



Curcumin in ocular diseases: therapeutic potential, mechanisms of action, and innovative delivery systems

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ABSTRACT

Background: Curcumin, a natural polyphenol derived from *Curcuma longa* L., has gained considerable attention in ophthalmology because of its potent anti-inflammatory, antioxidant, and immunomodulatory properties. This review evaluates the therapeutic potential of curcumin in ocular diseases and explores innovative strategies to enhance its bioavailability.

Methods: A comprehensive search was conducted in four major electronic databases—PubMed/MEDLINE, Scopus, Web of Science, and Google Scholar—using keywords related to curcumin, ophthalmology, and drug delivery systems. Studies published in English up to March 10, 2025, were included. Relevant articles were selected based on their focus on the therapeutic effects of curcumin and the application of advanced delivery methods.

Results: Curcumin shows promising therapeutic potential in various ocular conditions due to its anti-inflammatory, antioxidant, and anti-angiogenic properties. Studies highlight its beneficial effects in corneal neovascularization, promoting corneal wound healing, and dry eye disease. It also has demonstrated potential therapeutic effects against allergic and bacterial conjunctivitis, pterygium recurrence, anterior uveitis, and cataracts. Moreover, curcumin may be beneficial in glaucoma, age-related macular degeneration (AMD), and diabetic retinopathy, offering a multi-targeted approach to preserving vision and ocular health. However, its poor bioavailability remains a major limitation. Strategies to overcome this challenge include the development of structural analogs, bioavailability enhancers, and advanced drug delivery systems such as nanoparticles, liposomal systems, micelles, hydrogel-based systems, and nanoemulsions, all of which may enhance the stability, bioavailability, and controlled release of curcumin.

Conclusions: Curcumin has garnered attention in ophthalmology because of its multifaceted therapeutic properties, including anti-inflammatory, antioxidant, apoptosis regulating, antibacterial, and immunomodulatory actions. These properties have demonstrated promising results, highlighting the potential of curcumin in treating various ophthalmic conditions. Despite the promising potential of curcumin in ophthalmic therapies, addressing its poor bioavailability by using innovative drug delivery systems is crucial for maximizing its clinical effects. To address these challenges, substantial research has focused on enhancing the bioavailability of curcumin through the development of structural analogs, bioavailability enhancers, and advanced drug delivery systems. Innovative formulations, including nanoparticles, liposomal systems, micellar solutions, hydrogel-based systems, nanoemulsions, microspheres, and transferosomes, are promising approaches to improve the stability, bioavailability, and controlled release of curcumin, offering a hopeful avenue for its future application in ocular therapies.

KEYWORDS

curcumin phytosome, turmeric yellow, ocular surgery, eye disease, bioavailability, drug delivery system, therapeutic use

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INTRODUCTION

Curcumin, a natural polyphenol derived from *Curcuma longa* L., exhibits a diverse range of pharmacological properties, including antioxidant, anti-inflammatory, antimicrobial, antimutagenic, and anticancer effects [1]. Consequently, curcumin has been investigated for its potential role in preventing and treating various diseases, including diabetes, cancer, rheumatoid arthritis, atherosclerosis, pulmonary infections, chronic intestinal inflammation, allergic conditions, asthma, autoimmune disorders, psoriasis, and neurodegenerative disorders such as Alzheimer's disease [2].

Clinical studies have generally demonstrated a favorable safety profile and tolerability, while potential therapeutic effects varies according to the disease and formulation [3]. Despite its promising pharmacological profile, the clinical application of curcumin remains a challenge because of its poor aqueous solubility, low bioavailability, rapid metabolism, and systemic elimination. These pharmacokinetic limitations hinder its therapeutic efficacy and complicate dose optimization [4, 5]. Furthermore, the susceptibility of curcumin to photodegradation and autofluorescence complicates pharmacological assessments and limits its therapeutic reliability [4, 5].

Recently, curcumin has gained increasing interest in ophthalmology because of emerging evidence from both *in vitro* and *in vivo* studies suggesting its potential benefits for a range of ocular diseases [6]. Curcumin exhibits significant antimicrobial and immunomodulatory properties that influence the intricate interactions between infection, inflammatory responses, and oxidative damage, which are fundamental factors in the progression of numerous ocular disorders [1]. Curcumin may exert therapeutic effects in conditions such as corneal wound healing, dry eye disease, conjunctivitis, anterior uveitis, glaucoma, cataracts, age-related macular degeneration (AMD), and diabetic retinopathy [6].

