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Correlation of physical parameters of an oil in water emulsion with manufacturing procedures and stability

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Abstract

The effect of nine process variables for the manufacture of a semi solid paraffin-in-water emulsion prepared with two nonionic surfactants, steareth 21 and sorbitan oleate were examined initially and following ageing for 2 and 4 years. The techniques employed included differential scanning calorimetry (DSC), small angle X-ray diffraction (SAXD) and microscope (differential interference contrast (DIC) and crossed polars). A previous paper (Lashmar, *Int. J. Pharm.*, (1993) 59–67) used particle size analysis and rheological techniques to evaluate the emulsions. It was concluded that the total DSC enthalpy change was an important indicator of the stability of an oil-in-water emulsion and that the appearance of a sample under crossed polars could be used as a guide. SAXD was not found to be suitable for evaluation of process parameters. The thermal properties of the emulsions and their appearance under crossed polars suggested that the homogenisation speed of the manufacturing vessel probably was the single most important factor for the production of a stable emulsion and that extending the homogenisation time would improve the stability of the emulsion. Cooling the emulsion slowly appeared to benefit its stability, whereas the speed at which the water phase was added to the oily phase during the emulsification process, the emulsification temperature and the speed of the agitator during cooling seemed to have little effect on the stability of the emulsion. Adding the surfactants to the aqueous phase before emulsification and adding the oil phase to the water phase during the emulsification produced inferior emulsions. On cooling, the optimum stability was achieved when the agitator was stopped around the temperature corresponding to the lower cooling exotherm for the sample. Results from this and the previous paper (Lashmar, 1993) indicated that the droplet size and the rheological properties could be manipulated by process parameters without affecting the stability of the product. A later paper will investigate other techniques to evaluate emulsions and manufacturing parameters.

Keywords: Emulsion; Process variables; Stability; DSC; SAXD; Microscopy; Gel structure; Droplet size

1. Introduction

Emulsions are frequently used for topical delivery since they have high patient/consumer ac-

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ceptance. Oil-in-water emulsions in particular can be produced to a consistency and with in use properties that appeal (Becker, 1966; Breuer, 1983). Emulsions are thermodynamically unstable structures (Tadros and Vincent, 1983). They consist of two immiscible phases held together by an appropriate selection of molecules with both lipophilic and hydrophilic affinity. Often a mixture of surfactants, co-surfactants and other additives are used. The emulsion formulation employed in this study consisted of 1.36% w/w steareth 21, 0.64% w/w sorbitan oleate, 8% w/w cetostearyl alcohol, 12% w/w liquid paraffin with Dowicil 200 (0.20% w/w) as a preservative. Two emulsifiers and the co-emulsifier cetostearyl alcohol was selected since this combination is frequently used (Barry, 1983; Eccleston, 1986a).

The properties and the stability of emulsions can be affected by the manufacturing procedure (Becker, 1966; Bornfriend, 1978; Lin, 1978; Fox, 1984). The stability of emulsions still presents a major challenge to the formulator (Eccleston, 1986a; Rieger, 1991). For this reason the effect of various manufacturing procedures on emulsion structure and stability was studied.

In a previous paper, the effect of process variables on the structure and stability of the emulsion was investigated by means of rheological techniques and particle size studies (Lashmar, 1993). The study showed that the rheological properties were not always related to variations in the droplet size and that neither alone could be used to predict stability. The present work extends the previous evaluations employing SAXD, DSC and microscopical techniques to link process parameters with the stability of the emulsion.

2. Materials and methods

2.1. Materials

The components used for the manufacture of the emulsions are listed in Lashmar (1993). Ce-

Table 1
Variation from standard manufacturing procedure

Addition order		Addition method		Emulsification temperature	
Sample	Water to oil (1) Oil to water (2)	Sample	Phase composition	Sample	(°C)
A	1	A	b + c in oil	K	60
B	2	E	b + c in water	A	70
C	1 [a]	F	b in water c in oil	L	80
D	2 [a]	G	b in oil c in water	M	90
Addition rate		Homogenisation speed		Homogenisation time	
Sample	(ml/min)	Sample	(rpm)	Sample	(min)
A	200	A	1500	A	40
J	800	N	3500	O	80
				I	138
Cooling rate		Agitation speed		Agitation and temperature	
Sample	Rate	Sample	(rpm)	Sample	(°C)
P	1°C/ min	R	6	T	30
A	1°C/5 min	A	30	U	40
Q	1°C/10 min	S	60	A	45
				V	50

All samples were manufactured as sample A except for one process parameter, this parameter being listed above. The manufacture of sample A is described in detail in Lashmar (1993).

[a] Phase addition through the homogeniser.

[b] Steareth 21.

[c] Sorbitan oleate.

tostearyl alcohol BP (Henkel) which contained 48% cetyl alcohol and 49% stearyl alcohol, cetyl alcohol and stearyl alcohol (Sigma) both with a nominal purity of 99% were used for identification of DSC peaks. All materials were used as received.

2.2. Manufacture of emulsions

The reference emulsion (sample A) was made by heating the liquid paraffin, the sorbitan oleate, the steareth 21 and the cetostearyl alcohol together at 70°C. The homogeniser and the agitator set to 1500 rpm and 30 rpm, respectively, were started and water preheated to 70°C was added at 200 ml/min. The total homogenisation time was 40 min at 70°C. The batch was cooled at 1°C/5 min, and at 45°C the agitation was discontinued. All the emulsions were manufactured as sample A except for the parameter given in Table 1. Further manufacturing details are given in Lashmar (1993).

