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Effect of water content on the microstructure of an o/w cream

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Summary

The effect of water content on the microstructure of o/w creams containing a mixed emulsifier (i.e. sodium lauryl sulphate and cetostearyl alcohol) as emulgator and liquid paraffin as the oil phase was studied using both large-angle and small-angle X-ray methods. Thermogravimetric and differential scanning calorimetric methods were also used to study the microstructure of the creams. Lamellar structure was observed in the creams and the interlamellar spacings were calculated and found to become larger with increasing amounts of water in the creams. Water evaporated from the creams in two (stages I and II) or three (I, II and III) stages, depending on the water content of the cream; with large amounts of water (> 50%), water evaporated in three stages. In the cases of three-stage evaporation, the water was bound loosely between the lamellae and evaporated in pulses.

Introduction

o/w creams containing mixed emulsifiers of the surfactant/fatty amphiphile type (e.g. sodium lauryl sulphate/cetostearyl alcohol) have been regarded to be four-phase systems (Junginger et al., 1984; Eccleston, 1986). In addition to the bulk water phase and dispersed oil phase, there can also be found hydrophilic and lipophilic gel phases. The hydrophilic gel phase consists of double layers of surfactant and fatty alcohol molecules with layers of water fixed between the lamellae. The interlamellarly fixed water and the bulk water phases form the continuous phase of the cream. Water release, i.e. the amounts of bulk water and fixed water is an important criterion for drug release from o/w creams (Junginger et al., 1984, Müller-Goyman and Frank, 1986).

Previously (Niemi et al., 1989) it was found that release of hydrocortisone from o/w creams containing ionic emulgators with fatty alcohol was retarded as the amount of water in the cream increased up to 60% water content; above this, the release of hydrocortisone was enhanced. In that study it was assumed that increasing the amount of water changes the microstructure of the cream, thus affecting its release properties. The aim of the present investigation was to determine how water content affects the microstructure of the cream.

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Materials and Methods

Materials

The creams studied were similar to those described previously in detail (Niemi et al., 1989). Sodium lauryl sulphate (1%, Fluka) and cetostearyl alcohol (8%, Henkel Chemicals Ltd) were used as a mixed emulsifier. The water contents varied from 10 to 80% and the respective amounts of liquid paraffin (Ph.Eur.) used as the oil phase varied accordingly, to give a total of 100%. The creams were prepared by dissolving sodium lauryl sulphate in water and cetostearyl alcohol in liquid paraffin, both at 70°C. The two phases were mixed together at 70 ° C and blended mechanically as the cream congealed. To replace the evaporated water, the amount of water used to prepare the creams was 5% more than the amount stated in the recipe. Before they were tested, the creams were allowed to stand for about 4 weeks in opaque tubes at 20 ± 1°C.

Methods

The creams were assessed visually using binocular light microscopy with polarized plates (Nikon Optiphot).

Large-angle X-ray diffraction (ADXD) of the creams was measured using a Philips PW 1130 diffractometer under the following conditions: radiation Ni filtered CuK$_\alpha$ ($\lambda = 0.15418$ nm), voltage/current ratio 40 kV/20 mA, scanning speed 1°/min, divergence/receiving slits 0.5/0.3 mm. The reflected radiation was investigated by means of a scintillation detector. To study the cetostearyl alcohol and the mixture of cetostearyl alcohol and liquid paraffin, an Enraf Nonius Diffractis 583 diffractometer was used, with CoK$_\alpha$ radiation ($\lambda = 0.1790$ nm). The cream containing 20% water was studied with both types of equipments. The reflected radiation was investigated by means of an Si(Li)-semiconductor detector, divergence/receiving slits 1.0/0.3 mm.

Small angle X-ray scattering (SAXS) patterns for determining the interlamellar spacings in the creams were taken using a Kiessig camera constructed in our laboratory (Fig. 1) and an exposure time of 24 h. All experiments were carried out at 18° C. Ni-filtered copper radiation was used. The repeated distances (d) in SAXS experiments were calculated according to Bragg's law:

$$2d \sin \theta = n\lambda$$

where λ is the wavelength of the X-ray, n is the order of reflection and θ is half the scattering angle.

Differential scanning calorimetric (DSC) studies were performed with a Perkin Elmer DSC7 system. The scanning rate was 5°C/min, and weight of the sample was 5–10 mg.

