

Colloid Science

A study of the gel structure in a nonionic O/W cream by differential scanning calorimetry^{*})

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Abstract: The structure of a simple O/W cream and its separate components were investigated by differential scanning calorimetry. The results obtained for cetylstearylalcohol agree with those cited in literature. The thermal behaviour of the component poly(oxyethylene)₂₀ glycerolmonostearate (= PGM₂₀) was also investigated. It is pointed out that the thermal history of the PGM₂₀ batch may play an important role in a study concerning the structure of this surfactant. To both components water was added to study the effects of hydration. Hydration affected the transition temperatures of either component. The melting enthalpy per unit mass of cetylstearylalcohol was not influenced, in contrast with the melting enthalpy of the hydrocarbon fraction in PGM₂₀/water mixtures. It is supposed that hydration induces a tilt of the hydrocarbon chains with respect to the lattice plane in lamellar PGM₂₀/water mixtures. Cooling experiments indicated that, in samples containing sufficient water, 2 water molecules were tightly bound to the polyoxyethylene chains of the surfactant. The properties of simple creams containing cetylstearylalcohol, PGM₂₀ and water can be explained regarding their structure and considering the behaviour of the separate components.

Key words: Gel structure, nonionic surfactant, DSC, O/W cream.

Introduction

Ointments and creams are frequently used as topical administration vehicles for drugs. In their simplest form creams consist of water, oil and surfactant. The colloidal structures in pharmaceutical creams, which are built up of these components, not only determine the viscoelastic properties, but certainly will affect the release of water and drugs as well. For this reason characterization of such structures in existing formulations is important. Even more valuable is an insight into the interactions which cause the formation of these structures. In order to predict incompatibilities for example this insight is an indispensable tool. Furthermore, it enables one to understand the influence of certain structures on the release of water and drugs as well as on the viscoelastic properties of preparations, which are important for their practical application. Finally,

the formulations can be modified to achieve vehicles with particular properties.

Because of the advantages of creams containing nonionic surfactants to creams in which ionic surfactants are worked up [1], we decided to investigate the structural elements and the properties of a nonionic cream: Unguentum Hydrophilicum Nonionicum Aquosum, DAC [2]. The composition of this particular O/W cream is:

| | |
|---|------------|
| – Poly(oxyethylene) ₂₀ glycerolmonostearate (= PGM ₂₀) | 5.0 % W/W |
| – Liquid paraffin | 7.5 % W/W |
| – Cetylalcohol | 5.0 % W/W |
| – Stearylalcohol | 5.0 % W/W |
| – Glycerol | 8.5 % W/W |
| – White soft paraffin | 17.5 % W/W |
| – Water | 51.5 % W/W |

It may be expected that mainly the amphiphilic components PGM₂₀, cetylalcohol and stearylalcohol are responsible for the construction of the colloidal

^{*}) Dedicated to Prof. Dr. Elsa Ullmann on the occasion of her 75th anniversary.

network. Therefore, we started with research on systems containing these components and water.

In our study the following experimental techniques were used: small angle X-ray diffraction (SAXD), wide angle X-ray diffraction (WAXD), differential scanning calorimetry (DSC), thermogravimetry (TG), polarization microscopy (PM), transmission electron microscopy (TEM) and nuclear magnetic resonance spectroscopy (NMR). Measurements in which several experimental techniques were used, were carried out on samples of the same batches simultaneously.

Some preliminary results, mainly obtained by SAXD, have been published earlier [1]. In a following series of papers we will present a more detailed report of our results obtained by the techniques mentioned above. Here, results obtained by DSC are discussed.

First PGM₂₀ and mixtures of cetylalcohol and stearylalcohol were investigated. After that, water was added to study the interactions between the amphiphilic components and water. Subsequently, mixtures containing PGM₂₀, cetylalcohol, stearylalcohol and water were studied.

To observe possible time dependent effects, samples of the same batches were studied periodically. Alterations in our samples due to ageing will be discussed in a following paper.

To study the interactions between the polyoxyethylene part of the PGM₂₀ molecule and water more precisely a series of mixtures of polyoxyethylene 1550 and water was investigated. The results of this latter study are discussed in Reference [3]; in this paper we mention the most important findings only.

Experimental

The components cetylalcohol (Lorol C16^R, Henkel KGaA, 90–95 % cetylalcohol), stearylalcohol (Lorol C18^R, Henkel KGaA, over 95 % stearylalcohol), cetylstearylalcohol (Lanette O^R, Caesar & Loretz, Alcohol Cetylstearyllicus DAB 8), and PGM₂₀ (Tagat S₂^R, Th. Goldschmidt AG) were used without further purification. The water used was demineralized.

