

THE EFFECT OF TURMERIC ON ULCERATIVE COLITIS: A PERSPECTIVE

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ABSTRACT

Ulcerative colitis (UC) is a chronic inflammatory bowel disease with limited treatment options and potential side effects. Curcumin, derived from *Curcuma longa*, has demonstrated anti-inflammatory and immunomodulatory properties, making it a potential therapeutic choice for UC. This review summarizes the literature on the impact of curcumin on UC management and its mechanisms of action. The included studies demonstrated that curcumin supplementation can lead to clinical remission, improved endoscopic findings, and reduced inflammatory markers in patients with UC. Curcumin's ability to target multiple pathways involved in the pathogenesis of UC makes it a promising adjunctive therapy. However, there are limitations due to the various study designs, curcumin dosages, and formulations. More well-designed clinical trials are needed to establish optimal dosing and evaluate long-term safety and efficacy. In conclusion, curcumin shows potential as a complementary therapy for UC due to its anti-inflammatory properties. Although more research is needed, current evidence suggests that curcumin supplementation may offer clinical benefits in managing UC. Future studies should standardize formulations, optimize dosages, and investigate long-term effects.

Keywords: ulcerative colitis, curcumin, anti-inflammatory, immunomodulatory, complementary therapy.

INTRODUCTION

Ulcerative colitis (UC) is a chronic inflammatory disease that affects the colon and rectum. It is characterized by recurrent episodes of inflammation, ulceration of the intestinal mucosa, diarrhea, bleeding, abdominal pain, weight loss, and chronic fatigue¹.

Despite advances in conventional treatment, patients with UC face challenges in achieving and maintaining disease remission, requiring surgery in the most severe cases, total proctocolectomy¹⁻³.

The objective is to control inflammation and relieve symptoms through aminosalicylates, corticosteroids, and immunosuppressants. However, these approaches have unwanted side effects and are not always effective⁴.

In recent decades, the importance of alternative and complementary therapies in managing UC has increased. One of the promising approaches is the use of turmeric, also known as turmeric or turmeric, a spice used in Asian cuisine and valued for its medicinal properties in various cultures⁵.

Turmeric contains active compounds, with curcumin being the main component responsible for its therapeutic properties. Curcumin has been shown to have anti-inflammatory, antioxidant, immunomodulatory, and antimicrobial activity in preclinical and clinical studies⁵⁻⁷.

These properties demonstrate that turmeric is beneficial in reducing intestinal inflammation and relieving symptoms associated with UC. Although turmeric has gained interest as an effective therapy in UC, the scientific evidence available to date is limited and inconclusive⁸.

In vitro and experimental studies have shown promising effects of curcumin in reducing inflammation and protecting intestinal tissue. However, clinical studies are scarce and present contradictory results, making a deeper analysis of this issue necessary^{9,10}.

Burge et al. investigated how curcumin exerts protective effects in the intestine through protective molecular mechanisms in inflammatory bowel diseases, although it did not specifically focus on ulcerative colitis².

Studies suggest that curcumin reduces the production of pro-inflammatory molecules. In addition, curcumin is attributed to restoring the balance of the intestinal microbiota, which is fundamental in the symbiosis of the digestive tract³.

Zeng et al. analyzed the effects of curcumin on autoimmune diseases, including ulcerative colitis. Beneficial effects of curcumin and *Curcuma longa* extract were demonstrated; however, the meta-analysis included multiple conditions, and the

specific effects of curcumin on ulcerative colitis were variable depending on the type of study included⁴.

It is important to emphasize that clinical studies on the effect of turmeric on UC are limited and show contradictory results. Some studies suggest a reduction in symptoms and an improvement in inflammatory markers, while others found no significant differences compared to the control group⁹⁻¹¹.

Goulart et al. analyzed the effects of curcumin on ulcerative colitis and Crohn's disease. Curcumin has been found to reduce inflammation, improve symptoms, and regulate the gut microbiota. However, they emphasized the need for well-designed clinical trials to confirm such effects⁵⁻⁸.

