# Strategies to load curcumin into poly(2-hydroxyethyl methacrylate)-based disks to increase controlled release time for intraocular lenses

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## I. Introduction

The Canadian Council of the Blind estimates that 3.7 million Canadians were living with cataracts in 2019 [1]. Treatment involves replacing the diseased lens with a prosthetic intraocular lens (IOL). After surgery, patients apply eye drops with anti-inflammatories and antibiotics but the drugs' low retention times on the eye and poor diffusion through the eye limit their effectiveness. Furthermore, reactive oxygen species can promote epithelial to mesenchymal transition in lens epithelial cells contributing to posterior capsule opacification [2]. Curcumin inhibits these transitions at low concentrations of 10 μM [3], but easily degrades and is hydrophobic, which makes ocular delivery challenging [4]. We hypothesized solvent-based loading strategies would allow high amounts of curcumin to be loaded into IOL materials to protect the curcumin and allow controlled release over months.

## II. Materials and Methods

Hydrogel disks were made by polymerizing 71 mol% 2-hydroxyethyl methacrylate, 7 mol% methyl methacrylate, 21 mol% acrylamide, and 1 mol% ethylene glycol dimethacrylate through free radical polymerization (Irgacure-1173 and UV light). Disks were vacuum dried, loaded with curcumin using different acetone:water ratios, concentrations, and incubation times, and then blotted and vacuum dried to remove excess surface solution and absorbed solvents. After reswelling, disks were incubated in 3 mL of phosphate buffered saline (PBS) and replaced with fresh PBS periodically, measuring the releasate spectrophotometrically. At the end of the release studies, 2,2-diphenyl-1-picrylhydrazyl (DPPH•) assays were done on the remaining encapsulated curcumin (after its extraction) and compared to fresh solutions.

## III. Results and Discussion

The resulting disks were similar to IOLs with a water content of ~45%, transmittance of 90% (375-700 nm), and refractive index of 1.42 ± 0.002. Incubation of disks with curcumin solutions of high acetone:water ratios enabled high loading of curcumin without damage to the disks. Curcumin appeared to slightly reduce disk swelling, and Figure 1 shows its extended release for over 60 days with potential for greater than 90 days (three months) of release based on assessments of the remaining curcumin content, longer than many ocular delivery systems loaded using soaking techniques which deliver over days or weeks [5]. Release rates of 0.0029 ± 0.0002 μmol/day (Loading Ratio 1) and 0.0027 ± 0.0003 μmol/day (Loading Ratio 2) were observed in the release studies from Fig. 1 after 25 days ($p < 0.05$). Precipitate found on the disks suggest dissolution was the mechanism of release, protecting the curcumin. The curcumin remaining in the hydrogel disks after 60 days was measured to have the same scavenging capability to fresh solutions of matched concentration ($p > 0.05$). Curcumin typically degrades quickly in solution (60% degradation in one hour with light exposure) [4] but the disks protected the curcumin over the lengthy release studies.

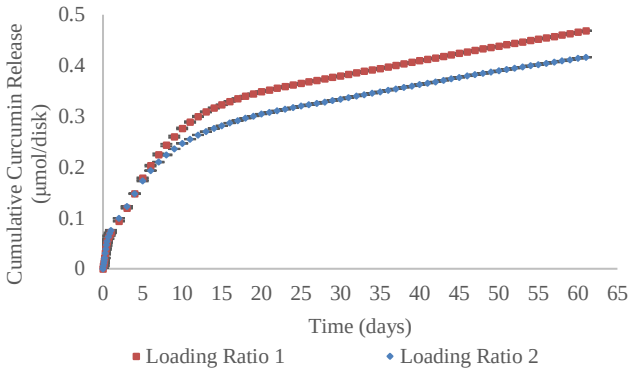


Fig. 1 Release of curcumin into PBS (pH 7.4, 37°C) (± 1 SD, n=3).

## IV. Conclusion

The acetone:water loading solutions enabled the high loading of curcumin into the hydrogel disks, with ratio 1 yielding greater amounts. After 25 days, its release was independent of loading and continued past two months. Curcumin loaded into poly(2-hydroxyethyl methacrylate)-based disks maintain activity upon release over extended periods of time.

## References

1. CCB, "The cost of vision loss and blindness in Canada", Deloitte Access Economics, Sydney, AUS, May 2021.
2. E. Kubo, et al., "Roles of TGF β and FGF Signals in the Lens: Tropomyosin Regulation for Posterior Capsule Opacity", *Int. J. Mol. Sci.*, vol. 19, no. 10, p. 3093, 2018.
3. H. Liu, et al., "Curcumin Inhibits Proliferation and Epithelial-Mesenchymal Transition in Lens Epithelial Cells through Multiple Pathways", *BioMed Res. Int.*, vol. 2020, no. 6061894, 2020.
4. G. Appendino, et al., "Shedding light on curcumin stability", *Fitoterapia*, vol. 156, no. 105084, 2022.
5. A. Topete, et al., "Intraocular lenses as drug delivery devices", *Int. J. Pharm.*, vol. 602, no. 120613, 2021.