First, the components were investigated separately. Next, we studied samples containing cetylalcohol, stearylalcohol and PGM₂₀ in the ratio 1 : 1 : 1 (W/W), corresponding to the ratio of these components in the DAC formulation, and water. The water concentration was varied between 0 and 90 % W/W and was determined by TG (Heraeus TGA 500 and Mettler TA 3000 system). The water loss found with TG was in good agreement with the amount of water used in preparing the samples (the maximum deviation was about 1 % of the sample weight). Cetylalcohol, stearylalcohol and PGM₂₀ were melted and stirred at 70 °C. Subsequently, water with a temperature of 70 °C was added and the mixture was cooled down

to room temperature under stirring. The samples were stored at room temperature in airtight glass containers. Samples containing only PGM₂₀ and water, or cetylalcohol, stearylalcohol and water were prepared and stored in the same way. Samples under investigation were 3 weeks old.

DSC measurements were carried out using the Mettler DSC 30 calorimeter (TA 3000 system). According to the ICTA agreements exothermal enthalpy changes are denoted with a positive sign.

Results and discussion

Mixtures of cetylalcohol and stearylalcohol

The polymorphism of cetylalcohol, stearylalcohol and their mixtures has been studied by Beer [4]. As in other multi-component systems the polymorphism is determined by composition and temperature. As shown by Beer [4] for the mixtures of cetylalcohol and stearylalcohol, the polymorphism can be affected substantially by impurities. The fatty alcohols we used in our study were probably not as pure as the alkanols Beer [4] used. The alkanols have been derived from natural oils and fats by transesterification and reduction. Therefore, they contained not only homologous compounds, but also small amounts of esters, fatty acids and unsaturated compounds. To examine the influence of these impurities on the polymorphic behaviour, we decided to investigate three mixtures of cetylalcohol and stearylalcohol. One of the mixtures contained equal weights of cetylalcohol and stearylalcohol. In the DAC ointment these components are present in this ratio also. The other mixtures contained excess amounts of either component (Table 1). Samples were cooled down from 25 °C to –150 °C (cooling rate 10 °C/min) and subsequently heated to 90 °C (heating rate 10 °C/min). The results were compared with the results obtained for Lanette O^R, which was treated in the same way (Table 1).

In all cases no pronounced heat effect was registered during cooling. During heating two endothermal effects were observed (Fig. 1). This agrees with the findings of Junginger et al. [5]. The low temperature peak denotes an enthalpy change due to the transition from the β_0 -modification to the α -modification [6]. For Lanette O^R this transition involves an enthalpy change of –86 J/g (Table 1). In both the α - and β_0 -modification the hydrocarbon chains are placed perpendicular to the lattice plane, forming bilayers (Fig. 2). The β_0 -modification has a nearly orthorhombic unit cell [6]. The α -modification is a plastic crystal in which the hydrocarbon chains are placed in a hexagonal array. The high temperature peak is due to the transition from the

Table 1. Polymorphic behaviour of cetylstearylalcohol

| Mixture | % W/W Lorol C16® | % W/W Lorol C18® | Transition temperatures and enthalpy changes | | | |
|------------|---------------------|---------------------|---|------------------|---------------------|------------------|
| | | | $\beta_0 - \alpha$ (°C) | ΔH (J/g) | α -Liq. (°C) | ΔH (J/g) |
| 1 | 33 | 67 | 34 | — | 52 | — |
| 2 | 50 | 50 | 31 | — | 50 | — |
| 3 | 67 | 33 | 31 | — | 49 | — |
| Lanette O® | — | — | 30 | -88 | 51 | -128 |
| Lanette O® | — | — | 31 | -84 | 51 | -128 |

α -modification to the liquid state and involves an enthalpy change of -128 J/g in the case of Lanette O^R (Table 1). No other transitions were observed.

From the results it can be concluded that the studied mixtures behave like mixtures of cetylalcohol and stearylalcohol of the same grade (over 99.5 %) Beer [4] used in his study. Apparently the impurities present in our batches of cetylalcohol and stearylalcohol do not affect the polymorphic behaviour in the studied composition range. This is an important conclusion for the application of these components in pharmaceutical ointments and creams.

Poly(oxyethylene)₂₀ glycerolmonostearate (PGM₂₀)

PGM₂₀ is an industrial product which contains about 3 % water. It has a molecular weight distribution, the hydrophilic chain can be branched and moreover, the glycerol part can be attached to different C-atoms in the oxyethylene chain. This is illustrated in Figure 3. Since the stearyl part of PGM₂₀ has been derived from natural fats and oils, the surfactant contains

some impurities comparable with those present in cetylalcohol and stearylalcohol. In Figure 4 A, a structure of PGM₂₀ is proposed. This structure is based on results derived by PM, WAXD and SAXD. PM and SAXD revealed that PGM₂₀ has a lamellar structure at 20 °C [1].

