INFLUENCE OF STERICALLY STABILIZING AGENTS ON THE STABILITY OF FAT EMULSIONS

J. S. Lucks, B. W. Müller, and R. H. Müller, Department of Pharmaceutics, Christian Albrecht University of Kiel, Gutenbergstr. 76-78, D-2300 Kiel 1

Parenteral fat emulsions have recently attracted attention as potential drug delivery systems. The drug is dissolved or dispersed in the internal phase. Many drugs have polar and non-polar moieties and act as surfactants. They penetrate into the surfactant layer around the oil droplet leading to instability (reduction in zeta potential, decrease in the microviscosity of the layer). Physical stability (e.g no coalescence) is an important parameter to be monitored, because droplets above 5 µm lead to capillary blockage. To increase the stability of drug-loaded and free emulsions by steric stabilization, ethoxylated surfactants of different chain lengths were incorporated at various lecithin/surfactant ratios. The hydrophobic moiety of the ethoxylated surfactant should comprise a similar structure to the fatty acid chains of the lecithin to provide a sufficient "anchoring" in the egg lecithin layer. Therefore ethoxylated glycerides (Tagat series) were chosen.

The emulsion stability was monitored by application of different laser light scattering techniques such as photon correlation spectroscopy (PCS), laser doppler anemometry (LDA), laser diffractometry (LD) and amplitude weighted phase structuration (AWPS). Different stress tests were applied to detect differences. Freeze thaw cycles, the addition of calcium ions to reduce the charge of the droplets and multiple autoclaving at 121° C proved to be suitable as accelerated stability tests. The addition of small amounts of ethoxylated surfactants (1%, 10%) to egg lecithin stabilized emulsions led to less stable systems with increased droplet coalescence. Mixed emulsions containing 50 % of the ethoxylated surfactant were more stable than egg lecithin emulsions but less stable than emulsions prepared with ethoxylated surfactant only (Table 1). The sterically stabilizing effect could be enhanced by elongation of the ethyleneoxide (EO) chains. At optimum concentration (i.e. 50% Surfactant + 50% Lecithin) no significant influence of the EO chain length could be detected (Table 2). Thus, the surfactant can be chosen with regard to toxicological considerations (e.g. minimum hemolytic activity).

Table 1: Long term stability of emulsions in dependence of incorporated amount of Tagat O (30 EO units) (diam. (nm))

Surfactant	0 Months	1 Month	3 Months	6 Months
Lecithin	294.8	297.8	573.6	606.4
1%	388.0	445.9	613.2	638.6
10%	214.6	209.7	2 Phases	2 Phases
50%	224.6	231.7	231.8	263.5
100%	237.1	242.2	237.3	256.6

Table 2: Long term stability of emulsions with 50% ethoxylated glycerides in dependence on the chain length (diam. (nm))

EO Units	0 Months	1 Month	3 Months	6 Months
20	215.8	221.3	207.2	240.9
30	224.6	231.7	231.8	263.5
100	227.7	228.6	256.3	282.4