Following the same line of research, Yin et al. conducted a systematic review and meta-analysis focused on curcumin-containing adjuvant therapy in ulcerative colitis. There was an improvement in clinical remission rates and a reduction in pathological phenomena. However, the authors inferred the need for robust and high-quality trials⁶⁻⁹.

Khare et al. highlighted nanomedicine applied to using natural products in treating inflammatory bowel disease. The potential advantages of nanotechnology in improving bioavailability and the targeted action of active herbal principles were highlighted. Such conduct would increase the effectiveness of curcumin in the treatment of ulcerative colitis⁷⁻¹⁰.

Zheng et al. explored the use of Chinese medicine in the treatment of ulcerative colitis and discussed the mechanisms of action associated with its therapeutic effects. While the study contains insights into the potential benefits of Chinese medicine, it is important to note its specific focus and the need for more research to validate the findings⁸.

Jadhav et al. reviewed the effectiveness of dietary supplements in inflammatory bowel disease, including curcumin and its benefits, along with other supplements, such as omega-3 fatty acids, probiotics, and vitamin D, in managing symptoms and reducing inflammation. However, it is important to consider that the review covered a wide range of autoimmune diseases, and the specific effects of these supplements on ulcerative colitis were different⁹⁻¹¹.

There are discrepancies in the results, which are attributed to different study protocols, variations in the dosage and quality of turmeric-based products used in the research, and the complexity and dependence on which stage of the disease the patients are in¹²⁻¹⁵.

An example of this is the study by Ebrahimzadeh et al. on curcumin supplementation in patients with ulcerative colitis and rheumatoid arthritis. The findings

were the potential benefits of curcumin in reducing inflammatory biomarkers in these conditions, although they are different pathologies¹⁰.

Another example of method heterogeneity was the study conducted by Cunha Neto et al. on the potential of curcuminoids from *Curcuma longa* as adjuvants in treating Crohn's disease and ulcerative colitis. The anti-inflammatory and antioxidant properties of curcuminoids and their effects on modulating immune responses in inflammatory bowel diseases were highlighted¹¹.

However, it is important to consider that the trial focused on the potential of curcuminoids as adjuvants and did not provide a comprehensive assessment of their effectiveness in ulcerative colitis specifically¹³.

Thus, there is an urgent need for well-designed clinical studies, larger samples, and standardized methods to evaluate turmeric's effectiveness in treating UC. Furthermore, it is essential to understand the mechanisms of action of curcumin at the cellular and molecular level to elucidate its therapeutic potential in clinical practice¹⁴.

In this sense, the present review aimed to critically analyze the scientific studies available on the effect of turmeric on UC, seeking to gather and evaluate the existing evidence. Discuss the possible mechanisms of action of curcumin, the results of the included studies, and the gaps and challenges found in this area of research.

This review is estimated to provide important information for researchers, health professionals, and patients interested in using turmeric as a complementary therapy in the fight against UC.

A deeper and more complete understanding of the potential of turmeric as a therapeutic approach will open new perspectives in managing this complex disease. It will help to improve the quality of life of patients with UC.

METHODS

This cross-sectional, observational, and integrative study consists of a review of the use of curcumin, derived from *Curcuma longa*, for ulcerative colitis management and its mechanisms of action. A search for studies was carried out in the PubMed/Medline, Scopus, Scielo, Embase, and Web of Science databases, in addition to Google Scholar, considered a source of gray literature, as it does not contain peer-reviewed articles. Studies related to the topic were selected using the following search strategy: ("Curcuma"[Mesh] OR (Curcumas) OR (Curcuma zedoaria) OR (Curcuma zedoarias) OR (zedoaria, Curcuma) OR (Zedoary zedoaria) OR (Zedoary zedoarias) OR (zedoaria, Zedoary) OR (Curcuma longa) OR (Curcuma longas) OR (longa, Curcuma) OR (Tumeric) OR (Tumerics) OR (Turmeric) OR (Turmeric)) AND ("Proctocolitis"[Mesh] OR (Rectocolitis) OR (Rectocolitis, Hemorrhagic) OR (Hemorrhagic Rectocolitis) OR (Proctocolitis, Hemorrhagic) OR (Hemorrhagic Proctocolitis) OR (Rectocolitis, Ulcerative)

