

MECHANISMS OF INSTABILITY IN W/O/W MULTIPLE EMULSIONS

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Water-in-oil-in-water (W/O/W) multiple emulsions have shown promise as drug delivery systems. Additives such as drugs can markedly upset the delicate balance of factors which maintain stability. If the processes of instability of these systems were better understood, it should be possible to formulate stable systems with many biopharmaceutical advantages. The stability of these systems composed of two emulsions is difficult to study and there is little published work on the subject. Davis *et al.*, (1976) have used freeze-fracture techniques; Kita *et al.*, (1977a,b) have measured migration of ions from the internal phase and a viscometric technique to follow breakdown of multiple emulsions.

Three different systems of water/isopropyl myristate (IPM)/water were prepared using various nonionic surfactants. The primary W/O system comprised in all cases IPM, Span 80 (2.5%) and water (50%). The multiple emulsion was prepared by emulsifying the primary system in an equal volume of water containing 2% surfactant: Brij 30 (system A), Triton X-165 (system B) and Span 80: Tween 80 3:1 (system C). System A had small multiple (oil) drops (mean diameter 8.6 μ m), 82% of which contained only one internal aqueous droplet. System B had somewhat larger multiple drops (mean size 19 μ m) with several smaller internal aqueous drops. System C comprising much larger multiple drops than A or B (mean size 25 μ m) contained large numbers of internal drops which were impossible to resolve.

Using conventional photomicrography, the decrease in the ratio of filled/empty multiple drops and in the number of internal droplets inside the multiple drops was observed. The internal droplets of emulsions A and B showed little change in diameter over a period of twenty weeks, and only slight changes in the mean size of the multiple drops were noted. Although these methods are tedious, they do provide some information on multiple drop stability. We have also used a modified time-lapse cinemicrography technique described by Dawson (1963) to study droplet movements for periods of up to twenty four hours, in the presence and absence of electrolyte in the internal and external aqueous phases. This has shown the internal droplets to be fairly stable in the early stages of the life of the emulsion. They appear to collide frequently but do not coalesce. Normal and high-speed cinemicrography have also been used. In the presence of electrolyte in the external phase, drops of emulsion A rupture, releasing the internal aqueous droplets. Drops of emulsion B, however, coalesce, behaving like a normal O/W emulsion, leaving the internal droplets intact. The main factors likely to influence coalescence in the constrained environment of the dispersed oil phase are the viscosity of the oil phase, interactions between the interfacial films and Brownian movement.

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