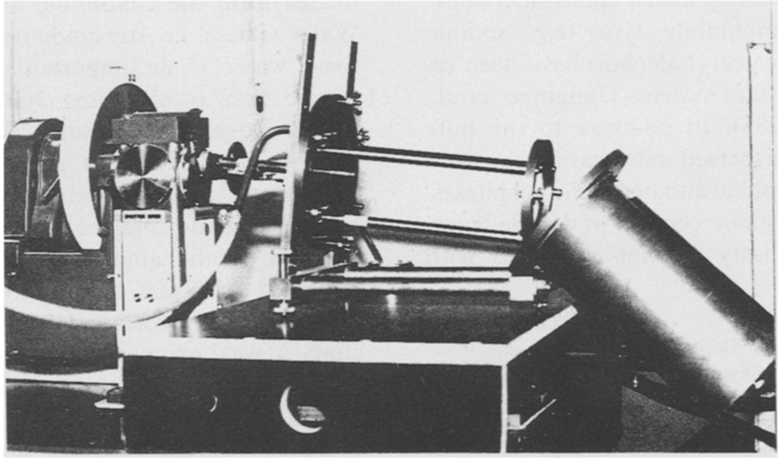

Fig. 1. Kiessig camera used in small angle X-ray measurements.

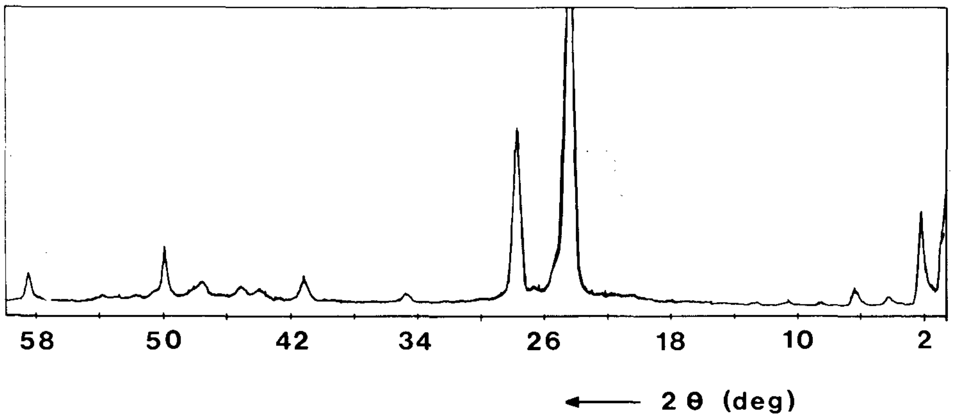

Fig. 2. Large angle X-ray diffraction pattern of cetostearyl alcohol. CoK$_\alpha$ radiation ($\lambda = 0.1790$ nm).

Thermogravimetric analyses (TG) were performed with Mettler TA 3000/TG50 and Perkin Elmer TGA7 systems. The heating rate was 2°C/min, weight of a typical sample was 4–10 mg, and the temperature range was 20–110°C.

Results and Discussion

With visual assessment no phase separation was found even in creams containing large amounts of water.

Cetostearyl alcohol in the creams

The X-ray diffraction patterns of cetostearyl alcohol (Fig. 2) and the mixture of cetostearyl alcohol and liquid paraffin (Fig. 3) show that, when cetostearyl alcohol was melted in the liquid paraffin, some of the characteristic reflections of cetostearyl alcohol could not be observed above the 2θ values of about 28°. Characteristics of the X-ray diffraction pattern for cetostearyl alcohol, the mixture of cetostearyl alcohol and liquid paraffin as well as of the cream containing 20% water are summarized in Table 1.