To establish which test could be used to identify critical process parameters the samples were studied following 2, 24 and 48 months storage at 30°C. The first data were generated 2 months after the manufacture of the samples, since it has been suggested that emulsion containing nonionic surfactants may take several weeks to reach equilibrium (Eccleston, 1982, 1985; Barry and Saunders, 1972; Barry and Eccleston, 1973).

2.3. Differential scanning calorimetry

DSC experiments were performed using the Perkin Elmer DSC-7 system with a TAC 7/DX/recorder. Preliminary experiments were performed to find the optimum combination of sample size and scan speed for comparing the samples. It was found that a scan rate of 10°C/min and 20 mg sample size gave good sensitivity but poor resolution, whereas a scan rate of 1.5°C/min improved the peak resolution but gave a large variation in the enthalpy. Both scan rates were, therefore, employed. DSC sweeps between 20 and 70°C followed by sweeps between 70 and 20°C were carried out for the emulsions and sample A spiked with 5% hydrated cetyl alcohol, cetostearyl alcohol and stearyl alcohol. The samples and reference (air) were placed in 50 μl hermetically sealed aluminium pans.

2.4. Microscopy

Each sample was examined using a Nikon Optiphot 2 at all the time points using differential interference contrast and crossed polars.

2.5. Small angle X-ray diffraction

SAXD spectra were collected using the synchrotron radiation source at the Daresbury laboratory, a slow quadrant detector and a 2.5 m camera length. The run time was 5 min/sample.

3. Results and discussion

3.1. Small angle X-ray diffraction

Fig. 1 shows the SAXD spectra for sample K. In general the spectra for all the samples were similar. Peaks 1–4 are orders of the interlamellar spacing, which varied from 213×10^{-10} to 229×10^{-10} m for the samples, but was on average 220×10^{-10} m. Peak 7 was absent on some of the

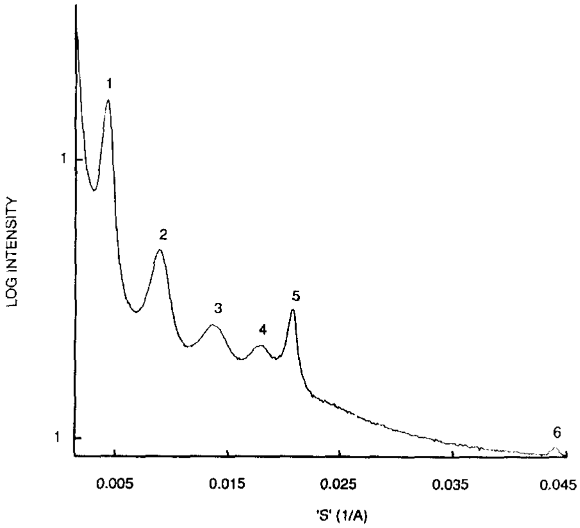


Fig. 1. SAXD spectra of sample K stored for 2 months at 30°C.