These findings highlight the potential of curcumin as an adjunctive or alternative therapy for ocular diseases. Thus, this review explores the pharmacological properties of curcumin in ocular diseases, highlights the challenges in ocular drug delivery, and discusses recent advances in curcumin formulations for improved ocular delivery.

METHODS

A targeted literature search was conducted to examine the therapeutic potential of curcumin in ocular diseases, with a focus on its mechanisms of action and innovative delivery systems. Four electronic databases were searched—PubMed/MEDLINE, Scopus, Web of Science, and Google Scholar—on March 10, 2025, for studies published in English. Search terms included “curcumin,” “ophthalmology,” “eye,” “therapy,” “inflammation,” “vascularization,” “antioxidant,” “immunomodulatory,” and various drug delivery systems such as “nanoparticles,” “liposomal,” “micellar,” “hydrogel,” “nanoemulsions,” “microspheres,” and “transferosomes.” Studies were included if they addressed the therapeutic effects of curcumin or innovative delivery methods in ophthalmic diseases. Additional relevant studies were identified through manual review of reference lists of selected articles.

RESULTS and DISCUSSION

Pharmacological Properties of Curcumin in Ophthalmology

Curcumin demonstrates a broad spectrum of pharmacological effects, including antioxidant, anti-inflammatory, antimutagenic, antimicrobial, and anticancer properties [7]. Table 1 summarizes the mechanisms by which curcumin exerts its therapeutic effects in ocular health. These activities render it a promising and adaptable therapeutic candidate, particularly when combined with advanced drug delivery systems [1].

Table 1. Mechanisms by which curcumin exerts therapeutic effects in ocular health

Effects	Mechanism of Action	Therapeutic Relevance
Anti-inflammatory [8-12]	Blocks pro-inflammatory signals (e.g., NF-κB, NLRP3), reduces cytokine activity (TNF-α, IL-1β, IL-6).	Regulates inflammation, supporting benefits for tissue repair while preventing chronic inflammation.
Antioxidant [13-19]	Activates NRF2 to enhance antioxidant enzymes (SOD, catalase, GPX), neutralizing ROS.	Protects ocular cells from oxidative stress, maintaining mitochondrial function and preventing damage.
VEGF Inhibition [13, 16, 17, 20-25]	Suppresses VEGF, controlling angiogenesis in conditions such as DR and AMD.	Prevents pathological neovascularization, potentially promoting proper blood vessel formation in the eye.
Apoptosis Regulation [13, 16, 17, 20-25]	Modulates Bcl-2/Bax ratio, preventing uncontrolled cell death while allowing elimination of damaged cells.	Protects ocular cells and ensures selective removal of damaged cells, aiding in tissue health.
Antibacterial Effects [8, 9]	Neutralizes ROS, inhibits bacterial biofilm formation, and supports controlled inflammation.	Reduces bacterial load, minimizes excessive inflammation, and enhances defense against microbial infections.
Immunomodulation [10-12, 26]	Modulates immune response, stabilizes extracellular matrix, and regulates endoplasmic reticulum stress.	Promotes tissue repair and regeneration, especially in autoimmune and infectious eye diseases.

Abbreviations: NF-κB, Nuclear factor kappa-light-chain-enhancer of activated B cells; NLRP3, NLR family pyrin domain containing 3; TNF-α; tumor necrosis factor-alpha; IL-1β, Interleukin 1 beta; IL-6, interleukin 6; NRF2, nuclear factor erythroid 2-related factor 2; SOD, superoxide dismutase; GPX, glutathione peroxidase; ROS, reactive oxygen species; VEGF, vascular endothelial growth factor; DR, diabetic retinopathy; AMD, age-related macular degeneration; Bcl-2, B-cell lymphoma 2; Bax, Bcl-2-associated X protein.

Table 2. Therapeutic applications of curcumin in ocular conditions [6].

Anatomical structure	Ocular conditions
Anterior segment of the eye	❖ Corneal Neovascularization ❖ Corneal wound healing ❖ Dry eye disease ❖ Conjunctivitis (allergic / bacterial) ❖ Pterygium ❖ Anterior Uveitis ❖ Cataract ❖ Glaucoma
Posterior segment of the eye	❖ Age related macular degeneration ❖ Diabetic retinopathy

Curcumin may exert therapeutic effects on various anatomical structures of the eye through the mechanisms described above [6], as illustrated in Table 2.