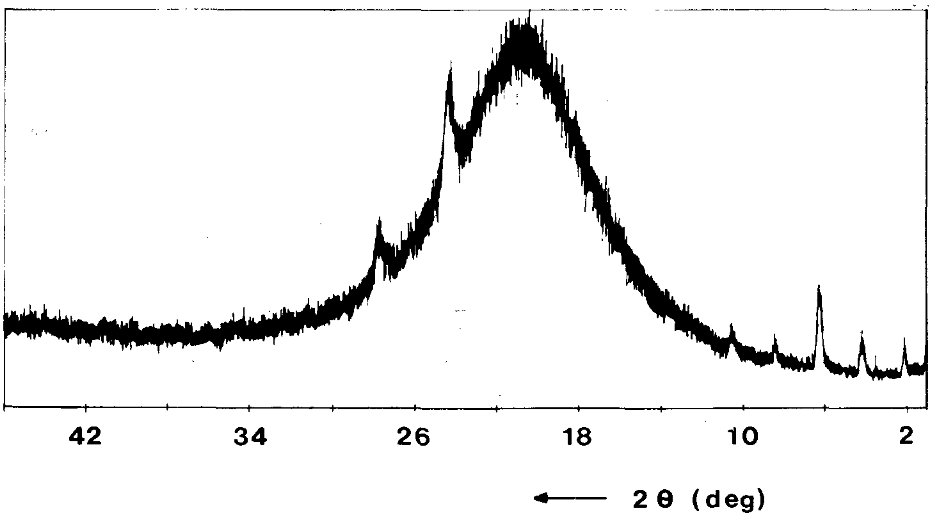

Fig. 3. Large angle X-ray diffraction pattern of the mixture of cetostearyl alcohol and liquid paraffin. CoK$_\alpha$ radiation ($\lambda = 0.1790$ nm).

TABLE 1

X-ray diffraction patterns of cetostearyl alcohol, a mixture of cetostearyl alcohol and liquid paraffin, and the cream containing 20% water ($\lambda = 0.1790$ nm)

Cetostearyl alcohol		Cetostearyl alcohol liquid paraffin		Cream with 20% water	
2θ (°)	d (nm)	2θ (°)	d (nm)	2θ (°)	d (nm)
2.25	4.55	2.25	4.55		
4.30	2.39	4.30	2.39		
6.30	1.63	6.30	1.63		
8.45	1.22	8.45	1.22		
10.6	0.97	10.6	0.97		
24.6	0.42	24.6	0.42	24.6	0.42
27.8	0.37	27.8	0.37		
34.7	0.30				
41.2	0.25				
44.0	0.24				
45.5	0.23				
47.5	0.22				
50.0	0.21				
58.5	0.18				

Furthermore, when water and sodium lauryl sulphate were added to the mixture, except for the typical pattern of liquid paraffin, only the strongest reflection of cetostearyl alcohol was observed, i.e. at a 2θ value of about 24.6° (Fig. 4). When the amount of water in the cream increased, the scattering from amorphous liquid paraffin became weaker; however, the cetostearyl alcohol peak at 24.6° remained. The calculated d value for that reflection of cetostearyl alcohol is 0.42 nm (Table 1).

In DSC measurements two melting endotherms of cetostearyl alcohol were observed, at 36.5 and 49.5 °C. These two melting endotherms could also be identified in the creams containing 20–70% water.

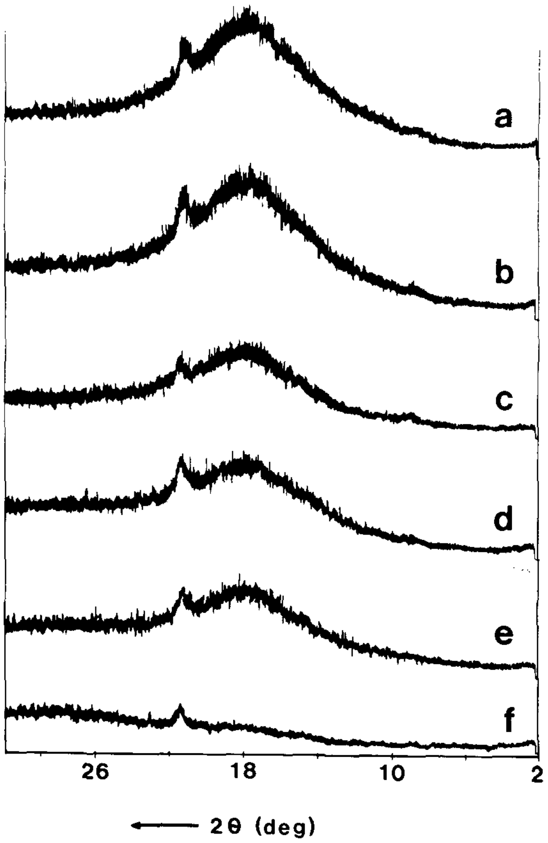

Fig. 4. Large angle X-ray diffraction patterns of creams containing different amounts of water. CuK_α radiation ($\lambda = 0.1542$ nm). Water amount in the creams: (a) 20%, (b) 30%, (c) 40%, (d) 50%, (e) 60%, (f) 80%.