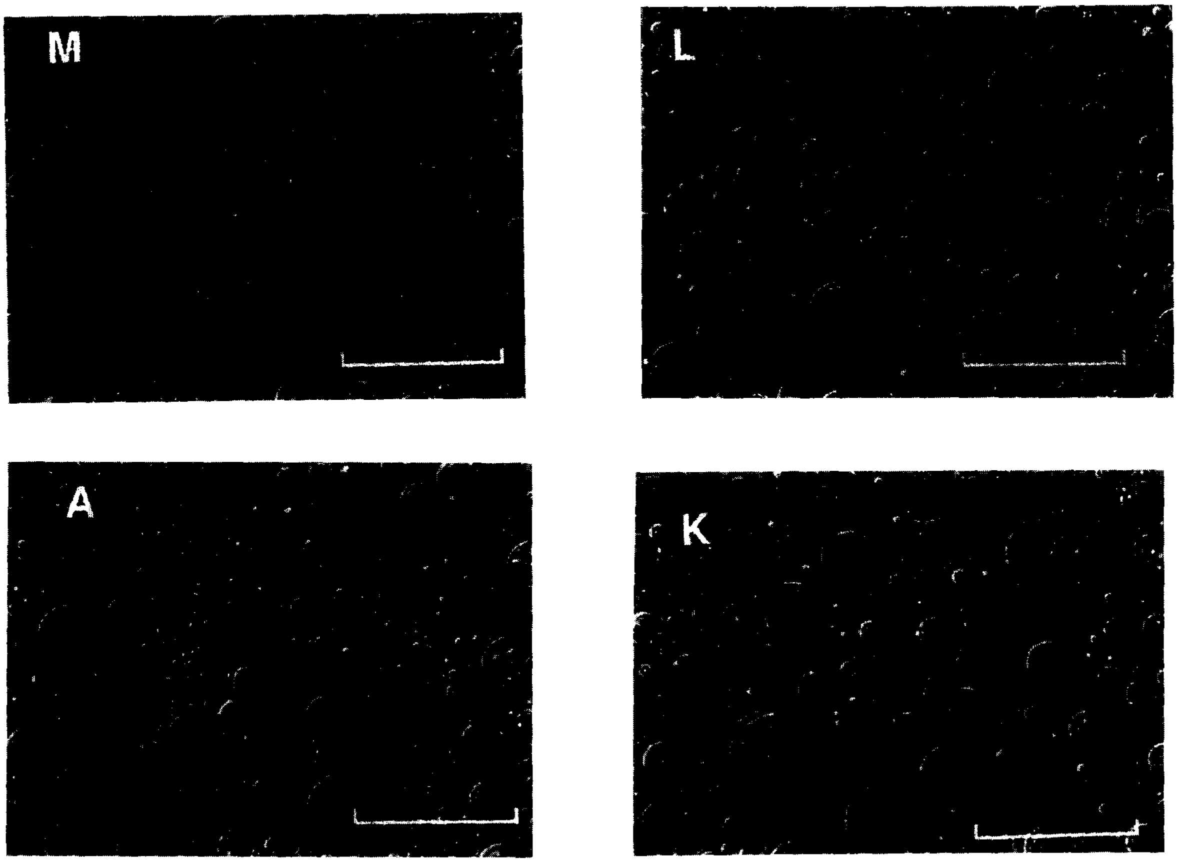


Fig. 2. DIC photomicrographs of the emulsion manufactured using an emulsification temperature of 90°C (sample M), 80°C (sample L), 70°C (sample A) and 60°C (sample K). Scale bar = 50 μm.

spectra, which could be ascribed to the interlamellar order. According to information from De Vringer et al. (1984), peaks 5 and 6 are likely to be diffraction peaks from cetostearyl alcohol crystals. The distance was 49×10^{-10} m in all the samples. The SAXD spectra show that at least

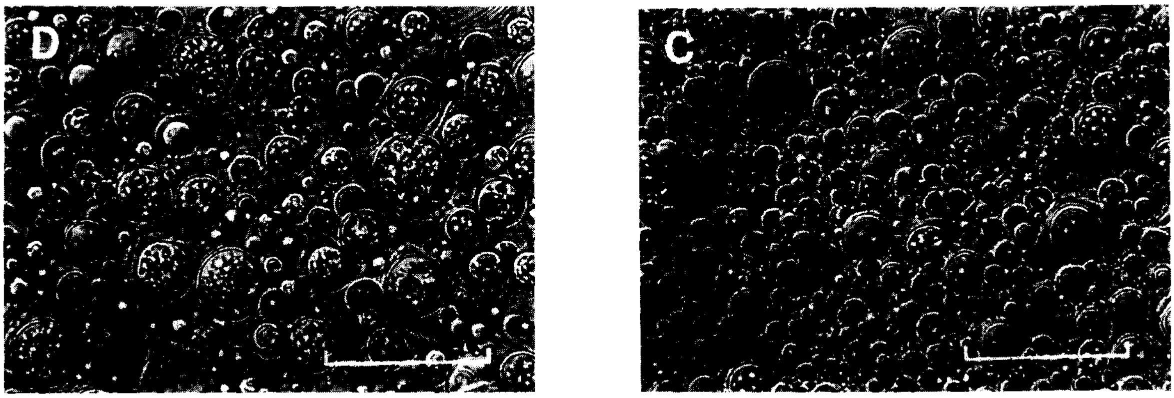


Fig. 3. DIC photomicrographs of the emulsion manufactured adding the water to the oil through the homogeniser (sample C) and adding oil to the water through the homogeniser (sample D). Scale bar = 50 μm.

two lamellar crystalline/gel structures exist in the emulsions and that the lamellar distances were very similar between the creams. SAXD could not be used to differentiate between process parameters.

3.2. Microscopy

DIC examination of the samples showed that there was a large number of 1–2 μm droplets and bilamellar structures surrounding the droplets in all the samples. The fraction of large droplets varied between samples. Using high homogenisation speed (sample N) produced an emulsion with almost 100% small droplets. Increasing the homogenisation time (samples O and I) also produced emulsions with a smaller than average number of large droplets as did high homogenisation temperature (sample M), shown in Fig. 2. This is in agreement with findings by Bornfriend (1978). Fig. 3 shows that adding the second phase through the homogeniser only produced a low number of large droplets if water was added to the oil phase (sample C), however, when oil was added to water (sample D) the sample contained a larger than average number of large droplets. This confirms that phase inversion during the manufacture of emulsions plays an important role in the uniformity of droplets in the sample as suggested by Becker (1966).

Between crossed polars the droplets appeared as distorted 'Maltese crosses' as shown in Fig. 4.

