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A quantitative examination of the structure of emulsions prepared using cetostearyl alcohol and cetrimide using Fourier transform infrared microscopy

J.D. Louden [1] and R.C. Rowe [2]

[1] *ICI Chemicals and Polymers Ltd, The Heath, Runcorn WA7 4QE (U.K.) and* [2] *ICI Pharmaceuticals, Alderley Park, Macclesfield SKO 2TG (U.K.)*

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Summary

Oil droplets in an emulsion consisting of liquid paraffin, cetostearyl alcohol, cetrimide and water have been quantitatively analysed by Fourier transform infrared (FT-IR) microscopy. All droplets analysed contained cetostearyl alcohol in excess of its solubility at room temperature. Calculations of the amount of cetostearyl alcohol in the aqueous phase revealed that twice as much had transferred across the oil/water interface in an emulsion containing 5% liquid paraffin compared to one containing 20% liquid paraffin. A mechanism to explain both this and the apparent inhomogeneity in the emulsions has been proposed.

Introduction

The mixed emulsifier of cetrimide and cetostearyl alcohol is frequently used in the preparation of antiseptic creams. The structure of these creams is very complex, consisting of droplets of liquid paraffin together with particles of cetostearyl alcohol dispensed in a gel network consisting of bilayers of cetostearyl alcohol swollen with water (Patel et al., 1985a; Rowe and McHanon 1987; Barry and Rowe, 1989). Although all the features have been identified using laser Raman spectroscopy (Louden et al., 1985) their actual quantitative composition remains the subject of conjecture. In this work we have used Fourier transform infrared (FT-IR) microscopy both to study qualitatively the structure of the emulsions and to analyse quantitatively the oil droplets for cetostearyl alcohol content. The latter is particularly of interest, since it provides information on the kinetics of the formation of the gel structure during production of the cream.

Materials and Methods

Preparation of the emulsions

All materials used were of Pharmacopoeial grade. Two emulsions were prepared according to the formulae in Table 1. The cetostearyl alcohol and liquid paraffin were heated to 80 °C and then dispersed in aqueous cetrimide solution at the

Correspondence: J.D. Louden, ICI Chemicals and Polymers Ltd, The Heath, Runcorn WA7 4QE, U.K.

TABLE 1

Emulsion formulations used in study

	Concentration (% w/w)	
	E_1	E_2
Liquid paraffin	5	20
Cetostearyl alcohol	10	10
Cetrimide	0.5	0.5
Purified water to:	100	100

same temperature. The mixture was stirred gently with a paddle stirrer for a period of 1 h before being allowed to cool to approx. 60 °C. The dispersion was then homogenized using a Silverson multipurpose high-speed mixer for a period of 15 min or until the setting part of the cream was reached. Both systems were allowed to stand for at least 2 weeks before being tested.

Fourier transform infrared microscopy

The FT-IR microscope used in this study was developed by AIRE Scientific Ltd and was coupled to a Nicolet 510 FT-IR spectrometer. The microscope utilised a 0.5 mm MCT (mercury cadmium telluride) liquid nitrogen cooled detector and a choice of 15 ×, 36 × and 52 × cassegrain mirror objectives.

Samples for analysis were in the form of a 20 μm thick film between two glass coverslips. Each sample was first examined on the microscope using white light illumination with either eyepieces or a close circuit television viewing system. The fea-