Samples of PGM₂₀ were cooled from 25 °C to -150 °C (cooling rate 10 °C/min) and subsequently heated to 80 °C (heating rate 10 °C/min). During cooling and heating several heat effects were observed. The reproducibility between samples of the same batch was good. A typical example of a heating curve is given in Figure 5. Above 31 °C the whole PGM₂₀ sample was molten and the heat flow had a constant value (not shown in Fig. 5). Just before the sample melted completely, an endothermal process was observed at 23 °C. At 25 °C the hydrocarbon chains, which melt at 31 °C, are in the crystalline state. At 20 °C part of the hydrophilic chains are in the liquid state, but also crystalline polyoxyethylene domains are present. At 20 °C PGM₂₀ can be considered as a gel, the liquid parts of the surfactant being held in a network of the crystalline hydrocarbon chains. On cooling down to low temperatures the pasty substance becomes brittle, due

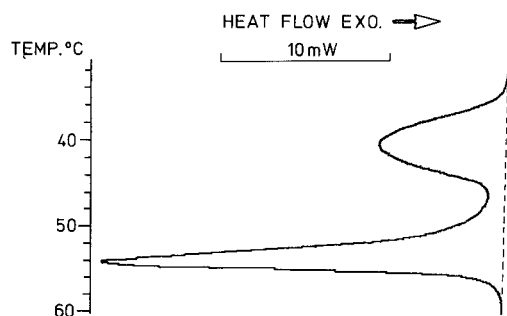


Fig. 1. DSC heating curve illustrating the polymorphic behaviour of cetylstearylalcohol. Heating rate 10 °C/min

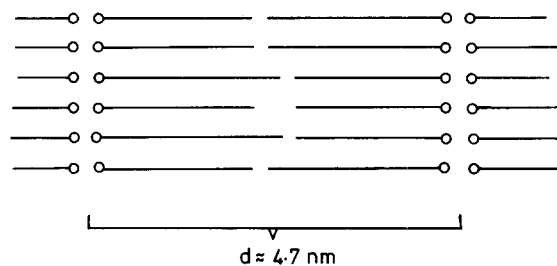


Fig. 2. Lamellar structure of a mixture containing equal weights of cetylalcohol and stearylalcohol: O = hydrophilic head; — = hydrocarbon tail

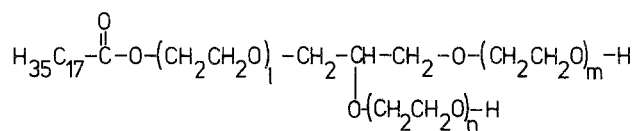


Fig. 3. Schematic representation of PGM_{20} : $l + m + n = z$; $z = 20$

to crystallization of the polyoxyethylene domains. Because the melting point of polyoxyethylene depends on its molecular weight and the polyoxyethylene domains of the surfactant have a broad molecular weight distribution (Fig. 3), the hydrophilic chains melt over a wide temperature range (Fig. 5). On heating, the last crystalline domains of the hydrophilic chains melt at 23 °C, a reasonable value compared with the melting points found for pure polyoxyethylenes with molecular weights of about 1000 [7–9]. That several peaks are observed in Figure 5 might be due not only to the fact that the PGM_{20} batch has a relatively broad molecular weight distribution, but also to the presence of impurities.

The thermal behaviour of PGM_{20} above 0 °C was further investigated to obtain values for the enthalpy changes at 23 °C and 31 °C. In order to acquire a better

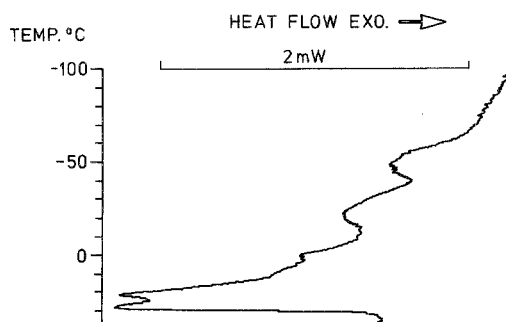
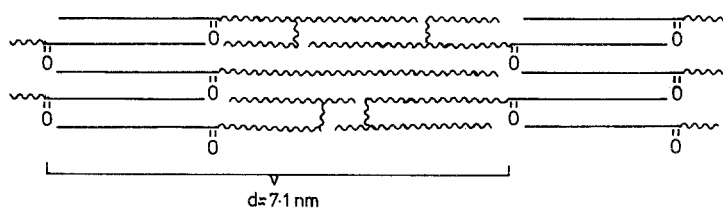
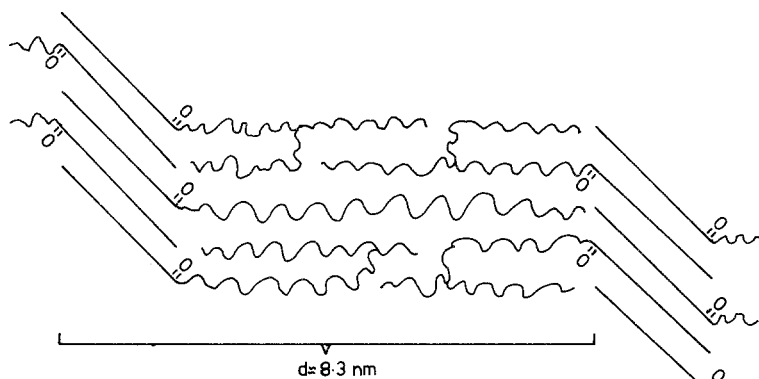


