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# Preventive and therapeutic potential of *Zard chob* (curcumin) in ophthalmic diseases: An integrative review of Unani and modern perspectives

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**Abstract**
Curcumin, also referred to as *Zard chob* in Unani medicine, is a bioactive polyphenolic compound derived from *Curcuma longa*. Historically held in high esteem for its anti-inflammatory, antioxidant, and wound-healing activity, curcumin has been gaining more interest in contemporary ophthalmology for its therapeutic applications in ocular diseases.

This is a review on the use of curcumin in the management and treatment of ophthalmological conditions based on evidence from Unani classical sources as well as recent biomedical sources.

Electronic databases like PubMed, Google Scholar, and Scopus were used to perform a literature search. Experimental, clinical, and observational studies have been included that assess the efficacy of curcumin in ocular diseases in the review.

Curcumin has shown impressive therapeutic promise in the treatment of allergic conjunctivitis, dry eye syndrome, corneal ulcers, corneal neovascularization, pterygium, uveitis, glaucoma, cataract, Thyroid Eye Disease (TED), and retinal conditions like diabetic retinopathy and age-related macular degeneration. Its therapeutic action is due to anti-inflammatory and antioxidant actions, downregulation of proinflammatory cytokines (e.g., IL-6, TNF-α), inhibition of angiogenic factors such as VEGF, and facilitation of neuroprotection. In spite of these encouraging effects, oral curcumin is plagued by low bioavailability and short metabolic half-life, which restricts its therapeutic use. Progress in drug delivery, including nano-formulations, phospholipid complexes, and hydrogels, has exhibited better results in preclinical and clinical environments.

Curcumin emerges as a safe, natural, and multifaceted adjunct or alternative treatment for various ophthalmic conditions. Its pharmacological properties validate traditional Unani applications, emphasizing the significance of blending traditional wisdom with contemporary science. Yet, additional large-scale, controlled clinical trials are necessary to determine standardized dosages, long-term safety, and efficacy, as well as optimization of delivery systems for efficient ocular use.

**Keywords:** Curcumin, ophthalmic disease, antioxidant, natural remedies, unani medicine.

## 1. Introduction
Traditional and complementary systems of medicine, such as Unani medicine, are sciences rooted in medieval times but still relevant in the modern era for the treasure trove of naturally occurring substances that play a significant role in health prevention and cure. Many natural remedies known in Unani medicine are proving beneficial in modern studies [1]. According to the Unani concept of disease, the abnormal occurrence of humors in the body and the temperament of the individual lead to the development of diseases. Therefore, diseases can be prevented by achieving the proper balance of humors in the body [2]. The eye is a complex organ consisting of multiple tissues and layers. Every layer and part of this complex sensory organ has its own unique metabolic and physiological activities. These parts of the eye are exposed to different external and internal factors that affect the functioning of this organ. The external factors include exposure to excessive sunlight, toxins, trauma, and other environmental factors such as workplace conditions. The internal milieu of the body is constantly producing reactive oxygen species (ROS). These molecules have adverse effects on ocular tissues. Several ophthalmic diseases, such as keratitis, uveitis, cataract, glaucoma, diabetic retinopathy, and age-related macular degeneration (AMD), have been attributed to increased levels of ROS, pro-inflammatory cytokines, and angiogenic factors in the body [3].

*Zard chob* (curcumin, turmeric) is a plant used across Asian countries as an anti-inflammatory, anti-angiogenic, anti-cancer, and anti-oxidant agent, in various ailments. In many cuisines, it is used as a traditional spice. The name *Zard chob* is a Persian word, and the unani term is Khalidoneon. The name khalidoneon comes from the bird called khitaaf which is yellowish-brown in color. According to the *Unani* concept, curcumin is a hot and dry substance. It has classically been used for respiratory, dermatological, and biliary ailments. It is also useful in traumatic skin abrasions. The book Muheetey Azam contains a detailed description of the curcumin plant. Several Unani texts mention curcumin's beneficial effects in various eye ailments. The curcumin powder and extract of the leaves improve vision, help in cataracts, and are useful in itching, tearing, and other eye conditions. Unani texts mention how the curcumin is to be boiled in water until only half of the fluid remains. That extract is then applied to the eyes [4-7]. Recent studies have shown the importance of curcumin in ophthalmic diseases. This review focuses on the role of curcumin in eye diseases. The literature search for this review was performed on search engines such as PubMed, Google Scholar, and Scopus.

