FORMULATION OF OILS: AN ALTERNATIVE OF SURFACTANT BASED SELF EMULSIFYING SYSTEMS

R T Clay, K Patel*, R S Cook, Product Development Laboratories, Pharmaceutical Division, May & Baker Ltd, Dagenham, Essex.UK. *Present address University of Kansas, USA.

Solvent deposition of drugs on to solid carriers has been proposed as a means of enhancing dissolution rates of poorly water soluble drugs (Ampolsuk et al 1974; Monkhouse and Lach 1972). Previous work has utilised insoluble carriers to provide an increased surface area, however the use of carriers soluble in the gastric contents should provide an alternative to the presentation of oils as self emulsifying soft gelatin capsule formulations which contain certain high proportions of surfactants (20-50%). A fractionated coconut oil (Miglyol 810) was chosen as a model to investigate the feasibility of such systems.
Formulations were prepared by dissolving Miglyol 810 in dichloromethane and mixing with lactose, anhydrous USP, in a mortar until the dichloromethane had completely evaporated. A range of formulations was prepared having loadings from 1 to 20%w/w. Subsequently a similar range of formulations was prepared by coating four size fractions of lactose, anhydrous USP, obtained by sieving. Samples of the initial formulations were prepared by dissolving formulation (1g) in demineralised water (10ml), the particle size distributions of the resulting emulsions were measured by laser light scattering (Malvern 3600E Particle Sizer). The median droplet diameters ranged from 2.8μm (1%w/w coating) to 8.0μm (15%w/w). For coatings greater than 15%w/w Miglyol 810 the median droplet diameter was reduced, microscopial examination showed that these emulsions contained large droplets, 100 to 200μm which either separate in the Malvern cell or are too large to be measured with the equipment parameters set to examine the smaller particle size ranges. To ensure that this phenomenon was not the result of emulsion preparation the 20%w/w coated formulation was examined at a range of dilutions 1g in 5 to 50ml; no significant difference was observed in the particle size distribution, thus indicating a formulation rather than a sample difference.
The effect of carrier particle size on emulsion formation was investigated using the four sieve fractions in table 1. The particle size distributions were measured on 1 in 10 emulsions by means of laser light scattering. At loadings above 10% the effect of carrier particle size becomes highly significant $P < 0.001$ in paired t-tests. At levels below 10% coating the loading becomes the major factor influencing the droplet size.

Table 1: Effect of particle size fraction of carrier and oil loading on the droplet size of the resulting emulsion.

Lactose Size Fraction (μm)	Median Droplet size(μm) vs Loading Miglyol 810 (%w/w) 1%	5%	10%	20%
<80	1.98	3.45	4.22	4.01
80-125	2.52	3.63	6.58	4.40
125-250	2.63	3.66	7.71	6.48
250-500	2.50	3.67	8.85	7.40

Further studies indicate the nature of the carrier and the solute content of the solution also affect droplet size. The factors of most importance being solubility, electrolyte and surfactant properties of the carrier. Coated electrolytes eg sodium chloride typically give droplet diameters > 20μm. However emulsions formed by non-electrolytes in various electrolyte solutions eg lactose carrier in sodium chloride solution are not significantly different from those in demineralised water.
It is proposed that this type of presentation offers a means of promoting the bioavailability of oil soluble drugs or drugs only available as oils without resorting to self emulsifying oil formulation having high surfactant concentrations.

D C Monkhouse & J L Lach (1972) J.Pharm.Sci. 61 No 9, 1430-1441.
C Ampolsuk et al (1974) J.Pharm.Sci. 63 No 1, 117-118.