Fig. 5. DSC curve of PGM_{20} . Heating was started immediately after cooling to –150 °C. Heating rate 10 °C/min

separation of the peaks, the heating rate was reduced. Samples were stored at –10 °C for 4 weeks and then heated from –10 °C to 40 °C (heating rate 4 °C/min). An example of the heating curve is depicted in Figure 6. The endothermic process at 23 °C takes 12 J/g. The melting of the hydrocarbon chains at 31 °C absorbs 18 J/g. Due to overlap of the peaks these enthalpy changes cannot be estimated very accurately. However, the latter value agrees reasonably well with the melting enthalpy of cetylstearylalcohol (Table 1), considering that PGM_{20} contains about 20 % W/W hydrocarbon chains.



(A)



(B)

Fig. 4. (A) Lamellar structure of PGM_{20} (20 °C). (B) Lamellar structure of a mixture containing PGM_{20} and 37 % W/W water (20 °C)

~~~~~ = polyoxyethylene chain  
 ~~~~~ = hydrated polyoxyethylene chain  
 ————— = hydrocarbon chain

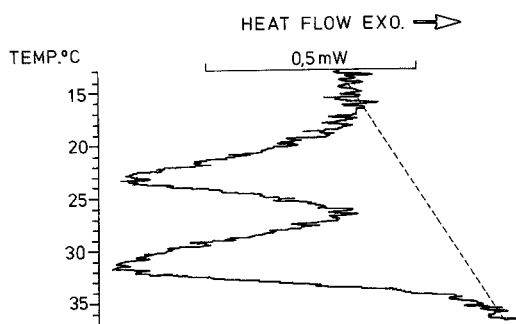


Fig. 6. DSC curve of PGM₂₀. Heated after storage at -10°C for 4 weeks. Heating rate $4^{\circ}\text{C}/\text{min}$

DSC measurements revealed that at room temperature (23°C) a transition takes place. WAXD experiments showed that if a molten sample is allowed to cool down to 20°C the sample solidifies, but the transition to the low temperature form is slow. Since samples are usually stored at ambient temperature, one should be careful in performing experiments without an accurate temperature control and sufficiently long adaptation time. To avoid adaptation problems PGM₂₀ samples were stored at -10°C prior to the experiments.

Mixtures of cetylalcohol, stearylalcohol and water

When sufficient water is added to liquid cetylstearylalcohol a solid hydrate will be formed on cooling [5]. X-ray diffraction revealed that an interlamellar water monolayer is formed between the hydrophilic alcohol groups. The addition of water affects the transition temperatures [5]: the β_0 to α transition temperature is lowered and the temperature at which the hydrocarbon chains change from the α to the liquid state increases. Further addition of water does not lead to swelling, but the excess of water is incorporated mechanically in the gel network and does not influence the transition temperatures.

We studied a mixture of cetylstearylalcohol containing 25 % W/W water to obtain values for the enthalpy change at the α to liquid transition of the hydrocarbon chains. The samples were heated from 5°C to 80°C (heating rate $5^{\circ}\text{C}/\text{min}$). The results are listed in Table 2. In the last column the calculated enthalpy changes per unit mass of dry cetylstearylalcohol are given. When these values are compared with the α to liquid enthalpy changes in Table 1, one may notice that the same value is found for cetylstearylalcohol in which no

Table 2. Melting enthalpy of hydrated cetylstearylalcohol

| Transition temperature ($^{\circ}\text{C}$) α -Liq. | % W/W Water | Enthalpy change $\Delta H(\text{J/g})$ of hydrated cetylst. alc. | calc. on dry cetylst. alc. |
|--|-------------|--|----------------------------|
| 56 | 25.1 | -96 | -128 |
| 56 | 26.2 | -95 | -128 |

water is incorporated. So, the interlamellar water monolayer has little or no effect on the melting enthalpy of the cetylstearylalcohol bilayers. However, the melting point is raised by 5°C . The increase of the melting point is probably an entropic effect. It is plausible that the molten hydrate is structured to a larger extent than molten anhydrous cetylstearylalcohol.

Mixtures of polyoxyethylene and water

The DSC experiments with which we studied a series of mixtures of polyoxyethylene 1550 and water are described in Reference [3]. In [3] we also extensively discuss the results of this study. Here only the most important findings are mentioned.