## 2. Curcumin

Curcumin is a yellow-colored polyphenol and principal curcuminoid isolated from the rhizome of the plant *Curcuma longa*. It was discovered in 1815, isolated by Vogel, and was synthesized by Lampe in 1913. The turmeric rhizome is popular as a spice and widely used in cookery, fabric dying, and the cosmetic industry [8, 9]. Curcumin can exist in various tautomeric forms, which are structures in which atoms are arranged in different arrangements; however, they can interconvert while retaining the same chemical formula. The two main tautomers of curcumin are the keto form and the enol form. Several studies have demonstrated the anti-inflammatory, anti-diabetic, anti-cancer, and anti-apoptotic effects of curcumin [10-12]. Curcumin is a safe agent, even at high doses of 4-8 g/day. However, its use as an oral agent is limited due to poor aqueous solubility, low bioavailability, limited absorption, and rapid metabolism and excretion. Topically, as an ocular formulation, it is hindered by poor corneal penetration, bioavailability, and unclear dosing [10, 12].
Several studies have reported the beneficial effect of curcumin in ophthalmic diseases. This review highlights the main uses of curcumin in such conditions.

## 3. Application of Curcumin in ophthalmic diseases

### 3.1 Allergic Conjunctivitis

The pathophysiology of allergic disorders is attributed to an immunopathogenic mechanism involving immunoglobulin E (IgE)-mediated and T helper 2 (Th2) cell-mediated responses. In a study conducted by Chung *et al*, mice were systemically sensitized to ovalbumin (OVA). Subsequently, they were challenged with the conjunctival instillation of OVA. Control mice were given an intraperitoneal curcumin solution twice before the conjunctival challenge. Mice that underwent systemic priming with local boosting with OVA had significantly higher levels of Ag-specific IgE antibody secretion. Conversely, systemic injection of curcumin before the OVA challenge resulted in a profound decrease of Ag-specific IgE antibody secretion, resulting in attenuation of the Th2-driven allergic conjunctival inflammation [13].
A commercially available eyedrop named Ophthacare, from a pharmaceutical company in India, containing 1.30% w/v curcumin is reportedly efficacious in the management of conjunctival xerosis (DED), and infective and/or inflammatory conjunctivital diseases [14]. Another eyedrop containing curcumin, called Haridra, was reported to have anti-inflammatory and anti-bacterial properties [15].