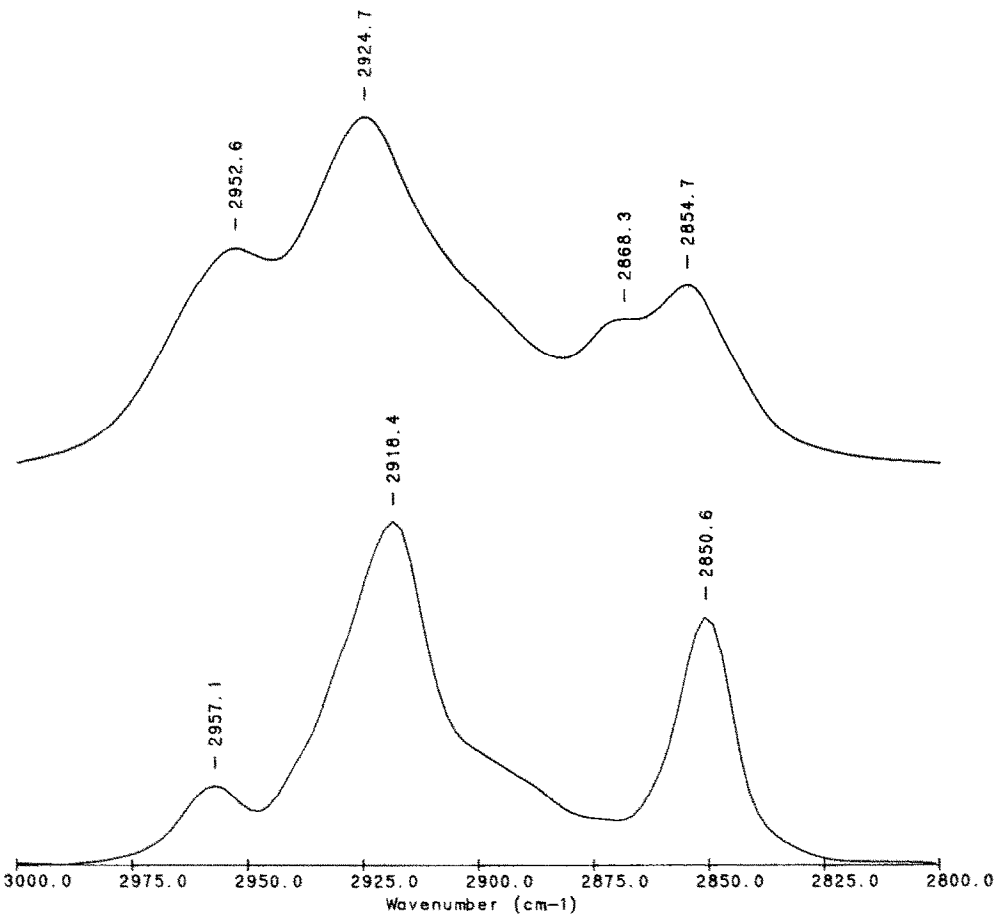

Fig. 1. Reference IR spectra for the liquid paraffin (top) and cetostearyl alcohol (bottom) used in this study.

tures of interest (oil droplets, polyhedral particles, gel network) were located and positioned centrally in the field of view and a video print obtained of the sample area. The specific area of interest, (typically 10×10 μm) was then isolated by means of the remote aperture (4 knife edge blades) located at the primary image position. Since the oil droplets were typically of the order of 20 μm diameter this process eliminated any interference from the surrounding medium.

The infrared energy was then transmitted through the sample and onto the MCT detector. Typically the IR spectra were recorded at 8 cm^{-1} resolution and 1000 scans using the $52\times$ cassegrain mirror objective and an aperture size of 10×10 μm.

Results and Discussion

Reference spectra

Fig. 1 shows the C-H stretching region of the IR spectra of batches of liquid paraffin and cetostearyl alcohol used in the preparation of emulsions. The paraffin spectrum consists of four peaks situated at 2952.6 cm^{-1} (antisymmetrical methyl C-H), 2924.7 cm^{-1} (antisymmetrical methylene C-H), 2868.2 cm^{-1} (symmetrical methyl C-H) and 2854.7 cm^{-1} (symmetrical methylene C-H). The cetostearyl alcohol spectrum consists mainly of two peaks situated at 2918.4 cm^{-1} (antisymmetrical methylene C-H) and 2850.4 cm^{-1} (symmetrical methylene C-H). Consequently, it is possible to use the C-H stretching region of the IR spectrum to differentiate between liquid paraffin and cetostearyl alcohol in the emulsions.

Qualitative examination containing 5% oil

Fig. 2 shows a differential interference photomicrograph of the emulsion containing 5% liquid paraffin. All the features associated with the known structure of these emulsions are evident; the spherical droplets of liquid paraffin (A), the polyhedral particles of cetostearyl alcohol (B) and the gel network surrounding these features (C). Examination of each of these features by the IR microscope gives the spectra shown in Fig. 3. The polyhedral particles and gel network give spectra identical to the reference spectrum of cetostearyl alcohol (Fig. 1) confirming the previous measurements made using Raman spectroscopy (Louden et al., 1985). However, while the IR spectrum of