When aqueous solutions of polyoxyethylene are cooled down to temperatures well below 0°C , water crystallizes. However, a part of the water does not freeze. From the non-freezing water fraction in samples containing over 50 % W/W water, it is concluded that 2 water molecules per polymer unit do not participate in the formation of ice. The polymer hydrate forms an eutectic with water at 50 % W/W water. The crystallization of the hydrate is a slow process and is accelerated at low temperatures. The eutectic melts at -16°C . The heat of fusion of the hydrate is about 100 J/g .

Mixtures of PGM₂₀ and water

We studied the thermal behaviour of mixtures of PGM₂₀ and water. Mixtures containing up to 70 % W/W water were heated from 5°C to 90°C (heating rate $5^{\circ}\text{C}/\text{min}$). In the heat flow scans only one peak was detected. The heat effect was endothermic and appeared when the hydrated surfactant changed to the liquid state, that is when the hydrocarbon chains of the surfactant melted. The melting temperature of the polyoxyethylene chains was lowered by the addition of water. Therefore, melting of polyoxyethylene was not detected in the studied temperature range. This

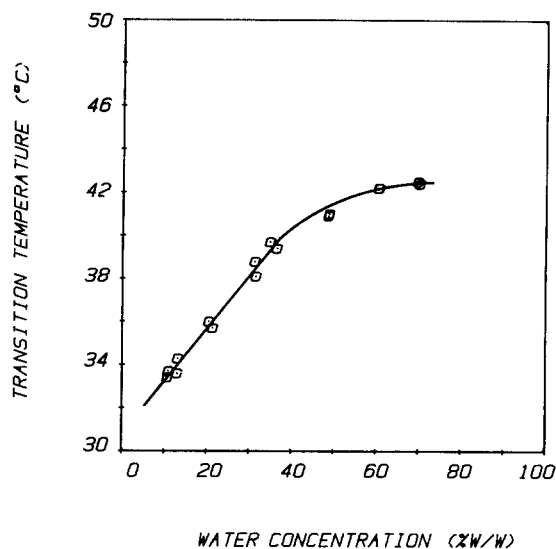


Fig. 7. Melting temperature of the alkyl chains in PGM₂₀/water mixtures plotted as a function of the water concentration

agrees with the findings of other authors [7, 10], who observed a decrease of the melting point of polyoxyethylene by addition of water.

In Figure 7 the transition temperatures are plotted as a function of the water concentration. Note that again, as with cetylstearylalcohol, hydration of the hydrophilic groups raises the melting point of the hydrocarbon chains. The maximum increase is about 11.5 °C.

Cooling the PGM₂₀/water mixtures to -60 °C showed that again 2 water molecules per oxyethylene unit are non-freezing water molecules. This agrees very well with the results obtained on mixtures of polyoxyethylene and water, where it was concluded that 2 water molecules per oxyethylene unit are tightly bound to the polymer chain at low temperatures [3]. If we now assume that at temperatures up to 50 °C this hydration number is still valid, the hydration water fraction in our PGM₂₀/water mixtures can be calculated. If we neglect the hydroxyl and carboxyl groups in the hydrophilic chains, the hydration of the surfactant should be completed at 37 % W/W water. From Figure 7 we see that the transition temperature rises directly proportional to the water concentration up to 37 % W/W water and levels off at higher water contents. This implies that above 37 % W/W water the transition temperature is still rising. This can mean that 2 water molecules are tightly bound to the oxyethylene unit, but that further addition of water still contributes to the hydration of the hydrophilic chains. This can explain

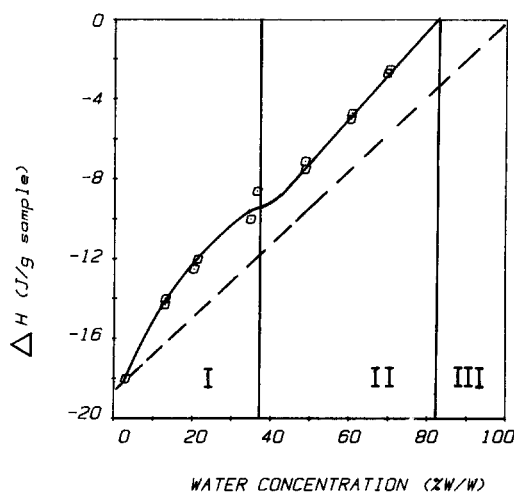


Fig. 8. Enthalpy changes at the melting point of the alkyl chains in PGM₂₀/water mixtures plotted as a function of the water concentration

why different experimental techniques yield different hydration numbers (see [3]).

In Figure 8 the enthalpy changes, connected with the melting of the hydrocarbon chains, are plotted as a function of the water concentration. The samples are divided in 3 regions. The classification is based on PM results. Samples containing 0 to ≈ 37 % W/W water (domain I) consist of a lamellar solid phase. In domain II (≈ 37 % to ≈ 82 % W/W water) a lamellar solid phase and an optically isotropic liquid phase coexist. The amount of liquid phase increases with increasing water concentration. Samples containing over 82 % W/W water (domain III) only consist of optically isotropic liquid.

