THE EFFECT OF MODIFICATION ON SOLUBILISATION AND MICELLAR PROPERTIES OF A NON-IONIC SURFACTANT

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Solubilisation in micellar systems offers an attractive way of formulating poorly water soluble drugs. For conventional polyoxyethylated non-ionic surfactants maximal solubilisation occurs at a hydrocarbon chain length of 16 C atoms. The reason why further increase of chain length does not result in an increase of solubilisation may be explained in terms of changes in the oxyethylene mantle close to the micelle core/mantle interface. When the alkyl chain length exceeds C_{16}, the chain is no longer liquid at 298 K, and some of the polyoxyethylene glycol intrudes into the core in order to depress its melting point and maintain a liquid micellar core (Elworthy and Patel 1982). This intrusion has the effect of destroying the ethylene oxide rich area next to the core which appears to be the main locus of solubilisation for the drugs.

In this present investigation we report the micellar and solubilisation characteristics of a novel non-ionic surfactant with a hydrophobic chain containing an ether linkage. The introduction of such a group into the hydrophobic region of the molecule has the dual function of decreasing the melting point of this region compared with a linear hydrocarbon chain and introducing a semi-polar core which should favour solubilisation of most drug substances (Patel et al, 1981).

$CH_3(CH_2)_6O(CH_2)_{10}(OCH_2CH_2)_{17}OH$, I, was synthesised from heptylbromide and 1,10 -decandiol by the Williamson ether synthesis and the purified product ethoxylated. The solubilities of five test compounds were studied in a 2% $^{w}/_{w}$ solution of I using the method of Arnarson and Elworthy (1980).

Table 1. Solubilising capacities (10^2g solubilisate/g surfactant) and aggregation numbers of I and $C_{18}E_{22}$*

	A	B	C	G	P	N
I	5.04	1.74	0.36	0.65	1.39	70
$C_{18}E_{22}$	4.20	2.11	0.60	0.86	1.11	111

A = azobenzene B = betamethasone C = cortisone acetate
G = griseofulvin P = phenylbutazone N = aggregation number
*$C_{18}E_{22}$ = $CH_3(CH_2)_{15}(OCH_2CH_2)_{22}OH$ (results from Elworthy and Patel 1982).

Total intensity light scattering indicates that replacement of one CH_2 group of the C_{18} chain with an ether oxygen reduces the micellar aggregation number by about 40%. The reduced micellising tendency is reflected in the CMC of 4.6×10^{-5} mol kg^{-1} for I (from surface tension measurements) compared with a value of 1.3×10^{-6} mol kg^{-1} for $C_{18}E_{22}$. The smaller micelle size which leads to solubilising capacities generally below that of $C_{18}E_{22}$ (Table 1) is thought to be not only a consequence of an increased hydrophilicity, but also of an adverse structural conformation of the monomer within the micelle which may affect micelle packing. Arnarson and Elworthy (1980) observed a similar effect by the introduction of a double bond (cis) in the hydrocarbon chain.

Arnarson, T & Elworthy, P.H. (1980) J.Pharm.Pharmacol. 32: 381-385
Elworthy, P.H. & Patel, M.S. (1982) Ibid. 34: 543-546
Patel, M.S., Elworthy, P.H. & Dewsnup, A.K. (1981) Ibid. 33: 64P