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Solubilization of testosterone propionate in oil-in-water lecithin-based microemulsions

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Nebulisation as a means of delivery is, in part, limited by the drugs aqueous solubility. There is therefore a need to develop aqueous-based formulations suitable for delivery to the lungs. Solubilization of a drug in a surfactant (SAA) system, in particular an oil-in-water (o/w) microemulsion, may offer a possible solution.

The aim of the study was to compare the solubilities of a poorly water soluble steroidal drug, tesoterone propionate (TP), in o/w microemulsions, with those obtained in micellar solutionsprepared using the same surfactants. The working hypothesis was that if the incorporated oil forms a distinct core in the interior of the surfactant aggregate it should provide an additional locus of solubilisation for the drug over the corresponding micellar system, thereby increasing solubilization. However if the oil was incorporated into the surfactant aggregate in a similar way to a cosurfactant, ie interchelated in the interfacial surfactant region, its effect on drug solubility within the microemulsion would be much less easy to predict because of the disruption caused to the head group region, known to be the major locus of drug solubilisation.

The surfactant systems studied were prepared from a combination of dimethyldodecylamine-N-oxide (DDAO) and lecithin at a weight mixing ratio of 1:2. DDAO was chosen as it has been previously shown to exhibit a high capacity for steroidal drugs (Lawrence and Devinsky, 1988). Microemulsions contained either ethyl butyrate, ethyl caprylate or ethyl oleate at a level of 2 wt%. The solubility of TP in the lecithin-based micelles, microemulsions and in the bulk oils was performed as described in Malcolmson and Lawrence (1993).

TP was most soluble in the most polar oil, ethyl butyrate, and least soluble in the least polar oil, ethyl oleate. From these results it may be expected that microemulsions containing ethyl butyrate would exhibit the greatest capacity for TP. However, with the exception of ethyl oleate all of the microemulsions tested exhibited a decrease in solubilisation of TP compared to the corresponding micellar solution (Table). In the case of ethyl oleate microemulsions solubilisation was similar to the equivalent micellar solution. These results suggest that the oils do not form a distinct central core in the surfactant aggregate but rather that they act as a cosurfactant altering the head group region of the surfactant aggregate, the primary locus of solubilisation.

Solubilization of TP in lecithin-based micelles and microemulsions

Total SAA Conc. wt%	Micelle	EO μe	EC μe	EB μe
12.5	0.75	0.89*	NF	0.73
15.0	0.86	1.02*	0.88*	0.70*
17.5	1.21	1.19	0.92*	0.87*
20.0	1.27	1.23	1.09*	1.11*
22.5	1.28	1.23	1.07*	1.13*
25.0	1.35	1.21*	1.33	1.16*

n = 4, NF = not formed

*significant difference between micellar and corresponding microemulsion (μe) system.

The results obtained in the present study suggest that the ability of an o/w microemulsion to increase the solubilisation of a steroidal drug over the corresponding micellar solution depends upon both the solubility of the drug in the dispersed oil and the nature of the incorporation of the oil into the surfactant aggregate. A similar observation has previously been reported by Malcolmson et al (1998) using the non-ionic surfactant, Brij 96.

Lawrence MJ & Devinsky F, (1988) J. Pharm. Pharmacol., 40(supp) 125P.