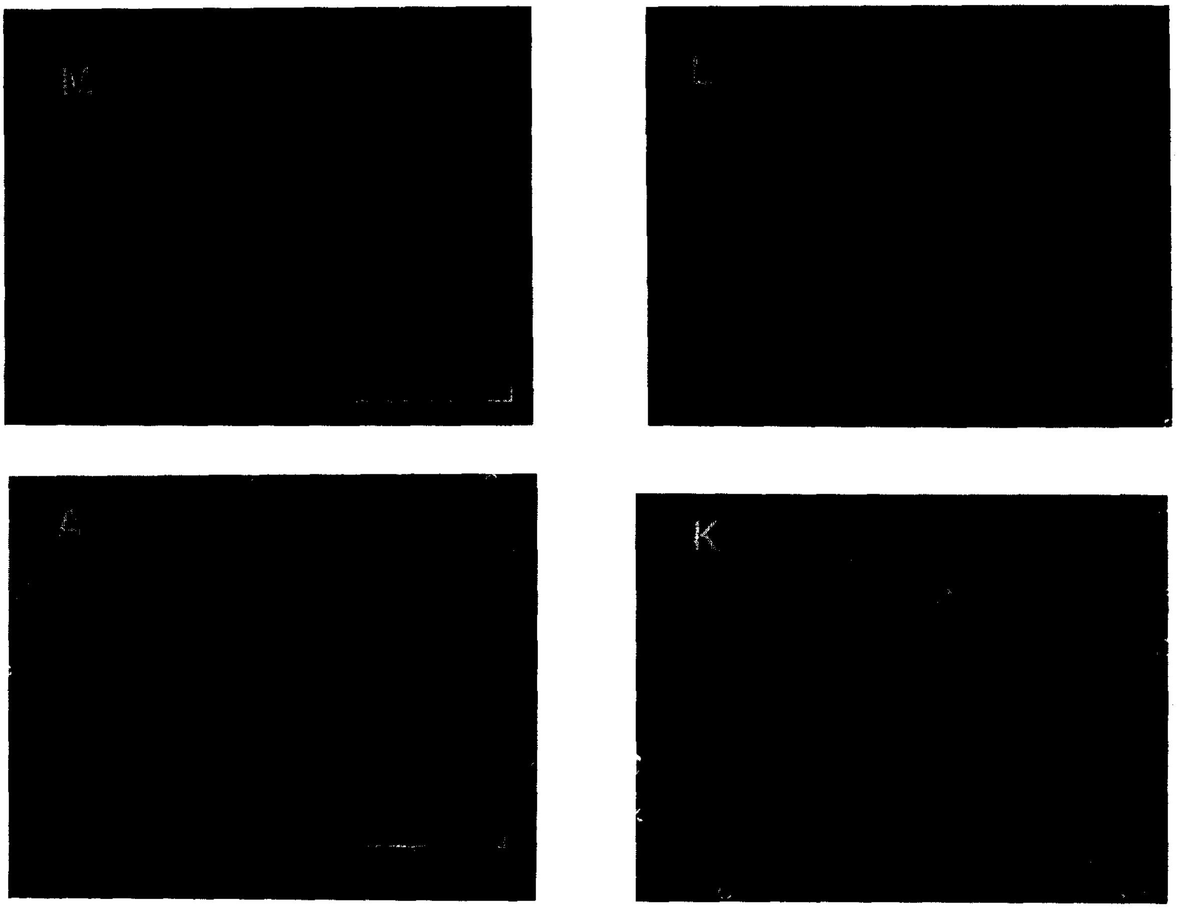


Fig. 4. Photomicrographs of samples emulsified at 90°C (sample M), 80°C (sample L), 70°C (sample A) and 60°C (sample K) and stored for 48 months at 30°C between crossed polars. Scale bar = 200 μm.

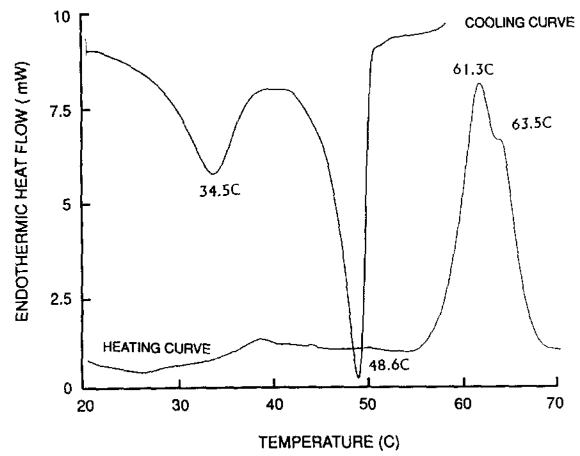


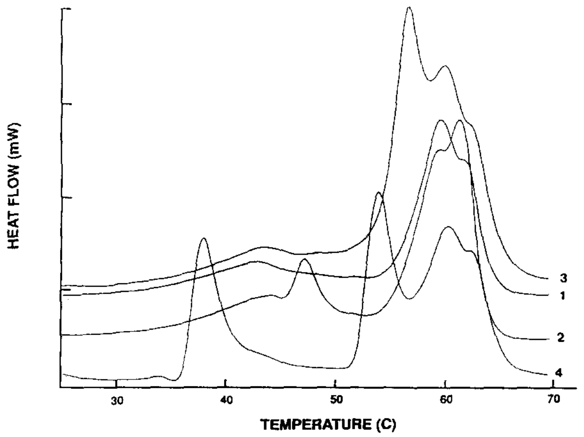
Fig. 5. DSC heating and cooling curves for sample A stored for 2 years at 30°C. Sample weight 20 mg, scanning rate 10 C°/min. The sample was held at 70°C for 1 min before the cooling curve was generated.

