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# The Anti-inflammatory Role of Curcumin in Osteoarthritis: An Overview of Molecular and Radiologic Changes

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**Abstract**
Osteoarthritis (OA) is the most common form of arthritis, causing pain and progressive disability in millions of people worldwide. The commonly prescribed medications for OA, including non-steroidal anti-inflammatory drugs, have many side effects which has led the scientists to consider safer drugs as an alternative. Therapeutic effects of Curcumin on OA are increasingly declared, and its various aspects in suppressing inflammation and reducing the disease progression are examined more thoroughly. This study aims to discuss curcumin and OA to help scientists working in these fields. In this brief review, we took a look at OA pathogenesis, the role of the immune system, and the biomarkers involved in the onset and progression of the disease. We focused on available data on the anti-inflammatory effect and mechanism of treatment by curcumin on OA.
**Keywords:** Curcumin, Osteoarthritis, Inflammation, Biomarkers

## 1. Background

Osteoarthritis (OA) is one of the most common and costly musculoskeletal diseases. Its prevalence is increasing in line with aging and increased obesity in the population worldwide. OA is characterized by the destruction of joint cartilage with associated degenerative changes in the adjacent bone and synovial tissues. Primary OA (which is idiopathic and without any background diseases) is more common than secondary one (which occurs with a previous injury or pre-existing condition). Microtrauma, abnormality in joint alignment, obesity, hemarthrosis, and history of infectious arthritis are among etiologies for OA.[1]

The role of inflammation in OA has been well recognized. Many anti-inflammatory medications are effective against OA,[2] but not without complications. The search for new medications with lower complications and the same efficacy are ongoing. One of the sources for new medications is herbal and traditional medication.[3,4] Curcumin is a herbal compound with anti-neoplastic; anti-aging; anti-oxidant, and anti-inflammatory properties.[5] Previous studies have indicated that anti-oxidative and anti-inflammatory agents can contribute to ameliorating OA.[6]

## 2. Inflammation

Activation of the immune system is a major trigger in the initiation and resumption of inflammation in OA. This is caused by an interaction between the wound healing cascade (including interleukin 4 [IL4], IL1, tumour necrosis factor alpha (TNF-α), transforming growth factor beta [TGF-β], etc), innate immunity (including macrophages, natural killer cells, neutrophils, etc), and adaptive immunity (including CD8+ T killer cells and CD4+ T helper cells).[6]

Atabaki et al. reported that 80 mg of curcumin daily for three months decreased circulating CD4+ and CD8+ T cells, Th17 cells, and B cells frequency and visual analog score, C-reactive protein (CRP) in OA patients. The treatment also enhanced circulating Treg cells.[7] Curcumin (100 μM encapsulated within nanoparticles for 6 hours) could suppress mRNA expression of pro-inflammatory mediators IL-1β and TNF-α, matrix metalloproteinases (MMPs) 1, 3, and 13, and aggrecanase ADAMTS5, and upregulate the chondroprotective transcriptional regulator CITED2 and as a result, decrease OA progression.[8]

Previously, it was stated that curcumin and related biochemicals with similar structures may become safer alternatives for non-steroidal anti-inflammatory drugs commonly used for the treatment of OA. Henrotin et al suggest that curcumin and relevant drugs as the new medication relieve OA by decreasing the inflammation

and inflammatory markers such as IL-1.[5] Evidence on the efficacy of curcumin in relieving the pain of patients with OA is limited. Pinsornsak and Niempoog showed the analgesic property of 1000 mg/d curcumin for 3 months in addition to diclofenac, although they did not evaluate anti-inflammatory markers.[9] In another study, Rahimnia et al conducted a double-blind placebo controlled randomized clinical trial on patients with knee OA. During 6 weeks, the patients received 1500 mg of curcumin per day. The authors found that superoxide dismutase and malondialdehyde, white blood count, TGF-β, IL-6, IL-4 reduced significantly.[10] Due to negligible changes in CRP and ESR amount, they demonstrated that improvement in clinical symptoms of OA in patients who were treated with Curcuminoid cannot be attributed to the anti-inflammatory properties of these phytochemicals.[10,11]