The broken line in Figure 8 represents the theoretical enthalpy change assuming that the absolute value of the enthalpy change is directly proportional to the hydrocarbon concentration. The measured enthalpy changes obviously deviate from the broken line.

Let us now discuss the properties of the samples in the 3 domains in more detail. For samples up to 37 % W/W water the deviation is most probably due to an increasing tilt of the stearyl chains with respect to the lattice plane. This is illustrated in Figure 4B. The tilt is induced by hydration. Hydration increases the diameter of the hydrophilic chains. The polyoxyethylene chains are forced apart and the lipophilic/hydrophilic interface also increases. This leads to a shift of the stearyl chains with respect to each other and therefore, to a

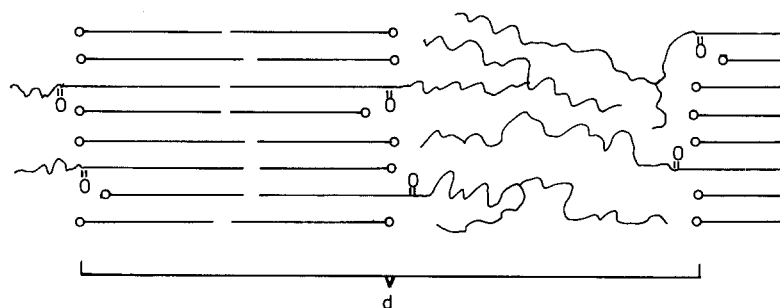



Fig. 9. Lamellar structure of a simple cream containing cetylstearyl alcohol, PGM₂₀ and water: ○ = hydrophilic head;  = hydrated polyoxyethylene chain; — = hydrocarbon chain

tilted structure. The proposed behaviour is supported by SAXD and WAXD results. This will be discussed in detail in a following paper.

It is calculated that at 37 % W/W water the tilt is about 40 degrees. This is probably the maximum tilt because further addition of water results in phase separation. A tilt of 40 degrees corresponds with a shift of the stearyl chains of 3 methylene groups. This should reduce the melting enthalpy per unit mass of hydrocarbon chains with 17 %. This value agrees very well with the DSC results.

In samples containing 37 to 82 % W/W water (domain II) a lamellar solid phase and an optically isotropic phase coexist. The liquid phase is probably a concentrated micellar solution. The formation of micelles is due to further hydration of the polyoxyethylene chains, which enlarges the volume of the hydrophilic groups once more and forces the stearyl chains further apart. The increase of the interface cannot be compensated by a further tilt of the hydrocarbon chains and therefore, the hydrocarbon chains get into the liquid state and the lamellar structure breaks down. Because the fraction of micellar solution increases with increasing water concentration and at 82 % W/W water only micellar solution is left, the measured enthalpy changes, calculated per unit mass of the total of hydrocarbon chains present in the sample, also decreases with increasing water content. The decrease of the crystalline fraction is supported by the findings of Dorset [11], who observed a disappearance of the wide angle X-ray reflections of the alkyl chain moiety on hydration of alkylethyleneoxides.

Extrapolation of a linear least squares fit through the data belonging to domain II to the $\Delta H = 0$ axis, yields a value of 82 % W/W water. This suggests that at 82 % W/W water only micellar solution is left and that the lamellar phase has dissolved completely. Further addition of water leads to dilution of the micellar solution

and possibly leads to alterations in the size and the shape of the micelles.

Mixtures of cetylalcohol, stearylalcohol, PGM₂₀ and water

We studied samples containing equal weight fractions of cetylalcohol, stearylalcohol and PGM₂₀. These components are also present in the DAC formulation in this particular ratio [2]. The water concentration is varied between 0 and 90 % W/W. Below 20 % W/W water the samples are solid-like [1]. Above 20 % W/W water the samples gradually become softer with increasing water concentration. Above 75 % W/W water phase separation is perceptible. In the range 20 to 75 % W/W water the samples can be considered as simple creams. In this range, the hydrocarbon part of the PGM₂₀ molecule is believed to form lipophilic bilayers together with the cetylalcohol and stearylalcohol molecules (Fig. 9). Hydrophilic layers consisting of the glycerolpolyoxyethylene chains, water and hydroxyl groups, alternate the lipophilic sheets.

The samples were heated from 25 °C to 80 °C (heating rate 5 °C/min). In Figure 10 a heat flow scan of a sample containing less than 1 % W/W water is shown. Endothermic peaks are observed at 32, 40 and 51 °C. The peak at 51 °C denotes the melting of cetylstearylalcohol. The other peaks belong to the β_0 - α transition of cetylstearylalcohol, to melting of mixed crystals of cetylstearylalcohol and PGM₂₀, and possibly to melting of separated PGM₂₀. The latter three processes overlap.

