International Journal of Pharmaceutics, 31 (1986) 281–282
Elsevier

IJP 01065

The stability of oil-in-water emulsions containing cetrimide and cetostearyl alchohol

R.C. Rowe [1], J. McMahon [2] and R.F. Stewart [2]

[1] *ICI Pharmaceuticals Division, Macclesfield, Cheshire SK10 2TG and*
[2] *ICI Corporate Colloid Science Group, Runcorn, Cheshire WA7 4QE (U.K)*

(Received March 21st, 1986)
(Accepted March 28th, 1986)

Key words: emulsions – cetrimide – cetostearyl alcohol – stability

In a recent paper on phase transitions in oil-in-water emulsions containing cetrimide and the fatty alcohols, it was stated that when the emulsions thin, the network entrapping the oil globules disintegrates resulting in droplet coalescence and eventual oil–water separation (Eccleston, 1985). We have extensively studied the thinning process in both ternary systems without oil and emulsions containing cetrimide and cetostearyl alcohol using a variety of techniques designed to elucidate the structural changes occurring in these systems (Patel et al., 1985a). While we would agree with the observation that the network entrapping the oil globules disintegrates, we have never observed coalescence and phase separation even after 36 months storage at 4°C.

The emulsion formulation we have studied consists of 0.5% w/w cetrimide, 10% w/w cetostearyl alcohol and 20% w/w liquid paraffin with hydroxybenzoates (0.28% w/w) as preservative prepared using a prolonged heating technique as described by Patel et al. (1985b). Differential interference contrast photomicrographs of the emulsion stored at room temperature and after 36 months storage at 4°C are shown in Fig. 1A and B (it should be noted that this system changed from an opaque cream to a pearlescent milky lotion after 9 months storage at 4°C, a state it maintained throughout the subsequent 27 months storage). It can be seen that while there is no perceptible change in the size of the oil droplets, there is a significant change in the overall structure with the droplets aggregating and a complete collapse of the network (feature × on Fig. 1A). In addition, when viewed under polarized light, the anisotropic crystals of cetostearyl alcohol recognized by their distinctive "Maltese Cross" structures (Barry and Saunders, 1970; Barry, 1971) and normally present in the room temperature sample could not be seen. When the thinned sample was equilibrated to room temperature and re-examined after 24 h, there did not appear to be any further change in its appearance when viewed under the microscope (Fig. 1C), even though the sample itself had thickened to form an opaque granular cream.

The changes seen in the sample are consistent with the proposed mechanism for thinning (Patel et al., 1985a; Eccleston, 1985), i.e. the breakdown of the network by fusion of the bilayer lamellae accompanied by changes in the crystalline form of the cetostearyl alcohol. However, there would appear to be sufficient cetrimide present at the oil–water interface to stabilize the emulsion against coalescence despite the fact that the continuous phase had decreased in viscosity. The aggregation of the oil droplets is interesting and may be due in

---

Correspondence: R.C. Rowe, ICI Pharmaceuticals Division, Alderley Park, Macclesfield, Cheshire SK10 2TG, U.K.

part to the restriction of their movement by the plates of cetostearyl alcohol formed by fusion of the lamellae (Patel et al., 1985a). These plates are responsible for the pearlescent sheen to the thinned sample and the granular nature of the equilibrated sample.

