EPITHEORESE KLINIKES FARMAKOLOGIAS
KAI FARMAKOKINETIKES, INTERNATIONAL
EDITION 13: 100 (1999)

Changes of Protective Enzyme Expressions and Cell Toxicity in Corneal and Retinal Cell Lines

P. Pappas[1], M. Sotiropoulou[1], P. Stephanou[1], L. Salminen[2] and M. Marselos[1]

1. Department of Pharmacology, Medical School, University of Ioannina, 451 10 Ioannina, Greece
2. Department of Ophthalmology, Medical School, University of Tampere, P.O. Box 607, 33101 Tampere, Finland

Aldehyde dehydrogenases (ALDHs) are a group of $NAD(P)^+$-dependent enzymes with similar activity and functional characteristics, catalyzing biotransformation of a wide variety of endogenous and exogenous aliphatic and aromatic aldehydes to their equivalent carboxylic acids. ALDHs are especially localized in organs with a high percentage of epithelial cells. Great interest has been shown for aldehyde dehydrogenase 3 (ALDH3) in the cornea, where much higher constitutive specific activity has been detected compared to liver cells. Moreover, ALDH1 represents 1-2% of the soluble proteins in human lens. Retinal pigment epithelial (RPE) cells have been shown to play an important protective role in the photosensitive cells of the eye against photo- and chemical toxicity. The metabolic capacity of RPE cells is high, as well as their ability to express several metabolic enzymes, such as cytochrome P450 isoenzymes and glutathione transferases.

In this study, determination of *in vitro* enzyme activities of ALDH3, ALDH1, and other drug metabolizing enzymes in human cell lines of corneal epithelial and retinal pigmented epithelial cells, is presented. In addition, several concentrations of drugs with known ophthalmotoxic properties (benzalconium chloride, Brij78, EDTA and tamoxifen) were tested to examine the possible use of these enzyme activities as drug toxicity markers. The levels of the above drug metabolizing enzyme activities agreed with cell toxicity and cell proliferation tests. Finally, the drug metabolizing battery of enzymes as a protective mechanism of ocular toxicity will be discussed.

This study was funded by an EU Grant (BM;H4-97-2324).