Eccleston and Beattie (1988), Barry (1983) and Fukushima et al. (1977) suggested that this appearance was due to the fatty alcohol/surfactant gel phase. In each sample some of the extinction crosses were brighter than others and the number of bright crosses varied between samples, suggesting that the appearance of a sample under crossed polars could be used as a guide to emulsion stability. Samples N, I and Q appeared to contain most bright extinction crosses and samples B, J and F the least.

3.3. Differential scanning calorimetry

Fig. 5 shows the up and down sweep for sample A after 24 months storage at 30°C. The scans for all the samples were similar. For each heating scan there was a major endotherm starting around 56°C, peaking at 61°C and with a shoulder peak around 63°C, a broad asymmetric low temperature transition was seen between 25 and 55°C. For each cooling scan there were two major exotherms, one starting around 50°C and peaking around 48°C and another starting around 40°C and peaking around 35°C. This agrees with findings by De Vringer et al. (1986) and Eccleston (1985). According to Eccleston (1985), the doubles may represent α gel and α gel-liquid crystalline transitions. As the emulsion deteriorates, the low temperature endotherm increased in intensity and the high melting endotherm reduced slightly, which agrees with the findings by Eccleston and Beattie (1988). On cooling the low temperature exotherm increased with time.

Cetostearyl alcohol emulsions made with nonionic emulsions is a multiphase system composed of α crystalline hydrates of cetostearyl alcohol, swollen bilayer gel phase of cetostearyl alcohol with the nonionic surfactants interspersed (Barry and Eccleston, 1973; Junginger et al., 1984; Eccleston, 1985). In stable emulsions the interlamellar distance is large providing a large proportion of bound water (Rowe and Brag, 1987). On storage the amount of interlamellar water gradually reduces, possibly accompanied by polymorphic phase transitions (Eccleston, 1986b; De Vringer et al., 1987), to more stable forms. A change in the distribution and oxidation of surfactants may also occur causing the lamellar gel phase to gradually separate into hydrated crystals and crystalline adducts of surfactants and alcohols (Eccleston, 1986b). The amount of hydrated fatty alcohol crystals could, therefore, be a marker for process efficiency and emulsion deterioration. Fig. 6 shows up and down curves for emulsion (A) spiked with 5% hydrated cetyl-, stearyl-and cetostearyl alcohol. Fig. 6 shows that neither free cetyl-nor stearyl alcohol is likely to have formed, since the peaks relating to the α and β-α crystal transformations (peak max. 38°C for cetyl alcohol and peak max. 48°C for stearyl alcohol) does not appear in scans of the emulsions. The melting endotherm for cetostearyl alcohol (peak max. 55°C) falls within the lower melting endotherm in the doublet of the emulsion. However, the exotherm on cooling falls within the higher temperature exotherm of the emulsion. From scans of the emulsions on storage it was established that the lower temperature doublet increased with the age of the sample for both the heating and cooling scan. An increase in the lower temperature doublet alone could, therefore, not be used as an indicator for a poor emulsion. A correlation of the ratio of lower to higher temperature doublet with process parameter and sample age (not shown) confirmed this. A decrease in the water content in the lamellar phase will increase the enthalpy changes of an emulsion (De Vringer et al., 1986), as will an increase in crystallinity. The total melting or cooling enthalpies for all the emulsions were found to increase consistently with storage time. Fig. 7 shows the heating scans with time for sample A. The heating enthalpies for all the samples are shown in histogram form in Fig. 8. The results are contrary to findings by De Vringer et al. (1987), which may be due to the shorter storage period employed by De Vringer et al. (1987) or due to differences in the emulsions tested. For the purpose of comparing the process parameters, low enthalpies were equated with preferred process parameters and high enthalpies with poor.



cooling curve

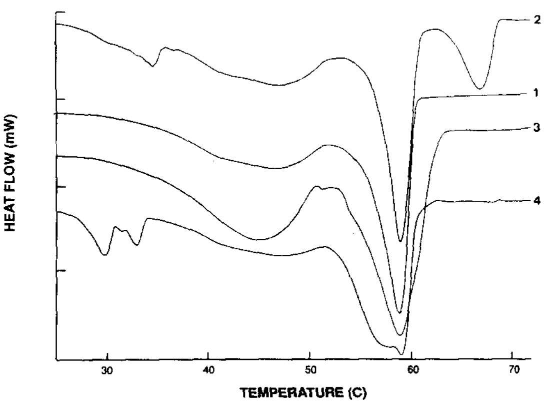


Fig. 6. Thermal behaviour of emulsion A (1), spiked with 5% hydrated cetyl alcohol (4), stearyl alcohol (2) and cetostearyl alcohol (3).

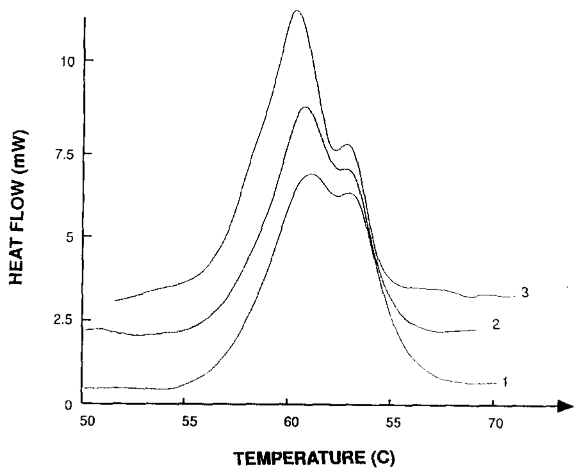


Fig. 7. Thermal behaviour of emulsion (A) manufactured to the standard procedures. (1) Sample stored for 2 months at 30°C, (2) sample stored at 30°C for 24 months and (3) sample stored at 30°C for 48 months.

