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An investigation into the mechanism of 'spontaneous' multiple emulsion formulation

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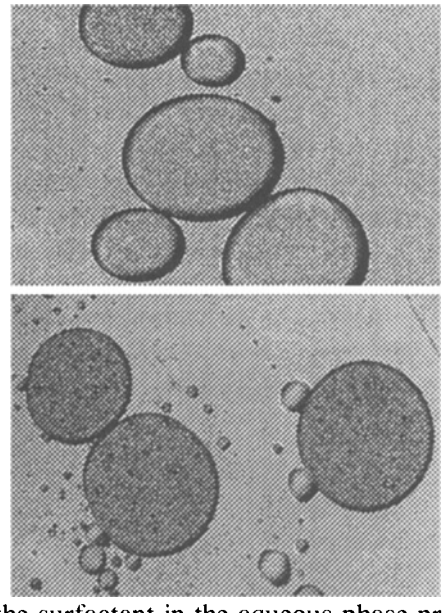
Multiple emulsions have been widely investigated as means of delivering drugs via the oral, topical and parenteral routes. In a previous study, Craig et al (1995) noted the formation of w/o/w multiple droplets from certain oil/surfactant mixes with very little agitation, opening up the possibility of spontaneous formation and thus simplifying current manufacturing process. However, the mechanism associated with the formation process is poorly understood. Lin et al (1975) investigated the effects of manufacturing protocol on the formation of multiple emulsions as manufacturing intermediates and postulated that a hydrophilic surfactant initially placed in the oil phase would form inverse micelles, thus solubilising a portion of the external water to produce a primary w/o emulsion. On continued mixing with excess water a w/o/w emulsion forms. In contrast, if the hydrophilic surfactant is initially placed in the external aqueous phase, this mechanism would become inoperative, hence no multiple drops would be formed and the final droplet size would be dependant on the intensity of mechanical agitation. The aim of this study is to examine the use of a novel oil-surfactant mix system as a means of 'spontaneously' generating multiple emulsions and to investigate the effect of surfactant location on multiple structure in order to elucidate a possible mechanism of formation. If the prior addition of the surfactant to the aqueous phase prevents multiple droplet formation, the hypothesis proposed by Lin et al (1975) may be applicable to the formation of these novel systems.

75μl of Tween 80 was placed in 300mls of distilled water to which 225μl of Labrafac Lipophile WL 1349 (Gattefosse s.a., France) was added (mix A). 250μl of an equivalent oil-surfactant mix was added to 300ml distilled water (mix B). Both were mixed for 10 minutes at 100 rpm using a rotor paddle. Each sample was examined under an Olympus BX 50 Differential Interference Contrast microscope. Particle size analysis was performed using a Malvern Mastersizer S.

Figures 1a and 1b:90% Labrafac Lipophile WL 1349/10% Tween 80; Surfactant placed in water (a) or added to oil (b)



Placing the surfactant in the aqueous phase prior to mixing fails to produce good quality multiple droplets. Small 'specks' can be seen in the oil globule (Figure 1a) in contrast to well-defined larger inner droplets formed on addition of an oil-surfactant mix (Figure 1b). The corresponding average medium size values were 294.9μm (SE:10.75) and 176.52μm (SE:1.95).

In conclusion, these results indicate that the Labrafac Lipophile WL-Tween 80 mixes may be used to form multiple emulsions with minimal agitation and that the behaviour of these systems is consistent with the hypothesis proposed by Lin et al (1975).

Craig, D.Q.M., et al. (1995) Pharm. Sci. 1: 559-495

Lin, T.J., et al (1975) J. Soc. Cosmet. Chem. 26: 121-139