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A COMPARISON BETWEEN NONIONIC MICELLES AND MICROEMULSIONS AS A MEANS OF INCORPORATING THE POORLY WATER SOLUBLE DRUG DIAZEPAM

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The ease of preparation, thermodynamic stability, optical transparency and ability to sterilise by filtration renders microemulsion systems an attractive prospect for use in drug delivery. In this investigation we attempt to determine whether these systems offer advantages over micellar preparations in the formulation of poorly water soluble drugs.

We compare the incorporation of a model poorly water soluble drug, diazepam (log P=2.6), in both micellar solutions of polyoxyethylene-10-oleyl ether (Brij 96), and in O/W microemulsion systems consisting of 2%w/w soyabean oil, with varying concentrations of Brij 96. The microemulsion systems were clear (disperse phase droplets less than 30nm), non-birefringent and stable before and after the addition of diazepam. Solubilities were determined by stirring a known excess of diazepam into each sample and allowing equilibrium to be achieved in a shaking water bath at 25°C for 8 days. The samples were then passed through a 0.22um filter and the concentration of the resulting clear preparations determined by dilution with 0.5%w/v sulphuric acid in methanol and subsequent absorbance readings taken at 284nm.

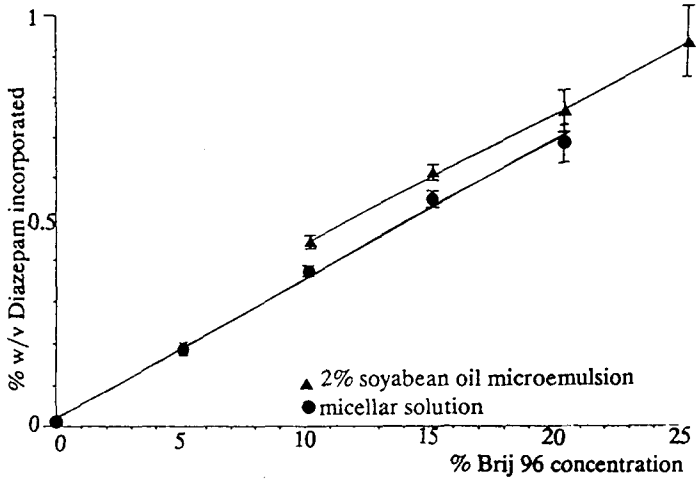

Fig.1: Percentage Diazepam incorporated vs Brij 96 concentration. Results are mean (n≥4). ±SD

Results (Fig. 1) indicate a trend for slightly higher incorporation of diazepam into the 2%w/w soyabean microemulsion systems compared with a micellar solution of the same concentration of Brij 96. This increase in solubility, although significant (P=0.05) at 10 and 15%w/w surfactant levels, is only small and can be explained partly in terms of drug solubility in the soyabean oil fraction (approx. 1.3%w/v). The weight ratio Diazepam/Surfactant remains relatively constant for the micellar systems (0.036+0.0014) but decreases from 0.044 for 10%w/w Brij 96 to 0.037 for 25%w/w Brij 96 microemulsions.

The similarity in the amount incorporated in both types of systems may be explained by consideration of the site of solubilisation. This has been studied using dimethoxytetraethylene glycol (DMTG) / water mixtures, in which pure DMTG is chosen to represent the local environment of dehydrated polyoxyethylene (Patel et al (1981)). Results show an exponential increase in diazepam solubility with increasing DMTG. This indicates that the major site of diazepam incorporation in both microemulsion and micellar systems is the region of concentrated, dehydrated polyoxyethylene chains that occurs close to the oil or hydrocarbon core.

It therefore appears that unless a drug has significant solubility in the dispersed oil phase of a microemulsion these systems offer little advantage over micellar ones for increasing the amount of drug which can be incorporated.

Patel, M.S. et al (1981) J. Pharm. Pharmacol. 33(suppl.): 64P