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TRANS-MEMBRANE TRANSFER OF MONO-CATIONIC TECHNETIUM PHOSPHINO-ETHANE HEART IMAGING AGENTS

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The transfer of a series of cationic ^{99m}Tc-based phosphino-ethane ligand complexes across a model membrane has been studied using the rotating diffusion cell (Albery et al 1976). These complexes, although structurally similar, exhibit widely ranging imaging behaviour and are consequently of differing value in terms of diagnostic imaging.

Heart imaging agents of the type described are known not to transfer across myocyte membranes via the Na^+K^+ATPase mechanism, but are thought to do so by a simpler route (Sands et al 1986). In these experiments isopropyl myristate (IPM) was used to represent the lipoidal nature of a biological membrane. Results showed that although the most lipophilic complex partitioned into the IPM membrane the efflux into the receptor compartment was negligible. The remaining six complexes are of low lipophilicity and demonstrated no transfer into the membrane.

In a second part of the experiment a 10% solution of oleic acid in IPM was used in the membrane. Long-chain fatty acid, in particular oleic acid, is recognised as the most used source of fuel in the myocyte cell under normal conditions (Bing 1965). In this part of the experiment transfer into the membrane was apparent for all complexes, the magnitude varying from complex to complex. Further, transfer into the receptor compartment was much more in evidence, again, in varying amounts. Table 1 shows the percentage depletion from the donor compartment and percentage transferred to the receptor compartment at the 100 minute timepoint using an oleic acid/IPM membrane. The '%membrane' column is the inferred percent complex resident within the membrane (n=1).

Table 1

Complex	%depleted	%transferred	%membrane
$[TcO_2(DMPE)_2]^+$	13	5.3	7.7
$[TcO_2(DEPE)_2]^+$	7	7	0
$[TcCl_2(DMPE)_2]^+$	42	3	39
$[TcCl_2(DEPE)_2]^+$	58	9	49
$[Tc(DMPE)_3]^+$	60	5.5	54.5
$[Tc(DEPE)_3]^+$	35	4	31

where,
DMPE= 1,2 *bis* (dimethyl phosphino)ethane
DEPE= 1,2 *bis* (diethyl phosphino)ethane

The proposed mechanism is that of facilitated diffusion as a result of ion-pairing between the cationic complex and the anionic carboxylate group of the oleic acid (which is predominantly ionised at pH 7.4). The differences in transfer into and out of the membrane reflect the stability of the ion-pairs and their consequent lipophilicity and may go some way in rationalizing the varied imaging behaviour of these similar complexes.

Albery, W. et al (1976) J.C.S. Faraday I. 72: 1618-1626
Sands, H. et al (1986) J. Nucl. Med. 27: 404-408
Bing, E. (1965) Phys. Rev. 45: 171-180