### 3.1 Dry Eyes

Dry eye disease (DED) is the most common ocular disorder worldwide. It has been defined by the Tear Film & Ocular Surface Society (TFOS) Dry Eye Workshop II (DEWS II) as an ocular surface disorder characterized by tear film instability, hyperosmolarity, and inflammation that disrupts the homeostasis of the ocular system. The pathophysiology of DED can be traced to the presence of proinflammatory cytokines like interleukins (IL) IL-6, IL-8, and IL-1β in the ocular surface cells. Oxidative stress also causes a buildup of ROS in the conjunctival cells, while hypoxia and inflammation cause the release of basic fibroblast growth factor (bFGF) and vascular endothelial growth factor (VEGF). These angiogenic factors are responsible for new vessel formation in the normally transparent cornea, haze, and ultimately, leading to poor vision [10]. In a study conducted by Borselli *et al*., 95 eyes of 45 patients were randomized to receive either a 0.25% hyaluronic acid-based tear substitute three times daily or the tear substitute with an oral curcumin-phosphatidyl complex (100 mg of curcumin and 200 mg of soy-phospholipid). The study found significant improvement in the bulbar redness and Ocular Surface Disease Index (OSDI) scores in the group that received oral curcumin along with the tear substitute [10]. Similarly, Kapil and his colleagues evaluated an oral bio-enhanced curcumin in 40 patients with mild-to-moderate DED. The patients were randomized to a tear substitute and oral placebo in one group and a tear substitute with oral curcumin. After three months of use, significant improvement in the curcumin group was seen in terms of OSDI score (P=0.002), tear meniscus height (P=0.002), tear volume (P=0.006), tear break-up time ($p$<0.001), non-invasive break-up time (P=0.026), lipid layer thickness (P=0.01), and decrease in bulbar redness (P=0.002) [16]. Jahromy *et al*. evaluated a curcumin-based ophthalmic nano-emulsion on atropine-induced dry eye in mice. The study reported that the nano curcumin-treated groups were able to increase and maintain their tear production till the end of the study (day 49) compared to the atropine-only group [14]. Radkar and colleagues have evaluated the effect of a novel oral supplement containing curcumin 200 mg curcuminoids, lutein 20 mg, zeaxanthin 4mg, and vitamin D3 600 IU in cases of mild to moderate dry eye. In the study, 60 individuals were randomized 1:1 to receive either the supplement or a placebo (soybean oil capsule) for eight weeks. The supplement group had significant improvements in the dry eye scores compared to the placebo group. The study concluded that the production, stability, and quality of tears are improved by the supplement, reducing ocular surface damage and tear inflammation [18]. In a study by Chen *et al*, human corneal epithelial cells were cultured in a hyperosmotic medium for 24 hours. Subsequent analysis found elevated levels of IL-1β, IL-6, and TNF-alpha. However, pretreatment with 5muM curcumin abolished the increased production of IL-1β and increased phosphorylation of P38 caused by the high osmolarity [19]. These studies have demonstrated that curcumin, on oral or topical administration, has a positive impact on DED through its anti-inflammatory and anti-angiogenic effects. However, there are concerns regarding the poor bioavailability of oral curcumin due to intestinal malabsorption and adverse effects like

gastroesophageal reflux, nausea, diarrhea, and dizziness. Therefore, topical application of curcumin is the preferred route.

### 3.3 Corneal Healing

Corneal wounds and ulcers can occasionally be non-healing and become management dilemmas. Several medical and surgical approaches have been employed to heal the cornea. The use of curcumin in corneal wound healing shows promise as a therapeutic or complementary agent. In rabbit experiments of alkali burn-induced corneal ulceration, a novel ophthalmic drop hydrogel of Curcumin nanoparticles encapsulated with β-cyclodextrin and hyaluronic acid was used to assess its effect on corneal healing. The study reported the agent to be highly effective in treating ulcerative keratitis, with a significantly reduced need for the frequency of medications, and overall better quality of the healed tissues [20-21].

Diabetic neuropathy is a common condition seen in diabetic patients. Affection of the trigeminal ganglion can cause neuropathic keratitis in these patients. Several studies have shown that polymeric micelle can act as an effective nanocarrier for hydrophobic drugs and to increase the drug's bioavailability. Guo *et al*. reported an intranasal nanomicelle curcumin agent that was found to promote corneal epithelial wound healing and recovery of corneal sensation [22].

However, Mehra *et al* have analyzed the effect of *Curcuma longa* aqueous drops and found there was markedly delayed and poor healing of superficial and penetrating corneal wounds. Also, there was reduced tensile strength of the corneal wounds. These actions were attributed to the cortisone-like activity of *Curcuma longa* [21].

### 3.4 Corneal Neovascularization

Corneal transparency is an important physiological factor for maintaining clear vison. Several etiological factors such as trauma, hypoxia, infection and inflammation cause the development of superficial or deep new vessels in the cornea. These fragile vessels cause chronic inflammation, with lipid exudation, scarring and corneal haze, impairing corneal transparency and ultimately vision. Corneal neovascularization occurs as a consequence of an imbalance between angiogenic factors such as VEGF, β-FGF on the one hand and anti-angiogenic factors like angiostatin, endostatin, or pigment epithelium derived factor (PEDF) on the other [23]. VEGF expression is associated with the activation of nuclear factor-kappaB (NF-kappaB). Curcumin has proven effective in inhibiting angiogenesis by decreasing VEGF mRNA levels and NF-κB phosphorylation. Curcumin has been reported to inhibit several signal transduction pathways, including the pathway leading to NF-kappaB activation [6].