Lamellar structure of the creams

The lamellar structure of the cream was confirmed by small-angle X-ray measurements. With increasing amounts of water, from 10 to 60%, the interlamellar spacing in the cream increased from

Fig. 5. Small angle X-ray diffractograms of creams containing different amounts of water.

	Amount of water (%)	Spacing (nm)
a	10	8.5
b	15	10.3
c	20	10.5
d	40	13.7
e	50	15.4
f	60	17.6

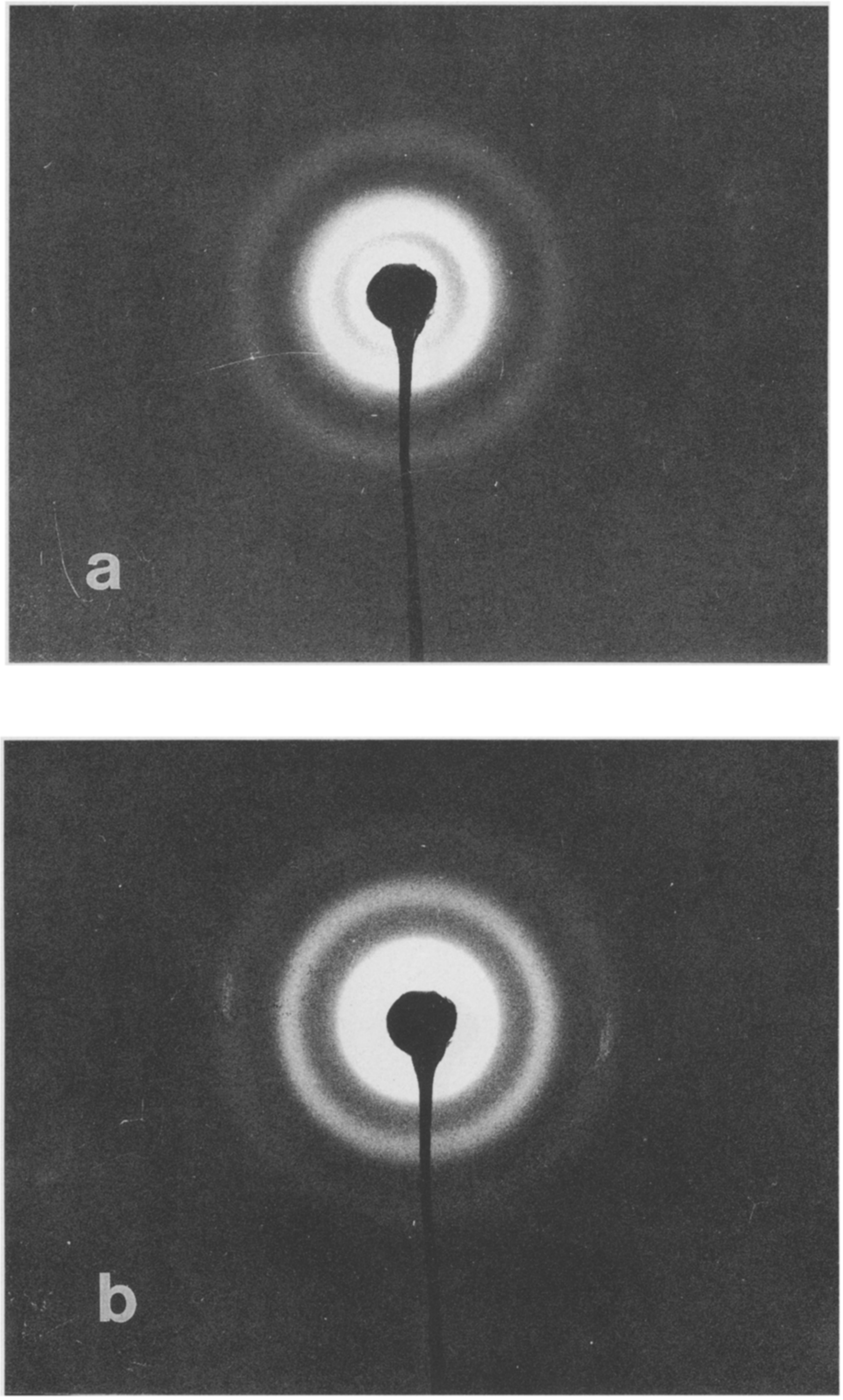

Fig. 5 (a,b).