OR (Rectocolitides, Ulcerative) OR (Ulcerative Rectocolitides) OR (Ulcerative Rectocolitis) OR (Ulcerative Proctocolitis) OR (Proctocolitis, Ulcerative) OR (Proctocolitides, Ulcerative) OR (Ulcerative Proctocolitides) OR (Proctosigmoiditis) OR (Rectosigmoiditis)). Cohort studies, systematic reviews, case-control, cross-sectional studies, case series studies, and randomized clinical trials were included. Experimental studies were used as exclusion criteria. Duplicate reports were excluded using the Rayyan software - Reviewer. Analysis, review, and selection of the studies were made by peers unthinkingly, from reading the title and summary of the study, with a third reviewer in case of disagreement between the other two reviewers.

RESULTS AND DISCUSSION

Ulcerative colitis (UC) is a chronic, relapsing inflammatory disease common in young adults. It involves genetic and immunological factors, indiscriminate use of antibiotics, diet, intestinal barrier disorders, and microbiota alterations, which increase the inflammatory response of the mucosa and rupture of the junctions between intestinal cells²⁻⁴.

Due to the chronic and intermittent nature of RUC, the treatment uses a combination of alternating medications. The goal is to reduce symptoms and induce remission. It all depends on the severity and complications of the disease. In mild to moderate cases, mesalazine or sulfasalazine are first-line therapy⁸⁻¹⁰.

In patients with severe RUC, corticosteroids, immunomodulators, or biological therapies are used, monotherapy or combination, which increases costs. Immunomodulators include thiopurines, methotrexate, and cyclosporine, which may take months to achieve the expected benefit⁵⁻⁷.

Using immunomodulators increases the risk of lymphoproliferative diseases and skin cancer, in addition to being toxic and ineffective in controlling the disease. Biological drugs (infliximab, adalimumab, and golimumab) are tumor necrosis factor antagonists, $\alpha 4\beta 7$ integrin inhibitors (vedolizumab), and anti-interleukin IL12 and IL23 (ustekinumab)¹⁻³.

Biological therapy reactivates latent infections, skin lesions, allergies, and systemic and hematological reactions. In this group, there are the Janus-kinase (JAK) inhibitors, tofacitinib, which acts on type I interferon, interferon- γ , and interleukins implicated in the pathogenesis of inflammatory bowel diseases (IBD)^{10,11}.

Based on the above, natural products, including curcumin, are tested in the management of UC. This active principle modulates cellular signaling pathways as a pleiotropic molecule as a polyphenol with anti-inflammatory, hypoglycemic, antioxidant, healing, neuroprotective and antimicrobial effects¹³⁻¹⁵.

Curcumin suppresses nuclear factor kappa-light-chain-enhancer of activated B cells (NF- κ B), interleukin-1 beta (IL-1 β), IL-6, and tumor necrosis factor-alpha (TNF- α)¹⁶. Therefore, such actions make curcumin a potential alternative for treating UC¹⁴⁻¹⁶.

However, the use of curcumin in clinical therapy has limitations to be improved, considering that it is a hydrophobic molecule with reduced intestinal absorption, limited bioavailability, metabolism, and rapid elimination by the body⁹.

Despite this, because conventional therapy has significant and not always effective side effects, there is a growing interest in the use of complementary treatments, which explains the use of curcumin, due to its anti-inflammatory properties, as an adjuvant in treating UC^{4,8-10}.

According to the scenario above, Coelho et al. reviewed the use of curcumin as a complementary therapy in UC. There was evidence of control of disease activity, reduction of symptoms, and pathological remission. However, the authors emphasize the need for better-quality clinical trials to confirm such findings and the ideal dosages of herbal medicine to prevent toxicity¹².

