SECONDARY EQUILIBRIA CONTROL OF CROMOGLYCATE ION FLUX THROUGH POLYAMIDE MEMBRANE

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Passive flux of ions through hydrocarbonaceous membranes is generally very low due to the high aqueous solubilities of the ions. This is of particular relevance for the absorption of drug molecules through biological membranes. Manipulation of such flux behaviour using various physicochemical secondary equilibria could afford possibilities for altering the passage of drug ions through such membranes as the cornea,skin and rectal mucosa. Sodium cromoglycate (SCG) is a large dianionic salt having pKa values of approximately 1.8. A detailed study on the interaction of this ion with some alkylbenzyldimethylammonium chlorides (ABDACs) to form both ion pairs and complex coacervates (Tomlinson and Davis 1978) has allowed us to study the movement of this drug through a model membrane (polyamide 6) using a simple stirred diffusion apparatus. Table 1 gives a summary of some of our findings where we have studied the effect of altering the alkyl chain length (n) and the concentration of the ABDAC on SCG and ABDAC flux.

Table 1 Effect of ABDAC concentration and hydrophobicity on SCG flux

Below solubility product (K_s),(free ions;ion pairs)

$$\log J = 0.212\,n - 13.8 \quad \text{(correlation coeff,0.999)} \qquad (1)$$

Above solubility product (free ions;ion pairs;coacervate)

$$\log J = -0.172\,n - 9.8 \quad \text{(correlation coeff,0.995)} \qquad (2)$$

Flux of SCG alone 5.36×10^{-13} $mol.sec^{-1}.cm^{-2}$.

(all measurements at 60° C, number of data points for equation 1 was 3, and for equation 2 it was 4).

We have shown previously (Tomlinson and Davis 1980) that below the solubility product SCG and ABDAC form 1:1 ion pairs, and this appears to be reflected in the value for the slope coefficient of equation 1, where each methylene group contributes 0.212 to the increase in log of the flux of SCG. Above the solubility product, an increase in ABDAC chain length causes a decrease in the flux of SCG, although it is shown by the intercept coefficients of equations 1 and 2 that the large concentrations of ion pairs in these systems has raised the SCG flux considerably. These data indicate that the flux of large organic ions through membranes can be greatly increased by the presence of ion-pair forming amounts of oppositely charged large ion,(in the case of SCG this can be at least a 100 fold increase),that this can be through manipulation of pairing ion hydrophobicity and/or concentration, and that this increase in flux is self limiting upon the solubility product being reached.

References

Tomlinson,E. and Davis,S.S. (1978)J.ColloidInterfaceSci. 66:335.
Tomlinson,E. and Davis,S.S. (1980)J.ColloidInterfaceSci. 74:349.

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