The mechanism of curcumin on neovascularization is attributed to inhibition of expression of the angiogenic factors, VEGF and bFGF. A study by Jung *et al* found eyes treated with topical curcumin had significantly smaller areas of neovascularization and lower levels of corneal VEGF mRNA levels, weaker immunofluorescent staining for phospho-NF kappaB, just one week after curcumin administration [24]. Subconjunctival injection of hexahydrocurcumin was found to inhibit gene-induced corneal neovascularization by reducing the expression of VEGF and bFGF [20]. In an experimental study, curcumin nanoparticle administration topically was associated with suppression of inflammatory cytokines, IL1β and TNF-α, reduced expression of VEGF, MMP 2- and -9, and ultimately distinct reduction in the corneal neovascularization [25]. Micro-RNAs (miRs) are small non-coding RNA molecules involved in RNA silencing and post transcriptional regulation of gene expression. Experiments with curcumin on human umbilical vein endothelial cells (HUVEC), which act as a model for corneal neovascularization, found significant changes in the expression profiles of multiple miRs. The study of curcumin exposed HUVEC cultures found that two miR members, miR-1275, and miR-1246 play determinant roles in the anti-angiogenic effect of curcumin by targeting molecules involved in NF-κB signaling transduction [26].

### 3.5 Pterygium

Pterygium is a degenerative disorder of the conjunctiva characterized by wing-shaped tissues developing and occasionally encroaching over the cornea. The only treatment for the condition is surgical excision. However, there is often recurrence of the condition and scarring of the cornea, affecting vision. Some studies have demonstrated the effect of curcumin on human pterygium fibroblasts (HPF). The studies reported significant inhibition of HPF proliferation and even apoptosis of the fibroblasts in a dose- and time-dependent manner. The expression of proliferating cell nuclear antigen (PCNA) was inhibited in the curcumin-treated HPF also [27, 28].

In another study, keratinocytes from excised pterygia were cultured and treated with 1.3% curcumin. TUNEL technique and Annexin-V/PI staining in flow cytometry demonstrated apoptosis of keratinocytes following the curcumin exposure [29]. Stati *et al* have reported that an aqueous extract of *Curcuma longa* can induce apoptosis of pterygium-derived human keratinocytes. The pro-oxidant effects of curcumin on mitochondria and their enzymes lead to the production of ROS, which have pro-apoptotic effects. Curcumin also has a strong anti-inflammatory effect, which is comparable to corticosteroids. Therefore, there is minimal scarring of the cornea following treatment after pterygium excision [30]. Biswas *et al* have reported positive therapeutic responses in pterygium patients after usage of Ophthacare eyedrops [14].

### 3.6 Uveitis

Uveitis is inflammation of the uveal tract, namely the iris, ciliary body, or choroid. It can be acute or chronic in nature. There are many etiologies for its causation, making it a common inflammatory condition of the eye. In a study of chronic anterior uveitis, 53 patients were treated with oral curcumin alone in a dose of 375mg, thrice daily, for 12 weeks. Another cohort received antitubercular treatment for one year and curcumin for 12 weeks. The participants were followed up for three years. All patients who received curcumin alone and 86% of the combined treatment group had improved vision, reduced pain, redness, and lacrimation. There was regression in the clinical features of uveitis, such as circumciliary congestion, aqueous flare and cells, keratic precipitates, and vitreous turbidity. However, 22% of patients in the curcumin alone group and 36% of patients in the combined treatment group lost their vision from complications of uveitis [31]. Similarly, Allegri *et al*. treated 106 patients with recurrent anterior uveitis with a combination of curcumin-phosphatidylcholine complex (Norflo) twice daily for 12 months as an adjunct to the treatment the patients were already receiving, such as corticosteroids or immunosuppressants. The study reported improvement in the subjective symptoms, including ocular discomfort, and signs of inflammation in more than 80% of the patients after a few

weeks of Norflo treatment [32]. There is also experimental evidence of the effectiveness of topically applied *Curcuma longa* aqueous extract on induced uveitis in rats. Studies found a lowering of TNF-alpha levels and reduced signs of inflammation after curcumin administration [33, 34].