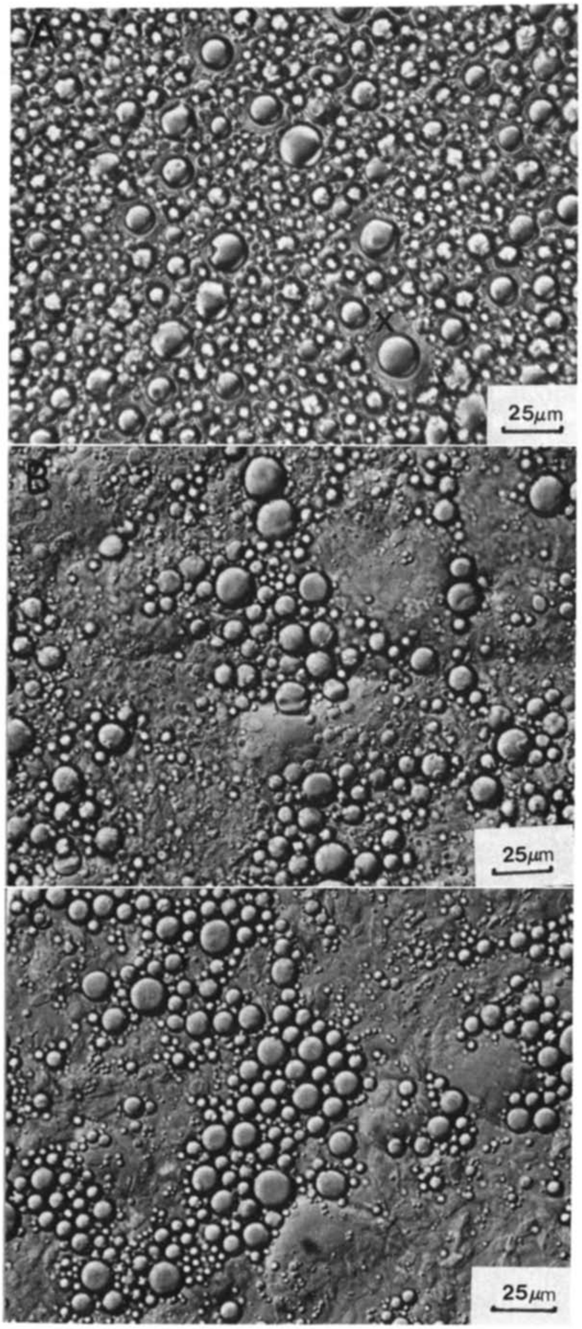

Fig. 1. Differential interference contrast photomicrographs of the emulsion (A) at room temperature, (B) after storage at 4°C for 36 months and (C) the thinned sample equilibrated to room temperature.

The cetostearyl alcohol used in this study was a synthetic blend and it is noteworthy that when substituted by a sample obtained from a natural source no thinning occurred. These two samples have recently been compared (Patel et al., 1985c) where it was found that sample obtained from the natural source contained a relatively high proportion of odd chain alcohols (C_{15} and C_{17}) in addition to a significant proportion of a C_{17} branched chain alcohol. It has been suggested (Patel et al., 1985c) that the presence of the C_{17} branched chain alcohols may be important in the formation of a more flexible more extensive network seen in ternary gels prepared using the natural cetostearyl alcohol. The implication of this present study is that the bilayers formed by such a homologue composition of alcohols are more resistant to fusion and breakdown.

Acknowledgements

The authors would like to express their gratitude to Mr. H.K. Patel and Mr. D.B. Mistry for their cooperation in this work.

References

Barry, B.W., Structure and rheology of emulsions stabilised by mixed emulsifiers. Rheol. Acta, 10 (1971) 96–105.

Barry, B.W. and Saunders, G.M., The self-bodying action of the mixed emulsifier cetrimide/cetostearyl alcohol. J. Colloid Interface Sci., 34 (1970) 300–315.

Eccleston, G.M., Phase transitions in ternary systems and oil-in-water emulsions containing cetrimide and fatty alcohols. Int. J. Pharm., 27 (1985) 311–323.

Patel, H.K., Rowe, R.C., McMahon, J. and Stewart, R.F., An investigation of the structural changes occurring in a cetostearyl alcohol/cetrimide/water gel after prolonged low temperature (4°C) storage. J. Pharm. Pharmacol., 37 (1985a) 899–902.

Patel, H.K., Rowe, R.C. McMahon, J. and Stewart, R.F., Properties of cetrimide/cetostearyl alcohol ternary gels; preparation effects. Int. J. Pharm., 25 (1985b) 237–242.

Patel, H.K., Rowe, R.C., McMahon, J. and Stewart, R.F., A comparison of the structure and properties of ternary gels containing cetrimide and cetostearyl alcohol obtained from both natural and synthetic sources. Acta Pharm. Technol., 31 (1985c) 243–247.