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Review article

# Cytoprotective mechanism of action of curcumin against cataract

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ABSTRACT

This review discusses the relationship between oxidative stress and cataract formation, molecular mechanism of curcumin action and potential benefits of treatment with the antioxidant curcumin. The first section deals with curcumin and endogenous antioxidants. The second section focuses on the action of curcumin on lipid peroxidation. Calcium homeostasis and curcumin will be discussed in the third section. The fourth section discusses the role of crystallin proteins that are responsible for maintaining lens transparency and the role of curcumin in regulating crystallin expression. The interaction of curcumin with transcription factors will be dealt in the fifth section. The final section will focus on the effect of curcumin on aldose reductase, which is associated with hyperglycemia and cataract. One of the strongest antioxidants is curcumin which has been shown to be very effective against cataract. This compound is better than other antioxidants in preventing cataract but its limited bioavailability can be addressed by employing nanotechnology.



**Contents**



*Abbreviations:* AGE, advanced glycation end products; AP-1, activator protein-1; ATP, adenosine tri phosphate; Cu, copper; CuZn SOD, copper zinc superoxide dismutase; COX-2, cyclooxygenage-2; DNA, deoxyribonucleic acid; FDA, Food and Drug Administration; Fe-iron, GSH, reduced glutathione; GPx, glutathione peroxidase; GST, glutathione S transferase; GSTP-1, glutathione S transferase promoter-1; $H_2O_2$, hydrogen peroxide; 4-HNE, hydroxy-2-trans-nonenal; HSP 70, heat shock protein 70; iNOS, inducible nitric oxide synthase; LEC, lens epithelial cells; MDA, malondialdehyde; microRNA, micro ribonucleic acid; MnSOD, manganese superoxide dismutase; mRNA, messenger ribonucleic acid; NADH, nicotinamide adenine dinucleotide reduced form; NF-κB, nuclear factor kappa B; NO, nitric oxide; $O_2^-$, superoxide anion; OH, hydroxyl radical; –SH, sulfhydryl group; SOD, superoxide dismutase; TBARS, thiobarbituric acid reactive substances; TPA, 12-*O*-tetradecanoyl-phorbol-13-acetate; TNF, tumor necrosis factor; UV, ultraviolet; VEGF, vascular endothelial growth factor.

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## Introduction

Both curcumin and cataract alone contribute to an ocean of research. Surprisingly, internet search using the terms 'curcumin and cataract' in combination resulted in only 17 'potential' papers (Table 1; source: science direct and pubmed). The use of curcumin as an antioxidant to prevent cataract formation was first brought into light by the work of Awasthi et al. in 1996 [1]. From then on, the study of curcumin as a potential anticataract agent has been one of the central areas of anticataract research. The main focus of this review is to analyze the available literature on the anticataract nature of curcumin and the mechanisms involved for potential use of this natural compound to prevent cataract.

## An introduction to cataract

Cataract is an eye disorder in which the transparency of the eye lens is lost (Fig. 1). There are three types of cataract, each defined by their location in the lens. Nuclear cataract is formed at the nucleus (inner core) of the lens and it usually occurs as a result of advancing age. Secondly, cortical cataract is formed at the cortex and resembles the spokes of a wheel which extend from outside of the lens to the centre and it is usually associated with diabetes. Lastly the sub-capsular cataract develops at the back of the cellophane like capsule that surrounds the lens. It is usually associated with people exposed to microwave radiation, diabetics, overweight individuals and intake of steroids [see http://www.visionaware.org/section.aspx?FolderID=6&SectionID=112&DocumentID=5676].

Eye lens contain three types of crystallin proteins – α, β and γ [2]. These crystallins tend to aggregate, forming clumps, when their native structure is disrupted and leads to loss of transparency. In this context chaperone activity of α crystallin is of great importance in maintaining β- and γ-crystallin proteins in their native state [3]. One of the chief factors that aids in cataract formation is age. With increase in age, the incidence of cataract formation accelerates due to modifications in the lens crystallin proteins [4]. In rodent models there is complete oxidation of protein cystein as they age whereas in humans not much loss is seen. Nevertheless other factors which contribute to the formation of cataract include ultraviolet (UV)-rays [5], xenobiotics [6–9], steroids [10] and secondary complications due to diseases [11–17].

The formation of cataract in humans is hypothesized to develop by the following mechanism [19]:

Aggregation and precipitation of lens protein
↓
Opacity of the eye lens
↓
Increase in refractive index of the eye lens
↓
Increased light scattering

Cataract, unfortunately, can only be prevented and the only treatment available to cure cataract is the surgical removal of the lens, known as phacoemulsification. Even though cataract surgery has become very successful, any complication during surgery or

**Table 1**
The following table summarizes the 18 papers which discuss the preventive action of curcumin on cataract.

| No | Cataract Model | Mechanism of action of curcumin | Reference |
|---|---|---|---|
| 1. | 4-HNE induced cataract | Activation of GST enzyme, GST8-8 isoenzyme–key role | [1] |
| 2. | Galactose cataract | Attenuation of apoptosis of lens epithelium and lens opacification, resistant to HNE opacification | [13] |
| 3. | Naphthalene induced cataract | Apoptotic effect of naphthalene is attenuated by curcumin | [70] |
| 4. | Galactose induced cataract | Low levels of curcumin maintain lens morphology | [11] |
| 5. | Selenium induced cataract | Curcumin elevates the levels of antioxidants and decreases the levels of lipid peroxidation products | [58] |
| 6. | Diabetic cataract-streptozotocin | Decreasing oxidative stress, improving antioxidant system, controlling polyol pathway, protein oxidation, protein content and crystallin distribution in the eye lens | [12] |
| 7. | Diabetic cataract-streptozotocin | Importance of α crystalline for lens activity and the role of curcumin in preventing α crystalline modification | [16] |
| 8. | Diabetic cataract-streptozotocin | Increase in α crystalline level due to diabetic condition. Curcumin administration attenuated α crystallin level | [17] |
| 9. | Diabetic cataract-streptozotocin | Curcumin suppresses sorbitol accumulation and prevents cataract | [15] |
| 10. | Naphthalene induced cataract | Inhibition of lens epithelial cell apoptosis | [18] |
| 11. | Selenium induced cataract model-rat | Inhibition of lipid peroxidation, aminoguanidine prevents reactive oxygen species formation, aminoguanidine is an inhibitor of nitric oxide synthase | [8] |
| 12. | Selenium induced cataract model-rat | Free radical scavenging activity | [6] |
| 13. | Selenium cataract model | Scavenges free radicals, reduce nitric oxide synthesis, maintenance of calcium ATPase | [9] |
| 14. | Galactose induced cataract | Prevents activation of polyol pathway | [32] |
| 15. | Posterior capsular opacification | Prevents formation of Morganian balls and posterior capsular opacification | [20] |
| 16. | Selenium induced cataract model-rat | Curcumin controls elevated expression of α and β crystallin, maintains calcium homeostasis in eye lens | [7] |
| 17. | Post capsular opacification | Curcumin inhibits HLE-B3 cell proliferation inhibited by RHB FGF | [83] |