The heating curves of samples containing over 20 % W/W water show only one peak, at 59 °C. In Figure 11 the heat flow scan of a sample containing 42.1 % W/W water is given. The endothermic heat effect at 59 °C is due to the transition of the hydrocarbon chains in the lipophilic bilayers from the α -modification to the

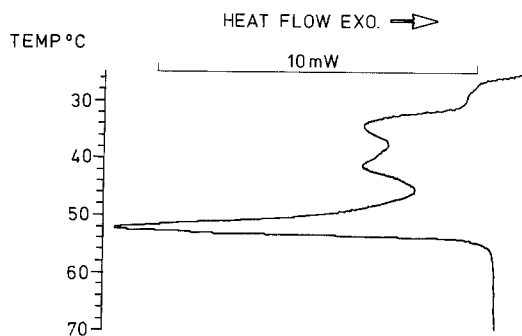


Fig. 10. DSC heating curve of a mixture containing cetylalcohol, stearylalcohol and PGM₂₀. Heating rate 5°C/min

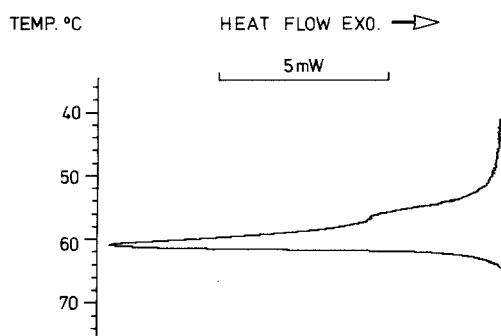


Fig. 11. DSC heating curve of a simple cream containing 42.1 % W/W water. Heating rate 5°C/min

liquid state. Notice the weak shoulder at the low temperature side of the peak. The shoulder is presumably connected with regions of hydrated cetylstearylalcohol in which no PGM₂₀ is incorporated (m.p. 56°C). We already noticed that as a result of hydration, the melting point of cetylstearylalcohol increases by 5°C to 56°C. The melting point of the hydrocarbon chains in PGM₂₀ is also raised due to hydration of its hydrophilic groups. A comparable effect is observed in this case. The melting point of the hydrocarbon chains in the lipophilic bilayers increases by 8°C to 59°C. The rise of the melting temperature has a value (8°C) between that of hydrated cetylstearylalcohol (5°C) and hydrated PGM₂₀ (11.5°C). This was expected from the structure of this lamellar system (Fig. 9).

In Figure 12 the enthalpy changes connected with the melting peak of the hydrocarbon sheets are plotted as a function of the water concentration. An extrapolated linear least squares fit intersects the ΔH -axis at -100 J/g. The calculated enthalpy change per unit mass of dry cetylstearylalcohol (including the stearyl chains of PGM₂₀) is -134 J/g. The latter value agrees with the values found for cetylstearylalcohol and hydrated cetylstearylalcohol (-128 J/g, Tables 1 and 2). Again we see that the melting point is raised, but the melting enthalpy is hardly affected by the hydrophilic layer between the lipophilic sheets. The extrapolated linear least squares fit intersects the composition axis at 100 % water, suggesting that the melting enthalpy of the hydrocarbon chains does not change by addition of water. This may be explained as follows: only 1 of about 11 alkyl chains in the lipophilic sheets belongs to a PGM₂₀ molecule, leaving plenty of space between the polyoxyethylene chains for hydration shells. Hence, in the simple cream the alkyl chains are not forced

apart due to hydration of the polyoxyethylene chains. So, addition of water does not influence the crystallinity of the hydrocarbon chains in these systems, in contrast with PGM₂₀/water mixtures, in which the crystallinity of the hydrocarbon chains is substantially affected.

Samples of the same batches are cooled down from 25°C to -60 °C (cooling rate 5°C/min). The cooling curves belonging to samples containing over 20 % W/W water show only one peak. The peak is exothermal and due to freezing up of the free water. In Figure 13 a cooling curve of a sample containing 50.1 % W/W water is presented. The sharpness of the peak is the result of supercooling of the free water below its depressed melting point, prior to crystallization.