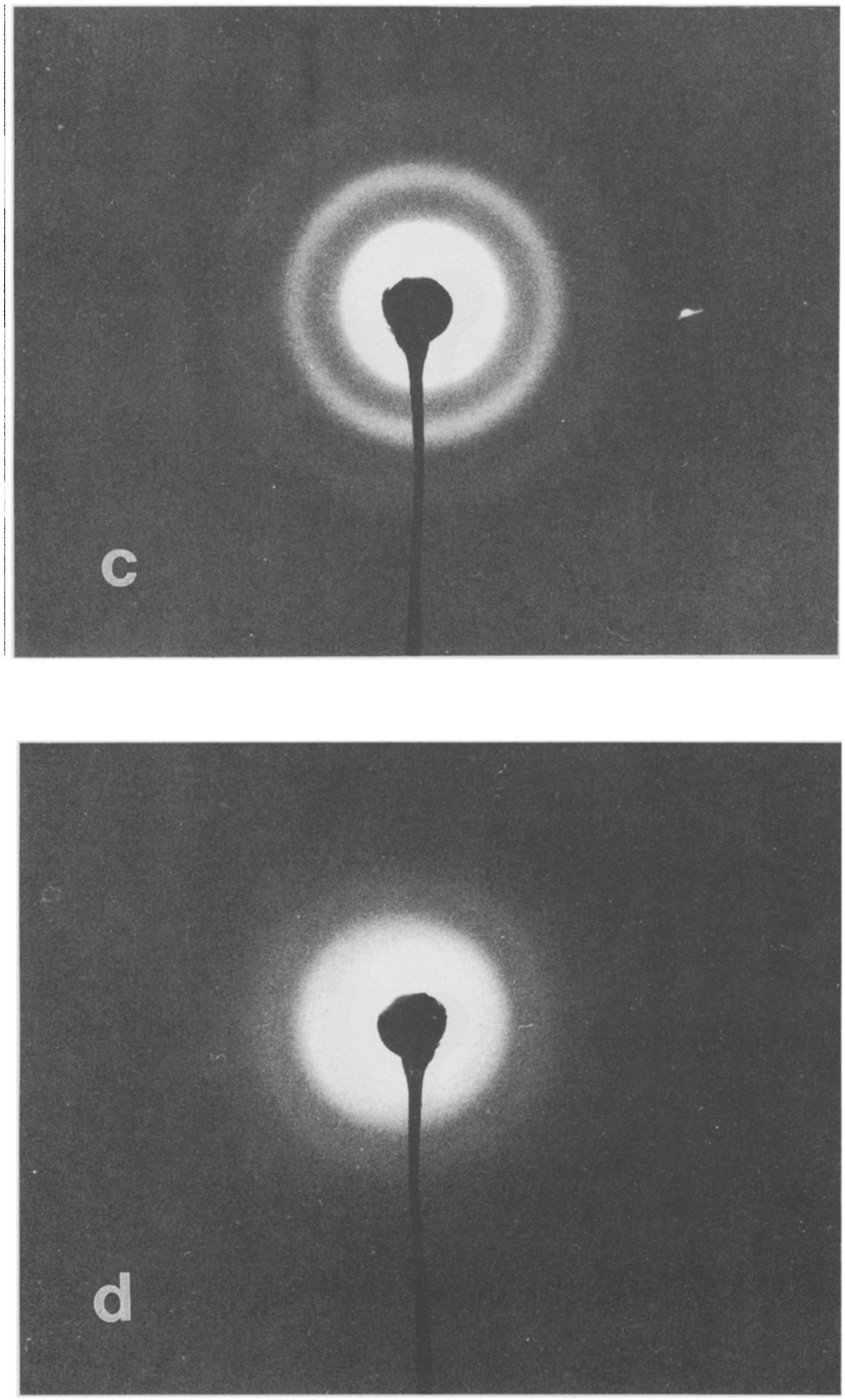

Fig. 5 (c,d).