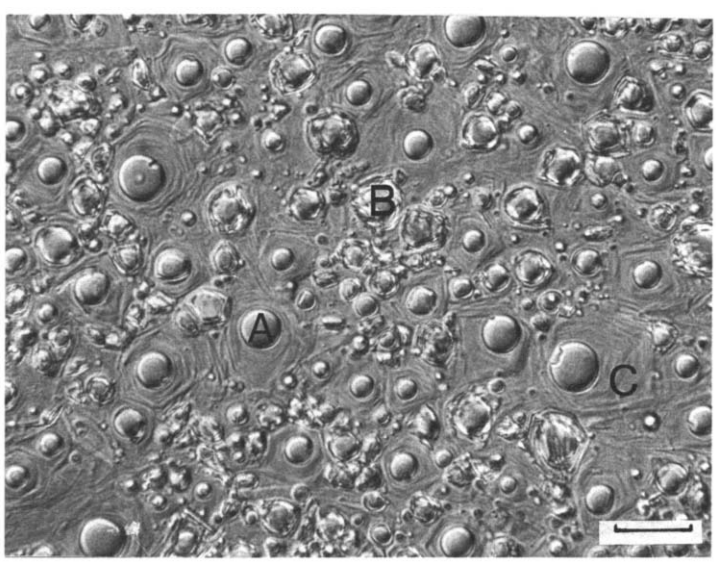

Fig. 2. Differential interference photomicrograph of the emulsion containing 5% oil. (A) Oil droplet, (B) polyhedral particle of cetostearyl alcohol, (C) gel network (bar = 25 μm).

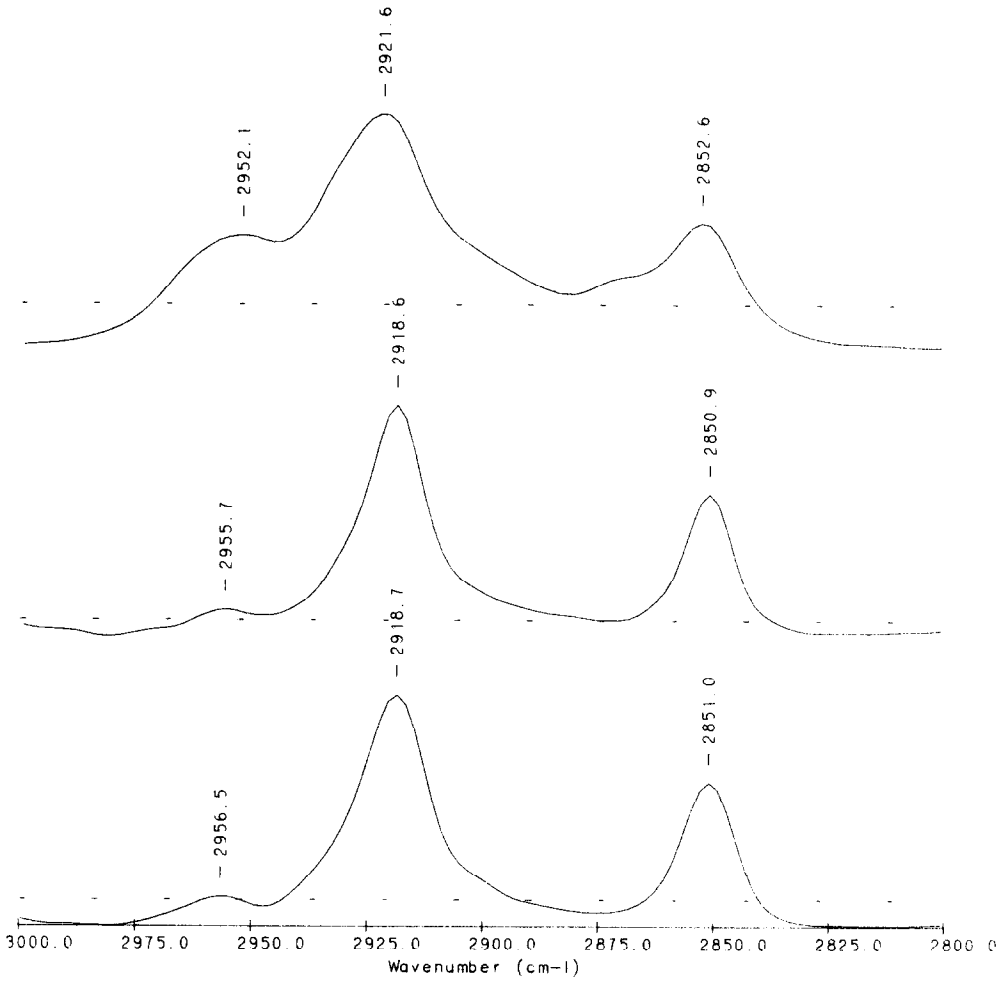

Fig. 3. IR spectra of the oil droplet (top), polyhedral particle (middle) and gel network (bottom).

the oil droplets is similar to the reference spectrum of pure liquid paraffin, there is a shift in peak positions especially those of the antisymmetrical methylene C-H at 2924 cm^{-1} and the symmetrical methylene C-H at 2855 cm^{-1}. This is consistent with the presence of some dissolved cetostearyl alcohol.