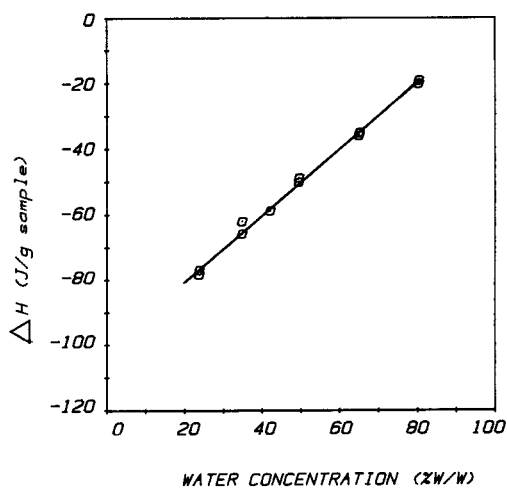


Fig. 12. Enthalpy changes at the melting temperature of the lipophilic sheets in a simple cream at various water concentrations

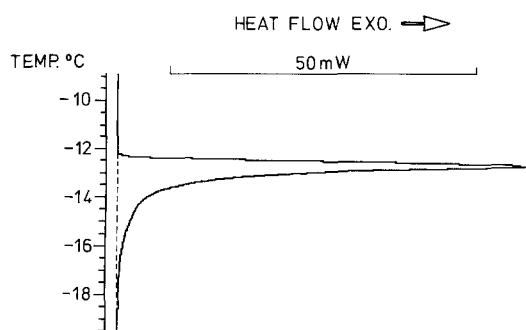


Fig. 13. DSC cooling curve of a simple cream containing 50.1% W/W water. Cooling rate 5 °C/min

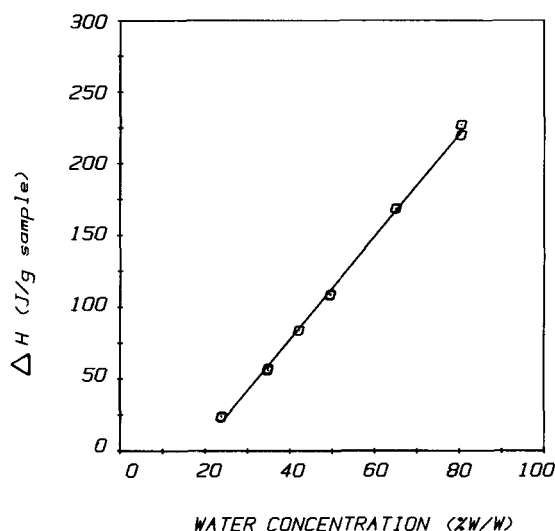


Fig. 14. Enthalpy changes due to freezing up of free water in a simple cream at various water concentrations

In Figure 14 the enthalpy changes due to freezing up of free water, estimated from the heat flow scans, are plotted as a function of the water concentration. An extrapolated linear least squares fit yields a value of 293 J/g at 100 % water. The heat of fusion of pure water at atmospheric pressure is 334 J/g. The observed deviation is the result of the heat of mixing, supercooling and melting point depression. The enthalpy corrections for these phenomena are discussed in [3].

The extrapolated linear least squares fit intersects the composition axis at 18.2 % W/W water. This value hardly changes when the measured enthalpy changes are corrected for the above mentioned phenomena. From the amount of polyoxyethylene present in our samples, it can be calculated that the intercept theoreti-

cally should be 17.5 % W/W water, if 2 water molecules per ether oxygen are tightly bound to the polyoxyethylene chains, as in polyoxyethylene/water mixtures [3] and in PGM₂₀/water mixtures. Therefore, the estimated intercept agrees very well with our assumption regarding the amount of tightly bound water.

It is interesting to notice that a study concerning drug release from these creams indicated that the fraction of water tightly bound to the polyoxyethylene chains does not contribute to the permeation of the extremely hydrophilic drug nicotinamide [12].

Conclusions

Small amounts of impurities normally present in technical grade cetylalcohol and stearylalcohol do not influence the polymorphic behaviour of mixtures of cetylalcohol and stearylalcohol in a wide composition range. On the other hand, addition of water lowers the β_0 to α transition temperature and raises the temperature at which the hydrocarbon chains change from the α to the liquid state; the melting enthalpy per unit mass of cetylstearylalcohol is not affected. Therefore, the increase of the melting point is probably an entropic effect.

When heating PGM₂₀ samples, a transition is detected at 23 °C. Therefore, the thermal history of PGM₂₀ samples may play an important role in studies performed at ambient temperature. Below 23 °C PGM₂₀ has a lamellar structure in which the hydrocarbon chains are in the solid state. Hydration increases the melting temperature of the hydrocarbon chains and induces a tilt of the hydrocarbon chains with respect to the lattice plain in solid lamellar PGM₂₀/water mixtures. Up to 37 % W/W water only a solid lamellar phase exists. The solid phase dissolves on further addition of water. Cooling experiments, performed with samples containing PGM₂₀ and over 37 % W/W water, show that 2 water molecules per oxyethylene unit are tightly bound to the hydrophilic chains. Heating experiments suggest that, at least at the melting temperature, additional water still contributes to the hydration of the surfactant.

Mixtures of cetylstearylalcohol, PGM₂₀ and 20 to 75 % W/W water can be regarded as simple creams with a lamellar structure. The properties of these creams (crystallinity of the hydrocarbon chains, melting enthalpy per unit mass of the hydrocarbon fraction, hydration effects, non-freezing water fraction) can be explained considering their structure and the behaviour of the separate components.

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