

Characterisation of the variation in the physical properties of commercial creams using thermogravimetric analysis and rheology

V.L. Peramal, S. Tamburic, D.Q.M. Craig *

Centre for Materials Science, School of Pharmacy, University of London, 29–39 Brunswick Square, London WC1N 1AX, UK

Received 7 February 1997; received in revised form 15 May 1997; accepted 21 May 1997

Abstract

A study was conducted to compare the physical properties of Aqueous Cream BP obtained from different manufacturers. The samples were studied using thermogravimetric analysis (TGA) and stress scan rheology as complimentary techniques. TGA studies showed two main peaks in the first derivative curves, corresponding to free and lamellar water. The profiles for creams obtained from different manufacturers showed marked variations between the samples, although the total water content was similar in all cases. Similarly, stress scans also showed marked differences between the creams, although no clear correlation between the thermogravimetric and rheological data was observed under the conditions used in the study. Three batches of cream from one manufacturer were then examined. Differences in the rheological properties were again observed, but less marked differences were seen in the TGA profiles. The study indicates that while the chemical composition of commercial aqueous cream may be controlled, considerable variations in the physical properties of these systems may be observed, both between different manufacturers and between batches from the same manufacturer. The implications of the poor correlation between stress scan rheological and thermogravimetric analysis data are discussed in terms of the use of these two methods in the quality control of creams. © 1997 Elsevier Science B.V.

Keywords: Cream; Emulsion; Rheology; Thermogravimetric analysis

1. Introduction

Pharmaceutical creams are semisolid emulsions which are widely used as a means of altering the

physical properties of the skin (particularly the hydration state) and as vehicles for the delivery of drugs. The structure of these creams has been the subject of considerable study, both for the purposes of optimising their physical properties (Eccleston, 1984) and understanding the mechanisms

* Corresponding author.

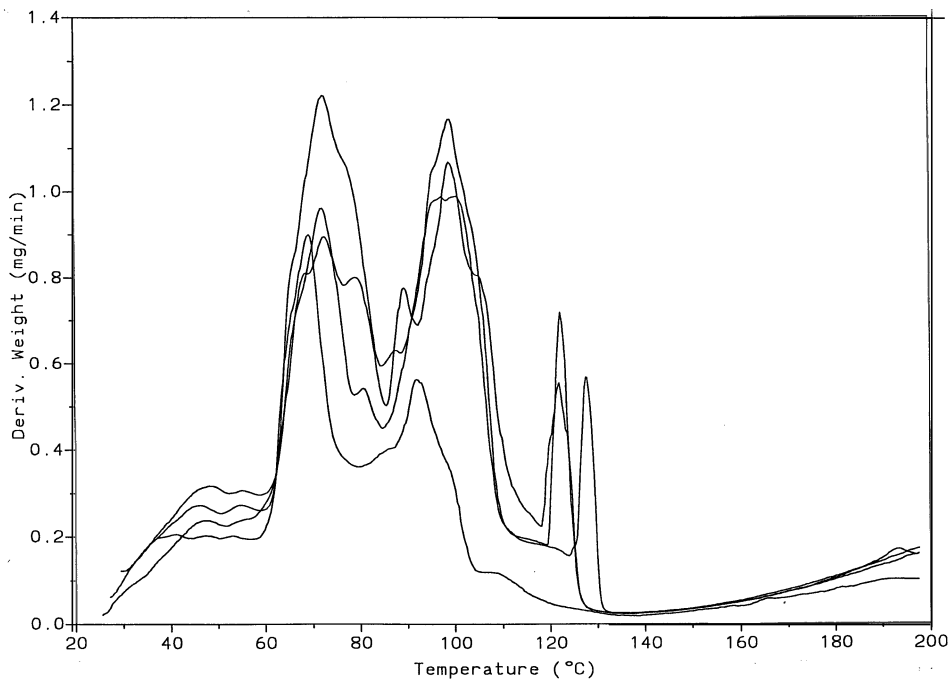


Fig. 1. Thermogravimetric analysis profiles of repeat samples taken from batch A.

by which drugs may be incorporated and released (Junginger et al., 1984; Mueller-Goyman and Frank, 1986). It has been proposed that o/w creams are composed of four phases; a hydrophilic gel phase composed of surfactant and fatty alcohol molecules with a layer of water arranged between lamellar structures, a bulk water phase, a lipophilic phase containing excess fatty alcohol in a hydrated state and a disperse phase (Eccleston, 1977, 1984; Junginger, 1984). It is interesting to note that despite the complexity, and hence variability, that may exist for these systems, the specifications for creams in, for example, the British Pharmacopoeia focus almost entirely on the chemical composition rather than the physical characteristics.

