

Glutathione: a vital lens antioxidant.

J Ocul Pharmacol Ther. 2000 Apr;16(2):121-35.

Giblin FJ.

Eye Research Institute, Oakland University, Rochester, Michigan 48309-4401, USA.
giblin@oakland.edu

The reducing compound glutathione (GSH) exists in an unusually high concentration in the lens where it functions as an essential antioxidant vital for maintenance of the tissue's transparency. In conjunction with an active glutathione redox cycle located in the lens epithelium and superficial cortex, GSH detoxifies potentially damaging oxidants such as H₂O₂ and dehydroascorbic acid. Recent studies have indicated an important hydroxyl radical-scavenging function for GSH in lens epithelial cells, independent of the cells' ability to detoxify H₂O₂. Depletion of GSH or inhibition of the redox cycle allows low levels of oxidant to damage lens epithelial targets such as Na/K-ATPase, certain cytoskeletal proteins and proteins associated with normal membrane permeability. The level of GSH in the nucleus of the lens is relatively low, particularly in the aging lens, and exactly how the compound travels from the epithelium to the central region of the organ is not known. Recently, a cortical/nuclear barrier to GSH migration in older human lenses was demonstrated by Sweeney et al. The relatively low ratio of GSH to protein -SH in the nucleus of the lens, combined with low activity of the glutathione redox cycle in this region, makes the nucleus especially vulnerable to oxidative stress, as has been demonstrated with use of *in vivo* experimental animal models such as hyperbaric oxygen, UVA light and the glutathione peroxidase knockout mouse. Effects observed in these models, which are currently being utilized to investigate the mechanism of formation of human senile nuclear cataract, include an increase in lens nuclear disulfide, damage to nuclear membranes and an increase in nuclear light scattering. A need exists for development of therapeutic agents to slow age-related loss of antioxidant activity in the nucleus of the human lens to delay the onset of cataract.