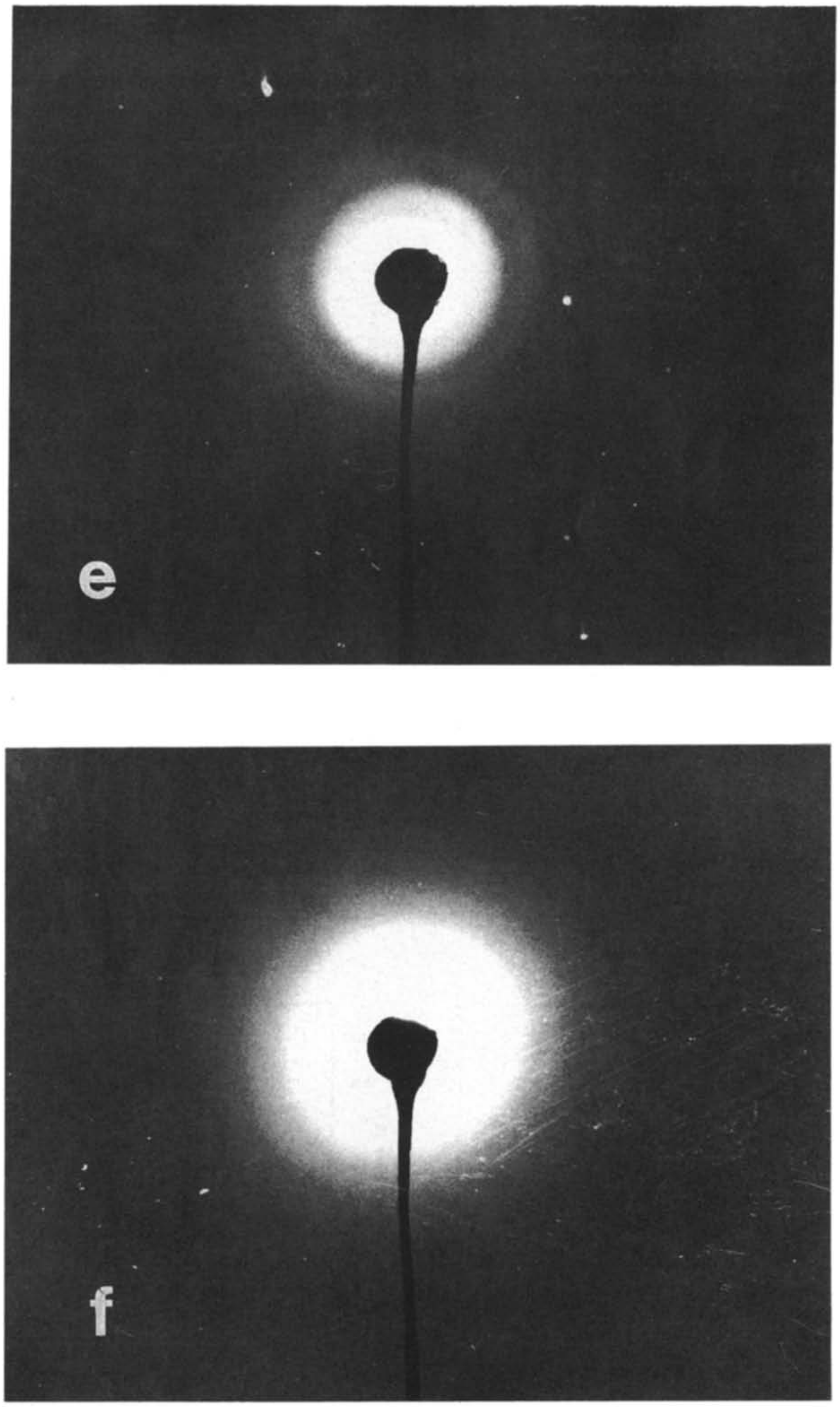

Fig. 5 (e,f).

8.5 to 17.6 nm (Fig. 5). This indicates an increase in the amount of water fixed between the lamellae formed by the amphiphilic molecules of sodium lauryl sulphate and cetostearyl alcohol and agrees well with previous findings (Junginger et al., 1979; Müller-Goyman and Frank, 1985; Bodde et al., 1986). A rough estimate suggests that the spacing of cetostearyl alcohol bilayers can be measured by