Quantitative examination of the oil droplets

In order to quantify the amount of cetostearyl alcohol present in the oil droplets a series of quantitative standards of cetostearyl alcohol dissolved in liquid paraffin were prepared and their IR spectra obtained (Fig. 4). It can be seen that as the concentration of the cetostearyl alcohol increases both the peak position of the antisymmetrical methylene C-H and also the peak height ratio of the symmetrical methylene and methyl C-H change. Figs 5 and 6 show the linear relationship between these changes and the cetostearyl alcohol concentration over the range 0–30% w/w.

Analysis of 11 droplets in the emulsion containing 5% oil and 18 droplets in the emulsion containing 20% oil led to the results listed in Tables 2 and 3. In general, there is good agreement between the two methods of analysis. An interesting feature is droplet/droplet variation in the cetostearyl alcohol concentration in both emulsions implying an inhomogeneity at the 'microlevel'. A similar inhomogeneity in the gel network has been

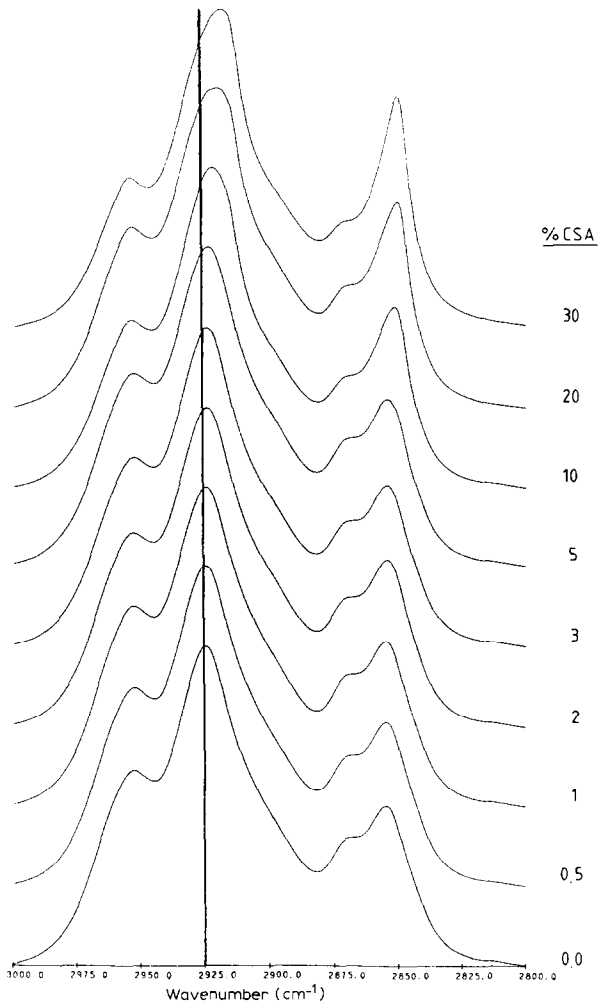

Fig. 4. IR spectra of calibration standards of cetostearyl alcohol dissolved in liquid paraffin.

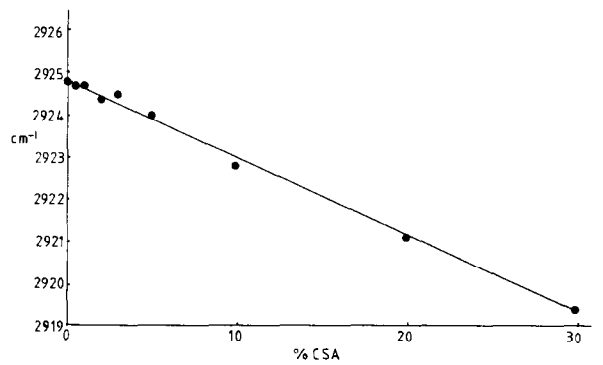

Fig. 5. Calibration graph of peak position vs cetostearyl alcohol concentration for standards.

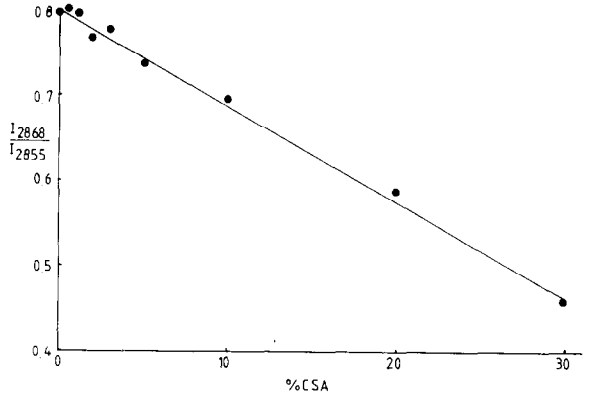

Fig. 6. Calibration graph of peak height ratio vs cetostearyl alcohol concentration for standards.

previously inferred from dielectric relaxation measurements (Dissado et al., 1987). However, in every droplet analysed the concentration of cetostearyl alcohol is in excess of its solubility in the oil at room temperature — approx. 2.0% w/w (Talman et al., 1967). Although no crystals were seen in the oil droplets in this work there are several reports of crystals being seen in oil droplets in similar emulsions (Talman and Rowan, 1968).