Clearly, the nature of the microstructure necessitates the development and use of a range of techniques which are capable of characterising these systems, both for enhancing the basic understanding of cream structure and to control the quality of the product. Methods that have been used to date include differential scanning

calorimetry (Eccleston, 1977; Junginger et al., 1984), thermogravimetry (Junginger, 1984; Rowe and Bray, 1987; Kallioninen et al., 1994, 1995), microscopy (Gstirner et al., 1969), reflectance measurements (Rowe and Patel, 1985), rheology (Barry, 1974), Raman spectroscopy (Louden et al., 1985), reflectance spectroscopy (Rowe and Patel, 1985) and dielectric analysis (Rowe et al., 1988; Goggin et al., 1994; Tamburic et al., 1996).

In this investigation, a range of proprietary Aqueous Cream BP samples were analysed using TGA and stress scan rheology in order to ascertain the extent to which the physical structure of these systems may vary between manufacturers and also between batches produced by the same manufacturer, as well as to compare two methods of cream characterisation. Stress scan rheology was chosen due to the widespread use of this method for the characterisation of creams, while TGA was used in order to investigate the water distribution within the system under study. It should be stated that the samples under study were simply purchased from community pharma-

cies, hence the age and storage conditions have not been controlled. However, the objective of the study was to investigate what variations, if any, a patient may experience on purchasing such a cream.

2. Materials and methods

Four batches of Aqueous Cream BP were obtained from different manufacturers (A–D), with a further two batches obtained from manufacturer D. The creams from the various manufacturers were similar in appearance, although the cream from A had a noticeably less firm consistency. All creams were used as received. TGA studies were conducted using a TA Instruments 2000 HiRes System. A purge gas of nitrogen was used throughout (0.25 barr) with a heating rate of 10°C/min (or, when stated, 20°C/min) from 20 to 200°C. A sample weight of 5–8 mg was used and each study was repeated three times. The data presented has been smoothed to a time interval value of 0.4 min. Rheological studies were conducted using a Carri-Med CSL 500 controlled stress rheometer (TA Instruments Ltd.), using cone and plate geometry. Stress scans up to 100 Pa were performed over a period of 2 min, followed by a decrease in applied stress over the same time interval. All studies were conducted at 25°C and were repeated five times. The coefficient of variation was found to be within 10% in all cases.

3. Results and discussion

3.1. Effect of experimental conditions on the TGA profiles of Aqueous Cream BP produced by manufacturer A

Before examining the profiles of the creams produced by different manufacturers, it was considered necessary to establish the effects of experimental variables on the data, notably the reproducibility of the profiles and the effects of scanning speed. Fig. 1 shows the first derivative TGA profiles for four repeat runs from Batch A

taken at random from the sample with a minimum of stirring. It can be seen from Fig. 1 that the general trends of weight loss are reasonably reproducible in terms of the presence of two loss peaks at approximately 70 and 100°C, although the magnitude values show variation. This variation may be a reflection of inhomogeneity within the creams or alternatively may be due to experimental factors such as loading of the sample, which is difficult to perform in a reproducible manner. It is interesting to note that one of the four profiles showed lower overall derivatives than the other three, indicating that the total water content was lower for this sample.

Fig. 2 shows the TGA traces for a batch of Aqueous Cream BP produced by manufacturer A, the profiles being run at 10 and 20°C/min. The traces show both the weight loss and first derivative curves. Junginger (1983, 1984) has stated that the two loss peaks correspond to bulk water and interlamellar water after melting of the hydrophilic gel phase, with the comparative areas under each peak corresponding to the ratio of the

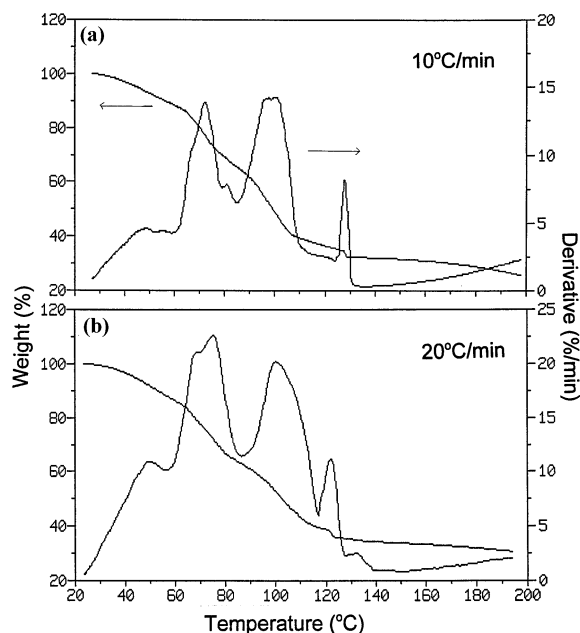


Fig. 2. Thermogravimetric analysis profiles of creams produced by manufacturer A performed at two scanning speeds, (a) 10°C/min, (b) 20°C/min.