3.4. *Order of addition*

The results of order of addition show that adding the water to the oil phase gives lower enthalpy values compared to oil to water addition. When one phase was added to the other through the homogeniser the differences were far smaller. A comparison of these results with the DIC droplet size findings (Fig. 3) suggests that introducing a phase through the homogeniser will improve the stability of a formulation without reducing the droplet size to any extent.

3.5. *The addition method*

The results from the addition method suggested that a more stable formulation was obtained when the hydrophilic surfactant (steareth 21) was melted together with the oily excipients before emulsification, whereas it made little difference if the hydrophilic surfactant (sorbitan oleate) was added to the aqueous or lipid phase before emulsification. Lin (1978), Lin et al. (1977) and Lin and Lambrechts (1969) found that placing both surfactants in the oil phase produced better emulsions. Above 15°C sorbitan oleate is a liquid which may explain the different results.

3.6. Emulsification temperature

Investigation of the emulsification temperature indicated that emulsification at 60, 70, 80 and 90°C produced emulsions with similar stability. Between crossed polars the samples also appeared similar, showing the same ratio of intense Maltese crosses to weak (Fig. 4). DIC photomicrographs of the samples (Fig. 2) show that the number of very large droplets increased with decreasing emulsification temperature. This agrees with findings by Bornfriend (1978) and Becker (1966). Small uniform droplet size has been used as an indicator for robustness (Lin, 1978). The all-important hydration of the hydrophilic part of the surfactants is temperature dependent (Carvell et al., 1986; Lyle and Tiddy, 1986). At high temperatures these groups are dehydrated preventing the molten fatty alcohol/surfactant phase from swelling, as the temperature drops the phase hydrates forming the characteristic multilamellar structures (Eccleston, 1986b; Eccleston and Beattie, 1988). Less force is required to reduce the oil droplet size at high temperature. These factors may explain why the droplet size decreases with increasing emulsification temperature while their comparative stability remains the same.

3.7. Addition rate

Lin (1978) showed that lowering the rate of aqueous phase addition during emulsification

