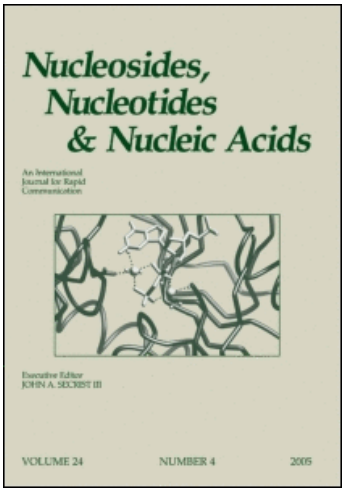

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CORNEAL PERMEABILITY of 5-IODO-2'-DEOXYCYTIDINE

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IDC is an antiherpetic agent which exhibits some advantages when compared to IDU, a better solubility in water allows higher concentrations for eye-drops, an improved antiviral activity by a greater specificity since the compound is phosphorylated by a viral induced specific thymidine-kinase and a subsequent lower toxicity for host-cells (*KURIMOTO, 1969 ; De CLERCQ et al., 1980*).

The objective was to know if IDC was able to pass through the cornea to reach active concentrations in aqueous humor and in which form, changed or unchanged.

We know that IDC can be deaminated in IDU by differents tissues as liver, kidney and blood (*PRUSOFF et al., 1979*). Our results show that when the contact is sustained between IDC solution and the eye IDC concentrations in aqueous humor and cornea are higher (30 $\mu g.ml^{-1}$ and 28 $\mu g.ml^{-1}$) than those described by *De CLERCQ et al.* as active on HSV_1 and HSV_2 in vitro (EC_{50} are 0.06 $\mu g.ml^{-1}$ and 0.3 $\mu g.ml^{-1}$ respectively). In addition, we followed penetration and metabolism by comparing IDU and IDC solutions on the eyes of the same animal. The eye-drops were applied every five minutes in order to maintain a high concentration of drugs on ocular surface. Furthermore, these conditions are suitable for therapeutic situations. Aqueous humors sampled after one hour and two hours of administration and processed by HPLC analysis show IDC concentrations of 0.9 and 2.0 $\mu g.ml^{-1}$ and for IDU 1.45 and 2.3 $\mu g.ml^{-1}$. The difference between IDC and IDU penetration is not significant. The absence of any detectable IDU in aqueous humor of the treated eyes by IDC solution suggests that deaminase activity of corneal tissues are pratically non-existant.

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The present study performed in the rabbit shows that IDC in a 0.15 % ophthalmic solution is able to penetrate, under unchanged form, through the cornea and achieve aqueous humor concentration which are compatible with antiherpetic activity.