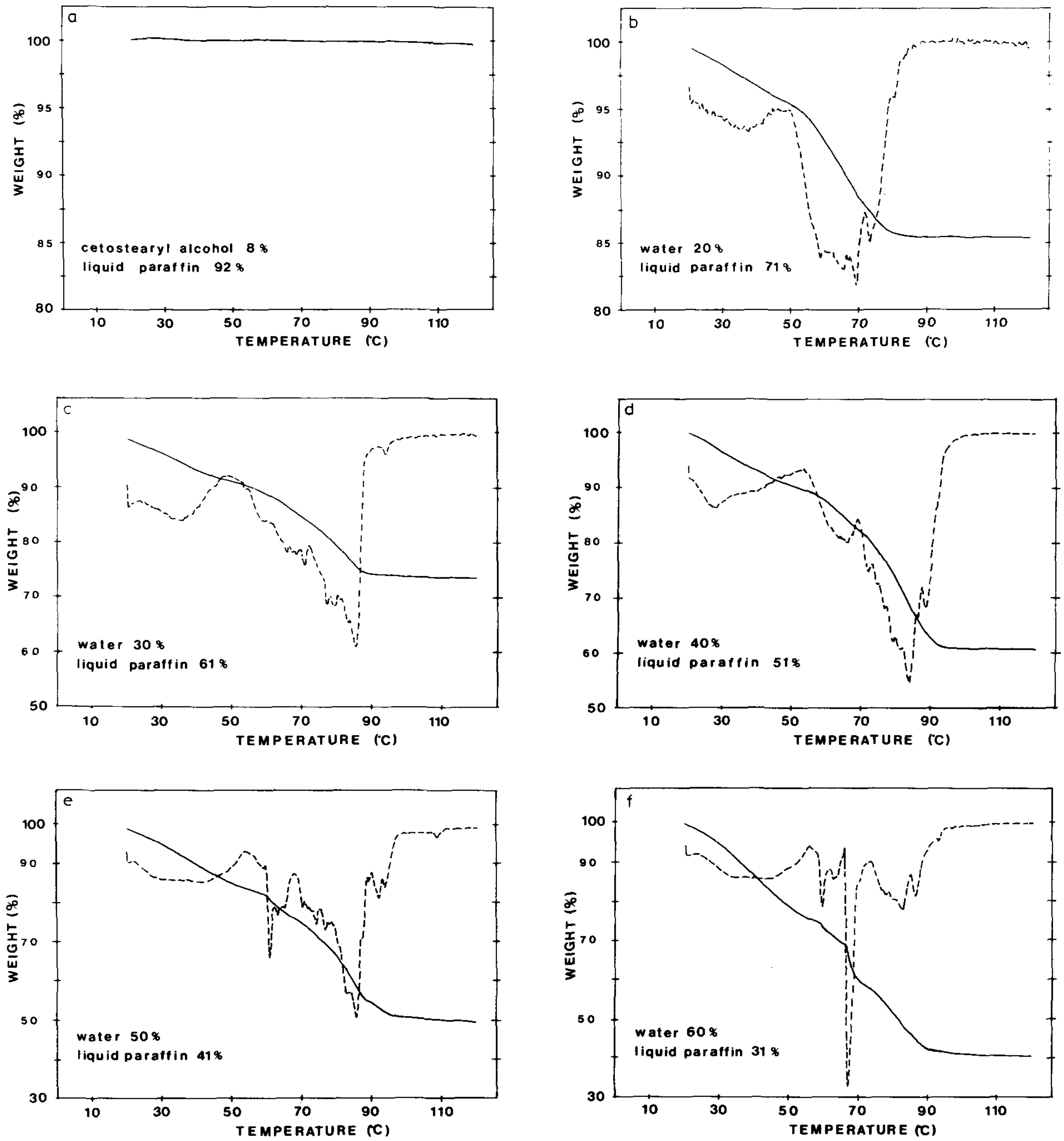

Fig. 6. Thermogravimetric curve measurements and their derivative curves for cream containing different amounts of water and of liquid paraffin (b–h). Thermogravimetric curve of the mixture of cetostearyl alcohol and liquid paraffin (a).