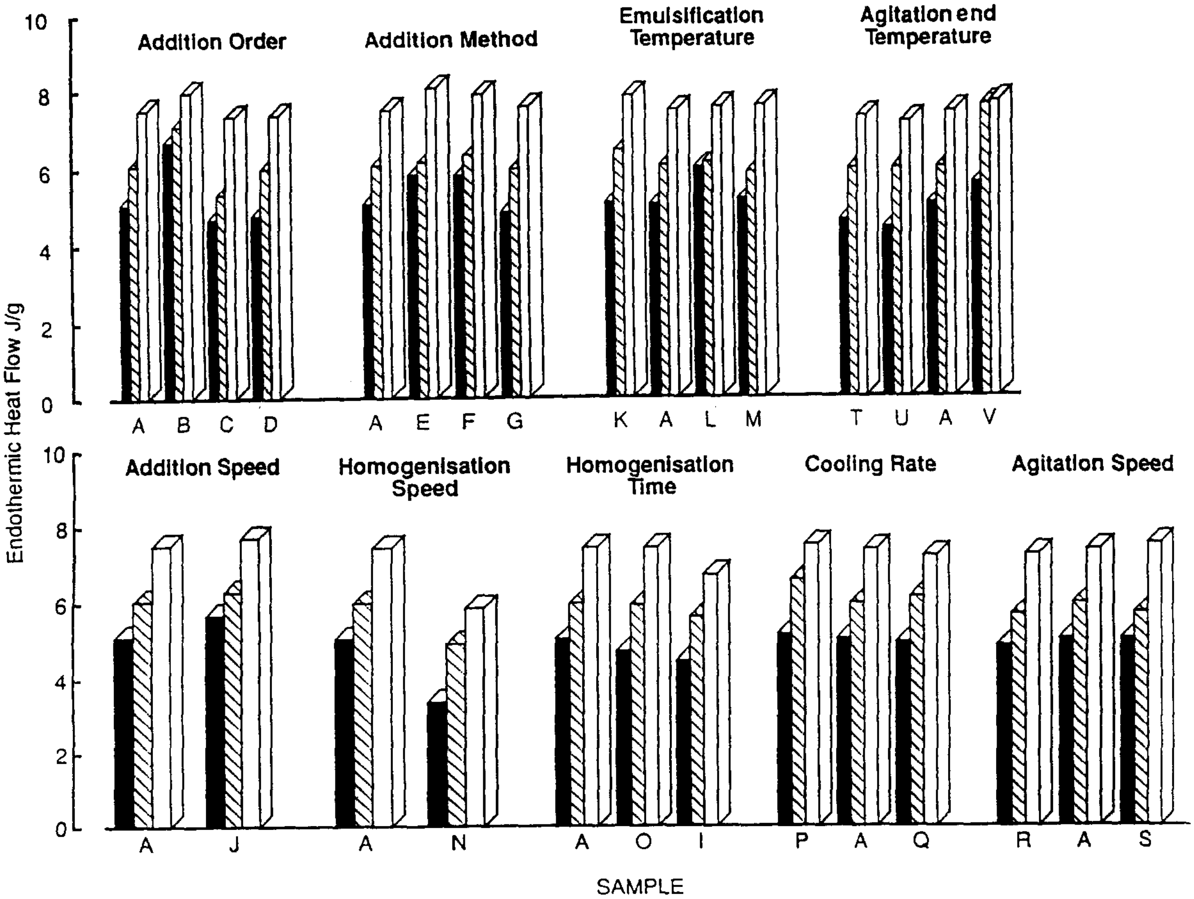


Fig. 8. Endothermic heat flow following 2 months storage at 30°C (filled bars), 24 months storage at 30°C (hatched bars) and 48 months storage at 30°C (empty bars).

produced better emulsions. Contrary to these findings, Fig. 8 indicates that it made little or no difference to the robustness of the emulsion whether the aqueous phase was added slowly or rapidly during the emulsification process. The different results may be due to differences in the total homogenisation times.

3.8. Homogenisation speed

This parameter had by far the greatest impact on the final quality of the emulsion, suggesting that the mixing efficiency of a manufacturing vessel will have a profound effect on the quality of the final product. With increased homogenisation speed the higher shearing forces disrupt the hydrocarbon chains of the oil and wax droplets exposing the surfactant chains to the water with formation of the additional gel phase (Eccleston and Beattie, 1988).

3.9. Homogenisation time

The results from the evaluation of the effect of the homogenisation time suggests, as expected, that increasing the homogenisation time will increase the robustness of the emulsions. Fig. 8, however, also shows that a substantial increase in the homogenisation time is required to improve the quality of the emulsion significantly.

3.10. Cooling rate

Bornfriend (1978) showed that the colloidal structures varied according to the cooling rate of the product. The rheological study of the emulsions indicated that slow cooling produced a less viscous product. Fig. 8 indicated that the stability of an emulsion cooled slowly is likely to be slightly better compared to a sample which is cooled quickly. Whether the findings are due to the slow cooling or the increased length of agitation is not known from this experiment. On cooling, the polyoxyethylene chains continually hydrate forming the multilamellar network with cetostearyl alcohol. The slower this process is, the more likely it is that more liquid gel structures will form (Eccleston and Beattie, 1988).

3.11. Agitation speed

The results from the evaluation of the effect of the agitation speed on the robustness of the emulsion indicated that this parameter had little or no effect on the predicted stability. Comparing the results from the cooling rate experiments with the results from the agitation speed experiments suggests that it is the slow cooling that provides the superior predicted stability.

3.12. Agitation end temperature

The results from the agitation end temperature investigation indicated that the optimum agitation end temperature was 40°C. Fig. 6 suggests that this may be related to the solidification profile. Agitation during the solidification process will speed up the equilibrium process (Eccleston, 1986) whereas agitation beyond the solidification point will disrupt the lamellar structures, confirming that emulsions containing cetostearyl alcohol are shear-thinning once the emulsion has solidified as suggested by Fox (1984) and Jass (1967).

A summary of the findings is shown in Table 2.

Table 2
Influence of each process factor in rank order based on the average percentage change in enthalpy for the standard manufacturing procedure (emulsion A)

Process parameter	Drop in enthalpy (%)	Increase in enthalpy (%)
Fast homogenisation speed	20	–
Long homogenisation time	9	–
Agitation end at 30°C	3	–
Slow cooling rate	1	–
Slow agitation rate	1	–
Fast agitation rate	–	1
Fast cooling rate	–	1
Emulsification at 60°C	–	3
Agitation end at 50°C	–	4
Adding Steareth 21 with water and sorbitan oleate with oil	–	5
Adding oil to water	–	7
Adding both surfactants to the aqueous phase	–	8

4. Conclusion

The study examined the effect of nine process parameters on the long term stability of an o/w emulsion using SAXD, microscopy and DSC to test the samples. The usefulness of the test methods were also assessed as part of the study. DSC enthalpy change was found, based on stored samples, to provide a means to determine the relative stability of an o/w emulsion. The procedure was reproducible (error ±2%) and owing to the short time needed for an experiment (approx. 10 min), it could be a suitable technique for process control and stability tests. The total heating enthalpy was the most sensitive DSC parameter. The total cooling enthalpy was found not to be as accurate for technical reasons. The use of a specific peak area was less reliable, probably since peaks from different crystal forms in the emulsion structure overlapped. Microscope examination using crossed polars provided a means of qualitatively differentiating between process parameters, however relatively small differences could not be separated. DIC microscopy suggested that the number of large droplets in a sample varied with the manufacturing process. Comparing the DIC microscopy findings with the results from the examination under crossed polars and DSC enthalpy results suggested that the droplet size range in a sample may not always be correlated with its stability. Notably, increasing the emulsification temperature caused the droplet size range to decrease whereas the heating enthalpies for the sample remained similar. The addition of the oil phase to the aqueous phase through the homogeniser produced a large number of large droplets without increasing the heating enthalpy for the sample. Using SAXD, no difference in quality between the samples could be detected.