Among ILs, IL-1β, IL-8, IL-18, activator protein 1 (AP-1)/nuclear factor-kappa B (NF-κB) are involved in inflammation pathway and pro-inflammatory conditions in knee OA and chondrocytes.[5,12,13] Moreover, Yeh et al after encapsulating curcumin found that Curcuminoid-loaded liposomes can downregulate the expression of inflammatory markers on osteoblasts, and induce a high osteoprotegerin/receptor activator of nuclear factor κB ligand (RANKL) ratio to preclude osteoclastogenesis and they finally concluded this compound can decrease the speed of OA progression.[13]

In a study conducted by Wang et al,[14] the pro-inflammatory role of TGF in synovitis and joint destruction was recognized. Furthermore, the TGF beta, prostaglandin E2 and matrix metalloproteinase-3 were also involved in OA and curcumin could reduce these factors in metacarpophalangeal joints in horses.

Curcumin and resveratrol also act synergistically in protecting human articular chondrocytes via inhibition of IL-1beta-induced NF-κB-mediated inflammation and apoptosis.[15] Meanwhile, it was confirmed that the stability and absorption of curcumin are increased by complexation with phospholipids.[16]

NF-κB[17] and other biomarkers in the family of the 'omics' (genomics, metabolomics, proteomics , and lipidomics) [18] shall be assessed for the efficacy of the anti-inflammatory effect of curcumin in OA patients in future studies, and this effect should be compared with the clinical changes.[19]

## 3. Radiologic Changes

There are limited studies on the radiologic changes in OA with curcumin treatment. In an animal study conducted by Taty Anna et al, curcumin improved radiologic features of Collagen-induced arthritis (an experimental autoimmune-mediated polyarthritis). They declared that daily treatment with 110 mg/mL/kg CL induced a significant mean difference in the ESR ($P$<0.01) and radiological scores ($P$<0.01) on day-28 compared to the olive oil-treated group."[20]

Wang et al in a prospective RCT study, evaluated the effect of *Curcuma longa* extract (80% turmerosaccharides and 20% curcumin extract, 2×500 mg capsules/day) on 36 cases of considerable OA with a moderate amount of ultrasound-defined effusion/synovitis (≥4 mm thickness in the suprapatellar region) for 12 weeks. There were no significant changes in MRI-defined effusion-synovitis volume between groups.[21] They concluded that *Curcuma longa* extract did not affect knee measures analyzed by MRI[21]; however it seems that the duration of the treatment may not be enough to change the imaging findings.

### Review Highlights

**What Is Already Known?**

Osteoarthritis is a common disabling musculoskeletal disease and its medications, including non-steroidal anti-inflammatory drugs, have many side effects. Researchers are therefore seeking better alternatives, including herbal medications.

**What Does This Study Add?**

Several studies have represented anti-inflammatory and analgesic effects of curcumins and these medications have shown to be a safe alternative treatment for OA.

## 4. Conclusion

Curcuminoids have represented a safe alternative treatment for OA in several studies. Future studies on the efficacy of curcumin in treating OA should focus on the mechanism of cartilage repair, target therapy of the effective inflammatory components, and new drug delivery systems such as subcutaneous delivery.[22] Approaches such as using synergistic treatments like vitamin D therapy that are effective on inflammatory conditions, and adding curcumin with promising non-pharmacological therapies such as acupuncture and cognitive behavior therapy to relieve chronic pain, should be attempted.[23,24]

### Authors' Contributions

AS, RG and RJ conceived of the presented idea and collected the data. NN worked out the details and wrote the manuscript with the supervision of AS. All authors contributed to the final manuscript.

### Conflict of Interest Disclosures

None declared.

### Ethical Approval

Not applicable.

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