Challenges in Ocular Drug Delivery of Curcumin

The therapeutic potential of curcumin is substantially hindered by its poor bioavailability, even when administered at high oral doses (12 g/d) [27]. Several factors contribute to this limitation, including retention of curcumin at the pre-enterocytic level by gastrointestinal mucus, which contains enzymes capable of modifying curcumin before absorption [27]. Additionally, curcumin interacts with enterocytic proteins that alter its structure, further impairing its absorption [27]. Once absorbed, curcumin undergoes extensive phase I (modification) and phase II (conjugation) metabolism, primarily in the liver, intestines, and gut microbiota, producing curcumin glucuronide and curcumin sulfate [28]. Double bonds are further reduced by cellular reductases, producing metabolites such as dihydrocurcumin, tetrahydrocurcumin, hexahydrocurcumin, and octahydrocurcumin. Some of these exhibit significant antioxidant activity, potentially contributing to the therapeutic effects of curcumin [29, 30]. However, limited solubility, rapid systemic metabolism, and degradation upon exposure to gastrointestinal fluids generally contribute to the poor oral bioavailability of curcumin [31]. Additionally, curcumin in solution is susceptible to photodegradation under UV exposure, complicating its physical handling [31].

Delivery of curcumin to the eye presents further challenges because of the pharmacokinetic and pharmacodynamic barriers of the ocular environment. Tear production, blinking, and clearance mechanisms limit drug retention and absorption, and the anatomical complexity of the anterior and posterior segments further reduces bioavailability [32]. Extensive research has focused on strategies to enhance curcumin bioavailability, including structural modifications, bioavailability enhancers, and advanced delivery systems [33]. Curcumin analogs, which are synthetic or modified derivatives, have been developed to improve pharmacokinetic properties. The curcumin molecule features a highly reactive β -diketone group—a key factor contributing to its low bioavailability; various analogs have been synthesized to address this issue [34]. Wang et al. designed the prodrug dephosphorylated curcumin, which demonstrated improved molecular stability in aqueous environments [35]. Similarly, Muangnoi et al. investigated the antioxidant properties of curcumin and its prodrug, curcumin diethyl succinate (CurDD), demonstrating that both protect against oxidative stress, with CurDD offering superior protection. This suggests that CurDD may be a promising therapeutic candidate, particularly for AMD [36].

Another approach to improve the bioavailability of curcumin involves bioavailability enhancers such as piperine, a bioactive component of black pepper that inhibits intestinal glucuronidation of curcumin, significantly increasing its systemic availability [37–39]. These strategies aim to optimize the therapeutic potential of curcumin by overcoming its pharmacokinetic limitations.

Advances in Curcumin Formulations for Ocular Delivery

Nanoparticles: Nanoparticle-based delivery systems have emerged as a promising strategy to enhance the stability, bioavailability, and controlled release of curcumin in ocular therapies [1]. A Pluronic-F127-stabilized curcumin nanoparticle system (<20 nm) demonstrated high solubility (4.3 mg/mL) and neuroprotective effects, significantly reducing retinal ganglion cell loss in glaucoma models [40]. Similarly, curcumin-loaded nanoparticles (170.2 nm) developed for dry eye disease exhibited high drug entrapment (90%) and sustained release, with *ex vivo* and *in vivo* studies confirming their safety and therapeutic potential [41]. In corneal neovascularization, methoxy poly ethylene glycol-poly [ϵ -caprolactone] nanoparticles improved curcumin retention, reduced angiogenic sprouting, and downregulated vascular endothelial growth factor (VEGF), inflammatory cytokines, and matrix metalloproteinases [42]. Additionally, they inhibited nuclear factor kappa B activation in lipopolysaccharide induced corneal cells without adverse structural effects [42]. These findings support curcumin nanoparticles as a promising therapy for various ocular diseases, including glaucoma, dry eye disease, and corneal neovascularization [40–42].

Liposomal Systems: Liposomal carriers enhance the bioavailability and stability of curcumin by encapsulating the drug within lipid bilayers, protecting it from degradation and improving ocular tissue penetration [43]. A variety of polyethylene glycol and d-alpha-tocopheryl polyethylene glycol 1000 succinate-based nanocarriers have been developed for ocular drug delivery, including nanoparticles [44, 45], micelles [46], and solid lipid nanoparticles [47]. These formulations improve drug retention, prolong release, and enhance therapeutic effects in ocular diseases.

