

## **Anti-Oxidant and Anti-Inflammatory Compounds in Retinal Degeneration Studies- from Molecular Mechanisms to Therapeutic Strategies**

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**Background:** Involvement of oxidative stress and inflammation are now established in major retinal dystrophies such as age-related macular degeneration (AMD) and diabetic retinopathy. Here we attempted to understand the molecular mechanism of protection of retinal cell death by a potent anti-oxidative compound, PBN and a potent anti-inflammatory compound, curcumin.

**Methods:** PBN was administered by IP injection to albino SD rats that were born and reared in cyclic dim light (5-10 lux), 0.5 hr before light damage at 2,700 lux for 6 hr. Alteration in gene expression was studied by microarray analysis. Curcumin, on the other hand, was fed to Wistar rats for 15 days with diet (AIN 76A + 0.2% curcumin), and followed by exposed to 1000 lux light for 3 hr; the mechanism of protection was studied by various biochemical and molecular analyses. As an in vitro model of oxidant stress, mouse retina derived 661W cells were used and stressed with H<sub>2</sub>O<sub>2</sub>.

**Results:** PBN treatment 0.5 hr before light damage restored > 90% photoreceptor functionality in SD rats whereas none-to-minimal ERG response was detected in the untreated rats. PBN treatment suppressed a host of inflammatory genes and oxidative genes such as *Icam1*, *Timp1*, *Ccl2*, *Lox12*, *Cox2*, and *HO-1*. Dietary supplementation of curcumin for 15 days restored 75-85% photoreceptor functionality, whereas control diet fed rats restored only 40-50% as analyzed by ERG. Curcumin diet reduced the level of pro-inflammatory molecule 4HNE and pro-oxidative peroxy-nitrite in the retina and blocked the activation of transcription factor NFκB. Curcumin treatment significantly up-regulated the level of HO-1 protein and gene expression, both in vivo and in vitro.

**Conclusions:** Understanding the molecular mechanism of action of PBN- and Curcumin- mediated protection of retinal structure and function in intense light induced damage could pave the way for their targeted application in retinal conditions that are suitable for pre-clinical trials. Successful evaluation of the protective mechanism of these compounds could result in novel augmentative therapy for AMD and diabetic retinopathy.