Based on the DSC and the crossed polar results, the homogenisation speed was found to be by far the most important parameter for emulsion stability, followed by the homogenisation time. Slow cooling improved the stability slightly, but the emulsification temperature, addition rate and agitation speed had little effect on the emulsion stability. Adding the surfactant to the aqueous phase before emulsification and adding the oil phase to the aqueous phase during the emulsification produced inferior emulsions. The agitation end temperature was found to have an optimum for the stability of the emulsion corresponding closely with the lower cooling exotherm.

References

Barry, B.W., Formulation of dermatological vehicles. *Dermatological Formulations. Percutaneous Absorption*, Dekker, New York, 1983, pp. 296-350.

Barry, B.W. and Eccleston, G.M., Influence of gel networks in controlling consistency of o/w emulsions stabilised by mixed emulsifiers. *J. Texture Stud.*, 4 (1973) 53-81.

Barry, B.W. and Saunders, G.M., Kinetics of structure build-up in self bodied emulsions stabilized by mixed emulsifiers. *J. Coll. Interface Sci.*, 41 (1972) 331-341.

Becker, P., *Emulsions: Theory and Practice*, 2nd Edn, Reinhold, New York, 1966, pp. 267-278.

Bornfriend, R., Effect of processing of the rheological behaviour of emulsions. *Cosmet. Toilet.*, 93 (1978) 61-69.

Breuer, M.M., Cosmetic emulsions. In Becker, P. (Ed.), *Encyclopedia of Emulsion Technology*, Dekker, New York, Vol. 2, 1983, pp. 385-424.

Carvell, M., Hall, D.G., Lyle, I.G. and Tiddy, J.T., Surfactant-water interactions in lamellar phases. *Faraday Disc. Chem. Soc.*, 81 (1986) 223-237.

De Vringer, T., Joosten, J.G.H. and Junginger, H.E., Characterisation of the gel structure in a nonionic ointment by small angle X-ray diffraction. *Colloid Polym. Sci.*, 262 (1984) 56-60.

De Vringer, T., Joosten, J.G.H. and Junginger, H.E., A study of the gel structure in a nonionic o/w cream by differential scanning calorimetry. *Colloid Polym. Sci.*, 264 (1986) 691-700.

De Vringer, T., Joosten, J.G.H. and Junginger, H.E., A study of the ageing of the gel structure in a nonionic o/w cream by X-ray diffraction, differential scanning calorimetry and spin-lattice relaxation measurements. *Colloid Polym. Sci.*, 265 (1987) 448-457.

Eccleston, G.M., Application of emulsion stability theories to mobile and semi-solid o/w emulsions. *Cosmet. Toilet.*, 101 (1986a) 73-92.

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.

Eccleston, G.M., The influence of fatty alcohols on the structure and stability of creams prepared with polyethylene glycol 1000 monostearate/fatty alcohols. *Int. J. Cosmet. Sci.*, 4 (1982) 133-141

Eccleston, G.M., The microstructure of semi-solid creams. *Pharm. Int.*, 7 (1986b) 63-70

Eccleston, G.M. and Beattie, L., Microstructural changes during the storage of systems containing cetostearyl alcohol/plyoxyethylene alkyl ether surfactants. *Drug Dev. Ind. Pharm.*, 14 (1988) 2499–2518.

Fox, C., Skin care: An overview and update on the state of the art of science. *Cosmet. Toilet.*, 99 (1984) 41–54.

Fukushima, S., Yamaguchi, M., Harusawa, F., Effect of cetostearyl alcohol on stabilisation of oil-in-water emulsion. *J. Colloid Interface Sci.*, 59 (1977) 159–165.

Jass, H.E., Effect of process variables on the stability of some specific emulsions. *J. Soc. Cosmet. Chem.*, 18 (1967) 561–598.

Junginger, H.E., Akkermans, A.A.M.D., Heering, W., The ratio of interlamellarly fixed water to bulk water in o/w creams. *J. Soc. Cosmet. Chem.*, 35 (1984) 45–57.

Lashmar, U.T., Correlation of rheological properties of an oil-in-water emulsion with manufacturing procedures and stability. *Int. J. Pharm.*, 91 (1993) 59–67.

Lin, T.J., Low-surfactant emulsification. *J. Soc. Cosmet. Chem.*, 28 (1978) 273–295.

Lin, T.J. and Lambrechts, J.C., Migration of surfactants in a two-phase system. *J. Soc. Cosmet. Chem.*, 20 (1969) 627–638.

Lin, T.J., Kurihara, H., Ohta, H., Prediction of optimum o/w emulsification via solubilisation measurements. *J. Soc. Cosmet. Chem.*, 28 (1977) 457–479.

Lyle, I.G. and Tiddy, G.J.T., Hydration forces between surfactant bilayers: an equilibrium binding description. *Chem. Phys. Lett.*, 124 (1986) 432–436.

Rieger, M.M., Stability testing of macrolmulsions. *Cosmet. Toilet.*, 106 (1991) 59–69.

Rowe, R.C. and Brag, D., Water distribution creams prepared using cetostearyl alcohol and cetrimide. *J. Pharm. Pharmacol.*, 39 (1987) 642–643.

Tadros, T.F. and Vincent, B., Emulsion stability. In Becher, P. (Ed.), *Encyclopedia of Emulsion Technology*, Vol. 1, Dekker, New York, 1983, pp. 129–285.