### 3.7 Glaucoma

Glaucoma is a neurodegenerative disorder characterized by the loss of retinal ganglion cells and their axons. There are several theories to explain the causation of glaucoma. These include the mechanical, vascular, biochemical, and genetic theories, among others [35].

There are reports of ROS playing a role in the development and progression of glaucoma. Yue and colleagues have used curcumin for its antioxidant properties to study glaucoma. Curcumin was given for six weeks in Wistar rats, and the survival of retinal ganglion cells (RGCs) was quantified. The changes in intracellular ROS and apoptosis were analyzed by using flow cytometry. The in vitro study demonstrated that BV-2 microglia pre-treated with curcumin had better cellular viability and significantly reduced ROS and apoptosis. The in vivo study was conducted by increasing IOP for 4 weeks. In this model, curcumin was protective for BV2-microglia cells and downregulated caspase 3, cytochrome c, and BAX, while bcl2 was upregulated. This shows that curcumin has neuroprotective properties by inhibiting oxidative injury [36].

Lin and colleagues have shown that trabecular meshwork (TM) cells are damaged in glaucoma. Pre-treatment with curcumin protects the TM cells against oxidative stress-induced cell death. Tm cells exposed to curcumin have reduced production of ROS, and there is significant inhibition of proinflammatory factors IL-6, ELAM-1, IL-1α, and IL-8. Curcumin also decreased the activities of the senescence marker SA-β-gal and lowered the levels of carbonylated proteins and apoptotic cell numbers [37].

Cheng and colleagues have also shown that TM cells are exposed to oxidative stress, which plays a crucial role in impaired conventional aqueous humor outflow and contributes to glaucoma. The researchers developed a thermosensitive chitosan-gelatin-based hydrogel that contains 20 μm curcumin-loaded nanoparticles and latanoprost. This dual-drug delivery system acts as a sustained-release agent. Curcumin decreases the oxidative stress-mediated damage to the TM cells by reducing inflammation-related gene expression, mitochondrial ROS production, and apoptosis [38].

### 3.8 Cataract

Oxidative damage to the lens is regarded as an important factor in the development of cataracts. Augmenting the antioxidant defenses of the lens is protective in cataractogenesis [39, 40]. As a powerful antioxidant, curcumin supplements induce expression of antioxidant enzymes, inhibit lens membrane lipid peroxidation, maintain the calcium homeostasis in the lens, support lens chaperone proteins, and regulate some transcription factors and enzymes which promote cataractous changes [41].

In a significant experiment by Awasthi *et al*, Lewis rats were initially treated with curcumin or corn oil as a control. Subsequently, the harvested lenses were exposed to 4-hydroxy-2-nonenal (4-HNE)/L, a highly electrophilic product of lipid peroxidation. The lenses turned opaque on exposure to the chemical. However, the curcumin-treated lenses were significantly more resistant to the 4-HNE-induced opacification. The study showed induction of glutathione S-transferase (GST) isozyme rGSl8-8 in the rat lens epithelium. It is assumed that induction of rGSl8-8 by curcumin had a protective effect since the isozyme preferentially utilizes 4-HNE as a substrate [40].

In an experimental model of selenite-induced cataract, male Wistar rats were pre-treated with curcumin. The study found the expression levels of HSP70 and the activities of 8-8-hydroxy-2-deoxyguanosine (8-OHdG) and malondialdehyde were significantly reduced, and the activities of catalase, superoxide dismutase, and glutathione peroxidase (GSH-Px) were increased in the curcumin group. The study concluded that curcumin attenuated selenite-induced cataracts by lowering the intracellular production of ROS, thereby protecting cells from oxidative damage [41]. Two similar studies of selenite-induced cataract also found that curcumin suppressed selenium-induced oxidative stress and cataract formation [42, 43].