Micelles and Micellar Solutions: Nanomicellar systems have emerged as a promising enhancement of the solubility, stability, and ocular delivery of curcumin by forming colloidal structures that improve drug dispersion and absorption in ocular tissues [48]. In vitro and in vivo studies demonstrated that compared to free curcumin solutions, curcumin-loaded nanomicelles significantly enhance cellular uptake and corneal permeation, exhibiting excellent ocular tolerance with no signs of irritation in rabbit models [49]. Additionally, the synthesized micellar curcumin formulations demonstrated negligible toxicity and good cytocompatibility, rendering them as promising nanocarriers for ocular drug delivery for conditions including hypertensive eye diseases [50]. Moreover, Guo et al. demonstrated that intranasal nanomicellar curcumin promotes corneal epithelial and nerve wound healing in a diabetic mouse model with corneal abrasion [51].

Hydrogel-Based Systems: Hydrogel-based systems have emerged as promising curcumin delivery platforms in ocular therapies, offering controlled and sustained drug release to maintain therapeutic levels and improve patient compliance [1]. Curcumin nanoparticles with β -cyclodextrin in a hyaluronic acid hydrogel significantly reduced dosing frequency compared to conventional treatments, enhancing tissue healing in ulcerative keratitis [52]. Additionally, an alginate-incorporated curcumin hydrogel demonstrated potential as a surgical graft in retinal tissue engineering [53].

Nanoemulsions: Nanoemulsions have emerged as an emerging strategy for ocular curcumin delivery by enhancing solubility, improving bioavailability, and enabling targeted drug delivery with minimal systemic side effects [54]. A curcumin-based nanoemulsion eye drop demonstrated promising therapeutic potential for dry eye syndrome in mice [55].

Microspheres and Transferosomes: Transferosomes have emerged as a promising ocular delivery platform for hydrophobic drugs, demonstrating good corneal biocompatibility and significantly enhanced corneal and conjunctival penetration [56]. These vesicular carriers enable deeper drug delivery, improving the therapeutic potential of curcumin for ophthalmic applications [56]. Additionally, curcumin microspheres have been explored as a floating drug delivery system for sustained oral administration, highlighting their potential for extended drug release [57].

This review highlights the promising therapeutic potential of curcumin in the management of ocular diseases, emphasizing its well-documented anti-inflammatory, antioxidant, and immunomodulatory effects. A major strength of this review is its focused synthesis of recent innovations in drug delivery systems for curcumin aimed at overcoming its limited bioavailability—one of the primary barriers to its clinical application. However, the review is limited by the heterogeneity of study designs and the predominance of preclinical data, which limits conclusiveness regarding clinical efficacy. Furthermore, variations in formulation strategies and outcome measures complicate direct comparisons across studies. Further research should prioritize well-designed clinical trials to validate the therapeutic benefits of curcumin in ocular diseases. In parallel, the continued development and standardization of advanced delivery systems are essential to ensure consistent bioavailability, targeted delivery, and sustained therapeutic action in ocular tissues.

CONCLUSIONS

Curcumin has garnered attention in ophthalmology because of its multifaceted therapeutic properties, including anti-inflammatory, antioxidant, VEGF inhibitory, apoptosis regulating, antibacterial, and immunomodulatory actions. These properties have demonstrated promising results in both in vivo and in vitro studies, highlighting the potential of curcumin in treating various ophthalmic conditions, such as corneal neovascularization, corneal wound healing, dry eye disease, conjunctivitis, pterygium, anterior uveitis, glaucoma, cataracts, AMD, and diabetic retinopathy. However, its therapeutic potential is significantly limited by its poor bioavailability. To address these challenges, substantial research has focused on enhancing the bioavailability of curcumin through the development of structural analogs, bioavailability enhancers, and advanced drug delivery systems. Innovative formulations, including nanoparticles, liposomal systems, micellar solutions, hydrogel-based systems, nanoemulsions, microspheres, and transferosomes, are promising approaches to improve the stability, bioavailability, and controlled release of curcumin, offering a hopeful avenue for its future application in ocular therapies.

ETHICAL DECLARATIONS

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