Calculations of the aqueous phase concentration of cetostearyl alcohol (assuming mean oil

TABLE 2

Peak positions, peak height ratios and cetostearyl alcohol concentrations of oil droplets in the emulsion containing 5% liquid paraffin

Peak position (cm^{-1})	Concentration (%w)	Ratio of 2868/2855 cm^{-1} peaks	Concentration (%w)
2920.2	25	0.524	25
2920.6	23	0.506	26
2920.6	23	0.545	23
2920.8	22	0.570	21
2921.4	19	0.573	20
2921.5	18	0.573	20
2921.7	17	0.573	20
2921.7	17	0.580	20
2922.2	15	0.598	18
2922.4	14	0.615	17
2922.8	11	0.637	15

TABLE 3

Peak positions, peak height ratios and cetostearyl alcohol concentrations of oil droplets in the emulsion containing 20% liquid paraffin

Peak position (cm^{-1})	Concentration (% w/w)	Ratio of 2868/2855 cm^{-1} peaks	Concentration (% w/w)
2919.1	35	0.473	29
2919.8	27	0.522	25
2920.2	26	0.543	23
2920.3	25	0.630	16
2920.3	25	0.512	26
2920.4	25	0.560	22
2920.5	24	0.547	23
2920.6	23	0.563	22
2920.6	23	0.517	25
2920.6	23	0.522	25
2920.7	23	0.541	23
2920.7	23	0.570	21
2921.4	19	0.610	17
2921.6	18	0.593	19
2921.6	18	0.585	19
2921.7	17	0.642	15
2922.1	15	0.643	15
2922.6	12	0.627	16

phase concentrations of 19.5% w/w and 21.5% w/w for the 5% and 20% emulsions, respectively) reveal that, while in the 5% emulsion 88% of the cetostearyl alcohol transfers across the oil/water interface, only 45% transfers in the 20% emulsion. It is generally assumed that the mechanism of transfer of the cetostearyl alcohol across the oil/water interface is by passive diffusion with the cetostearyl alcohol initially being solubilised by the cetrimide micelles in the aqueous phase and ultimately forming the lamellar smetic liquid crystals that constitute the gel network. However, although the calculated amounts of cetostearyl alcohol transferred are consistent with differences in the initial concentration in the two emulsions they are inconsistent with the mechanism of passive diffusion since the emulsion containing 20% oil will, by its very composition, have four times the interfacial area as compared to that containing 5% oil.

A possible reason for this apparent anomaly is in the assumptions made in the derivation of the laws of diffusion. It is generally assumed that the boundary conditions are such that the diffusing species is always rapidly and completely removed from the interface. However, in the case of an emulsion where the total interfacial area is related to the number and size of the oil droplets and the system is heterogeneous, i.e., the possibility of clustering of oil droplets is high, then these conditions cannot always apply. In such a system it is obvious that the situation will be exacerbated by increasing the oil phase concentration as in this study. The concept of clustering, and hence the production of non-ideal boundary conditions for each individual droplet, is consistent with the results on the variation in the cetostearyl alcohol concentration between droplets (Tables 2 and 3) since in some droplets diffusion could well be restricted, i.e. the residual cetostearyl alcohol concentration will be high while in others it could well be promoted, i.e., the residual cetostearyl alcohol concentration will be low.

Such a mechanism can also be used to explain the sensitivity of such formulations to variation in processing conditions (Patel et al., 1985b). It is well known, for instance, that the viscosities of these emulsions are affected by mixing conditions and the rate of cooling. Both factors will affect the amount of cetostearyl alcohol transferred across the interface and consequently the amount of gel network found, the first by affecting the droplet size and hence interfacial surface area, the latter by changing the time for diffusion to occur.

The results clearly show the potential of this relatively rapid, nondestructive technique in the quantitative analysis of these complex emulsions and in the understanding of the mechanisms of formation. The technique could possibly be used in the optimisation of processing conditions to eliminate batch to batch variation.

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