The role of ROS in the development of cataracts is well documented. Curcumin was found to increase the transcription of Peroxiredoxin 6 (Prdx6), a pleiotropic stress-response protein. This protein protects the cells from ROS-induced damage. Curcumin enhances specificity protein 1 (Sp1), Prdx6 mRNA, and protein expression, thereby reducing ROS expression and lipid peroxidation [44].

### 3.9 Thyroid Eye Disease

Thyroid eye disease (TED) is a chronic inflammatory condition of the orbital tissues characterized by congestion, proptosis, lid retraction, myopathy, and neuropathy. The pathogenesis of TED is attributed to an imbalance between pro- and anti-inflammatory mediators of inflammation. Inflammatory infiltrates, comprising lymphocytes, plasma cells, macrophages, and mast cells, occur frequently in TED. Some cells, like the B cells, T cells, and orbital fibroblasts, produce antibodies against several autoantibodies, including anti-thyrotropin receptor antibodies, insulin-like growth factor type 1 (IGF-1) receptor antibodies. The disease is usually treated with corticosteroids, occasionally in high doses, and immunomodulators. These agents have many side effects and are not suitable for all patients. Alternative and complementary agents like Curcumin can play a significant role in alleviating the orbital inflammation associated with TED [45, 46]. A study by Lee *et al* examined the therapeutic effect of curcumin on primary cultures of orbital fibroblasts from Graves' orbitopathy. There was a dose- and time-dependent decrease in the IL-1β-induced synthesis of inflammatory cytokines, including IL-6, IL-8, MCP-1, and ICAM-1 at both mRNA and protein levels. The study showed that curcumin inhibits the proinflammatory cytokine production, ROS synthesis, and adipogenesis in orbital fibroblasts [45].

In a study, 46 patients with TED were divided into three groups. One group was treated with 80 mg of Curcumin, another with 30 mg of Crocin, and a third group was designated as a placebo. The clinical activity score (CAS) was used to analyze the patients. During the period of the study, the CAS values, TNF-alpha, and IL-6 levels were significantly reduced across all groups. Overall, the curcumin group had 1 68% lowering of the CAS score, compared to 64% in the crocin and 51% in the placebo groups. These data were statistically insignificant. However, in patients with a CAS score of >4, there was a statistically significant effect on CAS, compared to the other two groups (P= 0.016) [47].

### 3.10 Retina

Several retinal disorders, including diabetic retinopathy (DR),

age-related macular degeneration (AMD), retinal ischemia-reperfusion injury (RIRI), proliferative vitreoretinopathy (PVR), and retinitis pigmentosa (RP), are attributed to oxidative stress, ROS overload, inflammation, and apoptosis. The early stage of diabetic retinopathy is characterized by increased levels of pro-inflammatory proteins, such as intercellular adhesion molecule-1 (ICAM-1), inducible nitric oxide synthase (iNOS) and vascular endothelial growth factor (VEGF). The release of pro-angiogenesis factors such as VEGF leads to new vessel formation and hemorrhage in the retina. These changes can affect visual acuity when they involve the posterior pole of the eye or due to a significant vitreous hemorrhage [48].

Curcumin protects the RPE cells from oxidative stress and damage induced by the inflammatory process by lowering TNF-α levels, downregulation of nuclear factor-jB (NF-jB), and inhibiting the gene expression of oxidation markers superoxide dismutase, glutathione, and maleic dialdehyde, which play a crucial role in cellular inflammation [49-53]. Curcumin has a novel function of inhibiting histone acetyltransferases (HATs), which are specific for CREB-binding protein and its homologue, P300. Alterations in these factors play an important role in the development of diabetic retinopathy [51]. The stromal cell-derived factor-1 induced migration of human retinal endothelial cells (HRECs), which is an important pathogenetic factor in DR, is also attenuated significantly by curcumin [52]. The proliferative stage of DR is a potentially blinding condition, characterized by new vessel formation and hemorrhages. Curcumin inhibits the proliferation and migration of retinal endothelial cells, which is a critical mechanism for the development of proliferative DR [51].