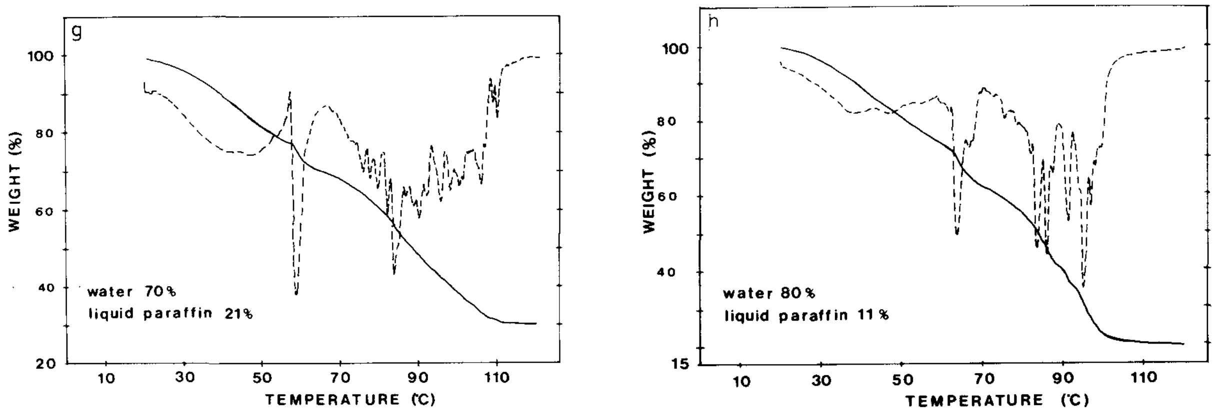

Fig. 6 (g,h).

extrapolation; when the interlamellar spacings are plotted according to the corresponding amounts of fixed water, the intercept with the ordinate is the spacing of cetostearyl alcohol bilayers. This estimate corresponds to the value for the cetostearyl alcohol molecule bilayers determined by De Vringer et al. (1984) . Above 60% water content, the lamellar structure could not be observed with SAXS.

Evaporation of water from the creams

According to the thermogravimetric curves and their derivative curves, no weight loss from melting of cetostearyl alcohol and liquid paraffin was found in the temperature range 20–110°C. From creams containing low percentages of water (i.e. 10–40%), the water evaporated in two stages, i.e. stages I and II (Fig. 6b–d, Table 2). The amounts of evaporated water in the different stages could be calculated from the areas under the thermogravimetric derivative curves. At temperatures below 50 °C the bulk water evaporated and thereafter the water fixed between the lamellae. Interestingly, changing the amount of water in the cream caused a third (stage III) evaporation, between the evaporation stages I and II; i.e. three separate stages of evaporation were found (Fig. 6e–h, Table 2). The third evaporation stage was observed to some extent already in the cream containing 40% water (Fig. 6d). This stage, however, was seen more clearly as the amount of water in the cream was increased. The amount of water evaporated in the temperature range 55–70 °C was about 7% of the total weight of the cream and remained at that level until the total amount of water in the cream was increased to 70%. With 80% water in the cream, the amount of water evaporated in this stage increased to 13%. With large amounts of water in the cream (70 or 80%), the water in stage II was bound loosely (Fig. 6g and h) and evaporated in pulses. The three stages,

TABLE 2

Weight loss (%) shown in thermogravimetric measurements of cetostearyl alcohol and liquid paraffin and creams containing different amounts of water (temperature range 20–110 °C) (accurately measured total amount of water in the cream is given in parentheses)

Amount of water in the sample (%)	Weight loss (%)		
	Stage I	Stage III	Stage II
0 0	–	–	–
20 (14.1)	4.2	–	9.9
30 (24.7)	7.7	–	17.0
40 (38.7)	10.2	7.1	21.4
50 (49.0)	15.4	7.9	25.7
60 (58.4)	23.8	7.0	27.6
70 (69.0)	22.3	8.0	38.7
80 (77.5)	24.7	13.0	39.8

however, were clearly observable. It has been suggested that the water in o/w creams may exist as free bulk water and fixed water in the liquid crystalline network around the oil droplets as well as in the liquid crystalline network in the bulk (Rowe and Bray, 1987). According to the results of our studies, the water in the creams evidently exists mainly as free bulk water and fixed water. With a large amount of water in the cream there is still another water phase, which is more tightly bound than the bulk water. It is, however, not organized like the fixed water between the lamellar structure of the amphiphile molecules; instead it is combined with the amphiphile molecules around the droplets of liquid paraffin. According to the thermogravimetric studies, evaporation of water from the cream seems to depend on the total water content of the cream; with low water content, the water exists mainly as fixed water and bulk water. When the water content of the cream is increased, water evaporates in three steps and is loosely bound. The loosely bound water in o/w creams may enhance the rate of release of the drug solubilized in the water phase. This may also explain the findings of a previous study (Niemi et al., 1989) in which the rate of release of hydrocortisone from similar o/w creams was decreased up to 60% water content in the cream but enhanced when the amount of water was higher than 60%.

Acknowledgement

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