BINARY AND TERNARY DIFFUSION OF TWO BIS-QUATERNARY NEURONAL BLOCKING AGENTS

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Reports on the physical chemistry of neuromuscular blockers have considered structure-activity relationships, enthalpies of dilution (Agharkar et al 1975), polarographic adsorption, and the effect of endogenous surfactants, e.g. bile salts, on their biological efficacy (Gaginella et al 1974). In the latter report it was concluded that bile salts at concentrations either above or below the C.M.C. were not of physiological importance in the absorption mechanism of these compounds. Our multicomponent diffusion studies show that there is an interaction of flows between simple salts mixed with these quaternary drugs although no biological effect of such an interaction can be inferred from this (Fleming & Johnson 1981).

The technique of Gouy interferometry permits measurement of the four diffusion coefficients, D_{ij}, in the simplified Fick's Law equation for a ternary (two solutes [1,2] and a solvent) system:

$$J_i = - D_{ii}(\partial c_i/\partial x) - D_{ij}(\partial c_j/\partial x); \quad (i,j = 1,2; \ i \neq j)$$

As in diffusion coefficient measurement by photon correlation spectroscopy (PCS) the diffusing system is not disturbed by sampling but in the Gouy case a concentration gradient must be established and so flow coupling, which may include ion association effects, can be studied through the volume-fixed cross-term $(D_{ij})_v$. The diffusion coefficient-concentration data below were obtained by the Gouy method applied to some ternary solutions containing hexamethonium bromide ($HexBr_2$), decamethonium bromide ($DecaBr_2$), and KBr.

Binary diffusion results for the two quaternaries alone show a decrease in diffusion coefficient with increase in concentration over the range studied (approx. 0.027 to 0.28 mol l^{-1}), with the larger compound having the lower value for a given concentration. Ternary data for one composition of each system are summarised below.

		$HexBr_2$ - KBr - H_2O $\bar{c}_1 = 0.14$, $\bar{c}_2 = 0.42$	$DecaBr_2$ - KBr - H_2O $\bar{c}_1 = 0.12$, $\bar{c}_2 = 0.42$
i	j	$10^9(D_{ij})_v$	$10^9(D_{ij})_v$
1	1	0.666	0.547
1	2	-0.013	0.017
2	1	0.224	0.242
2	2	1.816	1.686

Units: $\bar{c}_i$, mol l^{-1}; $(D_{ij})_v$, $m^2 s^{-1}$

The D_{ij} values show that quaternary flow has a significant effect on KBr flow and that the simple salt has little effect on quaternary transport. Estimates of D_{ij}'s at infinite dilution is possible through Gosting's equations (1956), which show that quaternary flow is increased if the solute 2 cation is changed to one of lower molar conductivity, so D_{12} would be more positive if NaBr rather than KBr had been used in our work. However inclusion of a sodium bile salt in this calculation confers four-component properties on the system through the lack of a common ion, so Gosting's equations cannot be used reliably although it is likely that the D_{ij} would reflect bile salt - quaternary interaction.

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