Age-related macular degeneration (AMD) is the most common cause of blindness in Western populations [53]. One of the important risk factors for developing this disease is the light-induced retinal degeneration caused by oxidative stress. There is an accumulation of lipids, nucleic acids, and proteins in the macula. This stage is called the “dry type” of AMD, with the appearance of yellowish deposits called drusen. There is a “wet type” of AMD, with the development of neovascular membrane and retinal bleeding. Administration of curcumin (0.2%) was found to inhibit the photoreceptor changes [54]. A study of blue light-induced toxicity on human RPE cells laden with A2E, a lipofuscin implicated in AMD, has shown protective effects of Curcumin extract and its curcuminoids. Curcumin, demethoxycurcumin, and bisdemethoxycurcumin in a concentration of 15 µm, were found to reduce the mRNA levels of c-ABL and p53, which play a role in RPE apoptosis [55].

Retinitis pigmentosa (RP) is a disease characterized by degeneration of photoreceptors and ultimately blindness. There are different types of RP. The autosomal dominant form is due to the P23H mutation in the rhodopsin gene and the formation of insoluble aggregates. Curcumin treatment causes dissociation of these aggregates and prevents photoreceptor apoptosis triggered by ROS [48, 50].

Proliferative vitreoretinopathy (PVR) is a sight-threatening condition that develops following surgery for a rhegmatogenous retinal detachment. There is a proliferation of retinal and immune cells, leading to the development of an epiretinal membrane, which leads to tractional retinal detachment. Curcumin (10-20g/ml) was found effective in inhibiting the proliferation and migration of RPE cells. It also causes apoptosis of RPE cells by increasing the Ca++ concentration, and also through the caspase pathway [48, 53].

Retinoblastoma (RB) is a common childhood cancer that develops from the retina. Studies have demonstrated that curcumin inhibits cell proliferation, induces apoptosis, and reduces the invasive and migratory activities of the RB cells. Curcumin deactivates the Janus Kinase-signal transducer and activator (JAK/STAT) signaling pathway by regulating mRNA-99 [56]. Conjectural reports of the effects of curcumin on inhibiting the growth of RGCs by cell cycle arrest, induction of apoptosis with up-regulation of Bcl-2-associated X protein (BAX), and the downregulation of Bcl-2 [57]. Curcumin decreases the expression of MMP-2, MMP-7, focal adhesion kinase (FAK), Rho A, and ROCK-1, growth factor receptor-bound protein 2 (GRB2). These actions of curcumin can prove useful in the treatment of retinoblastoma.

## 4. Conclusion

Curcumin, traditionally known as *Zard chob* in Unani medicine, has emerged as a promising natural agent with broad therapeutic potential in ophthalmology. Its multifaceted biological activities, particularly its anti-inflammatory, antioxidant, anti-angiogenic, and neuroprotective effects, have shown significant efficacy in managing a wide range of ocular diseases. These encompass uncomplicated and complicated conditions like dry eye, allergic conjunctivitis, corneal ulcers, neovascularization, pterygium, uveitis, glaucoma, cataract, thyroid eye disease, and retinal disorders like diabetic retinopathy and age-related macular degeneration.

Both experimental and clinical researches considered in this article confirm the age-old traditional practice of using curcumin in Unani medicine. The synergy between ancient wisdom and contemporary scientific findings justifies its use as a safe and effective adjunctive therapy. Nevertheless, the therapeutic use of curcumin is limited by low bioavailability, fast metabolism, and low eye absorption. These drawbacks are being met by novel drug delivery systems such as nano-formulations, hydrogels, and bio-enhanced complexes that have shown enhanced efficacy and patient outcomes.

With its broad range of action and excellent safety profile, curcumin presents a promising addition to the therapeutic armamentarium for ophthalmic diseases. However, to formalize dosages, refine formulations, and confirm long-term safety and efficacy, additional large-scale, well-designed clinical trials are required. Inclusion of curcumin in the mainstream practice of therapeutic ophthalmology, preceded by ancient wisdom and supported by current scientific data, has tremendous potential to enhance ocular health outcomes worldwide.

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