Such findings are validated by other studies highlighting curcumin's anti-inflammatory, antioxidant, and immunomodulatory properties as a therapeutic option for UC^{13,14}.

Sadeghi et al. observed a reduction in disease activity and levels of inflammatory markers with curcumin supplementation. However, it reinforced the thesis that studies with more patients are needed to obtain scientific validation on the subject¹⁵.

In this sense, we evaluated the specific action of curcumin in blocking the activation of nuclear factor-kappa B (NF- κ B), one of the signaling pathways involved in inflammation. Although curcumin effectively controls inflammation in UC, determining the optimal dosage and treatment regimen is crucial¹⁶⁻¹⁸.

Challenges were highlighted by Goulart et al. and Iqbal et al. through trials where they inferred that curcumin therapy increases the probability of achieving remission in patients with UC. However, different product concentrations and duration of treatment must be considered when interpreting the results^{5,19-21}.

Although there is promising evidence of the therapeutic potential of curcumin in UC, some extensive reviews on treating gastrointestinal diseases, such as that by Atefi et al.¹⁷, provided broader analyzes not specifically focused on UC. In addition, other studies have focused on using curcumin in inflammatory bowel diseases in general, without specificity for treating UC^{16,22,23}.

Banerjee et al. evaluated the combination of curcumin and mesalamine in mild and moderate cases of ulcerative colitis. This association was more effective than a placebo in clinical and endoscopic remission. However, this is a pilot study, and

additional research is needed to evaluate the long-term effects of turmeric as a new therapeutic alternative²⁴.

According to Masoodi et al. the effectiveness of curcuminoids in improving the symptoms and well-being of patients with ulcerative colitis is evident. Dietary supplementation containing curcuminoids significantly reduced disease activity associated with patients' clinical well-being compared to the control group²⁵.

Grammatikopoulou et al. analyzed randomized clinical trials that investigated the adjuvant therapy of curcumin in the regression of ulcerative colitis, obtaining a positive effect on remission rates²⁶.

In the study by Bommelaer et al. oral curcumin's effectiveness in preventing Crohn's disease recurrence in operated patients did not show significant differences compared to placebo. Due to the specificity of Crohn's disease, the results obtained cannot be extrapolated to UC, even in the case of inflammatory bowel disease²⁷.

Finally, Fernández et al. evaluated the use of alternative, complementary medicine (CAM) in patients with inflammatory bowel disease, including ulcerative colitis. There was a high prevalence of the use of CAM in the sample group, including turmeric-based products. Still, the study did not provide significant results on the effectiveness of curcumin among patients with the disease²⁸.

From these principles, it is important to stress that patients and healthcare professionals should consider the highlighted evidence when deciding to use curcumin as part of UC treatment. Still, caution is advised until more research is available to provide a solid basis of scientific evidence²²⁻²⁶.

Most studies have limited samples, therapeutic regimens, and varying treatment times that make direct comparisons of results difficult. Furthermore, robust clinical trials are needed to confirm existing findings and establish safety guidelines regarding the use of curcumin in the treatment of UC^{27,28}.

CONCLUSION

In conclusion, curcumin shows potential as a complementary treatment for ulcerative colitis (UC). Preclinical studies demonstrate its anti-inflammatory properties and ability to impact key signaling pathways in UC pathogenesis. Clinical trials and meta-analyses indicate positive outcomes, including improvements in disease activity, remission rates, and patient-reported outcomes with curcumin supplementation.

However, limitations related to study designs, curcumin formulations, and dosages prevent definitive conclusions. Further well-designed randomized controlled trials using standardized curcumin preparations and dosages are needed to establish efficacy, optimal treatment duration, and long-term safety in UC.

Curcumin's favorable safety profile and potential as an adjunct therapy make it a promising addition to current UC treatment options. Future research should focus on addressing knowledge gaps and providing evidence-based recommendations for curcumin's clinical use in managing UC.

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