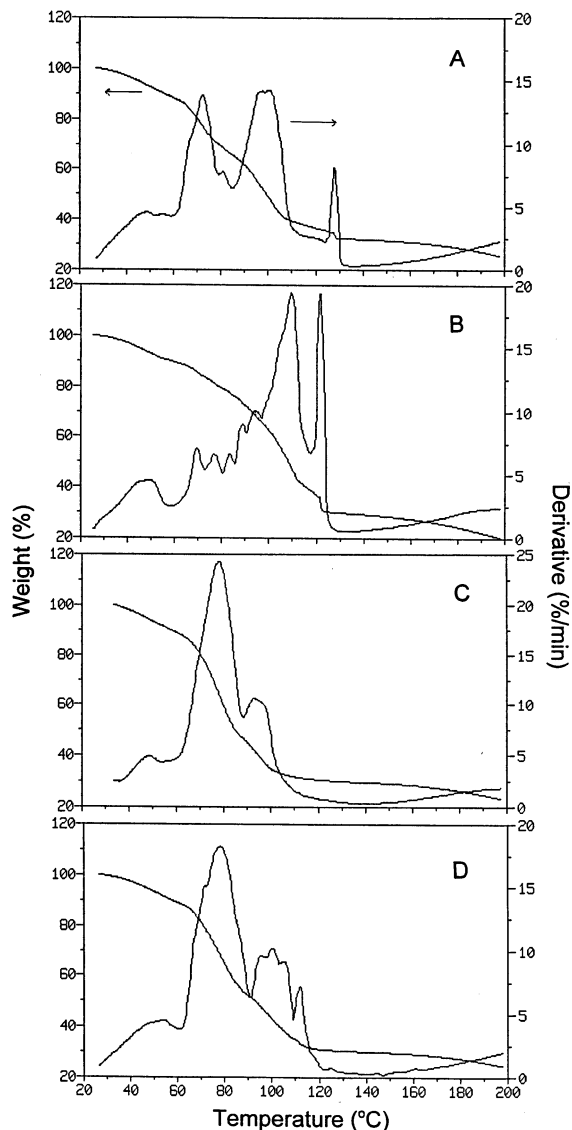


Fig. 3. Thermogravimetric analysis profiles of creams produced by manufacturers A–D performed at 10°C/min.

two water types. However, the analysis of the derivative areas (or direct measurement of weight loss) carries concomitant assumptions; in particular, the water may be in dynamic equilibrium between different states, while the invasive process of heating the sample will cause changes to the cream structure which will inevitably alter the temperature ranges over which water is released.

Both these considerations imply that the peak area analysis should be used as an indication of the water distribution rather than an absolute measurement. In addition, Rowe and Bray (1987) noted three peaks for cetostearyl alcohol cream systems, suggesting that the lowest and highest peaks corresponded to free and interlamellar water, although the origin of the second peak was less clear.

Examination of Fig. 2 indicates that in addition to the two main peaks, the curves show low (< 60°C) and high (> 120°C) temperature weight loss peaks in the first derivative curve. The low loss curve, corresponding to approximately 7–10% of the total weight (or 10–14% of the total water content) may correspond to free water which is able to diffuse to the surface at a faster rate than the evaporation process itself, hence the process represents free surface evaporation. The bulk water evaporation would then correspond to the rate limiting step being unbound water diffusing through the cream matrix, a process which would be limited by two phenomena. Firstly, the quantity of water in this state will be steadily decreasing, hence the rate of loss will decrease. Secondly, being a semi-solid system, the loss of water is likely to increase the viscoelastic moduli of the cream (below the melting of the lamellar phases), hence the diffusion will become slower as water loss takes place. This second consideration renders analysis of the kinetics of loss from these systems extremely difficult. The disruption of the lamellar phases will then result in a further water loss process. The final high temperature loss peak may be due to a number of mechanisms, either relating to residual water being strongly bound within the system or possibly a caking effect, whereby the residual water becomes physically entrapped within the dehydrated matrix. While not referring to such a well-defined water loss peak, Junginger (1984) suggested that high temperature loss processes may be due to water bound to the long chain alcohol as a semi-hydrate. Calculation of the molar ratios of water in this binding state compared to the cetostearyl alcohol content gives a value of approximately 10:1, which indicates that the weight loss is unlikely to correspond to water of hydration in this case.

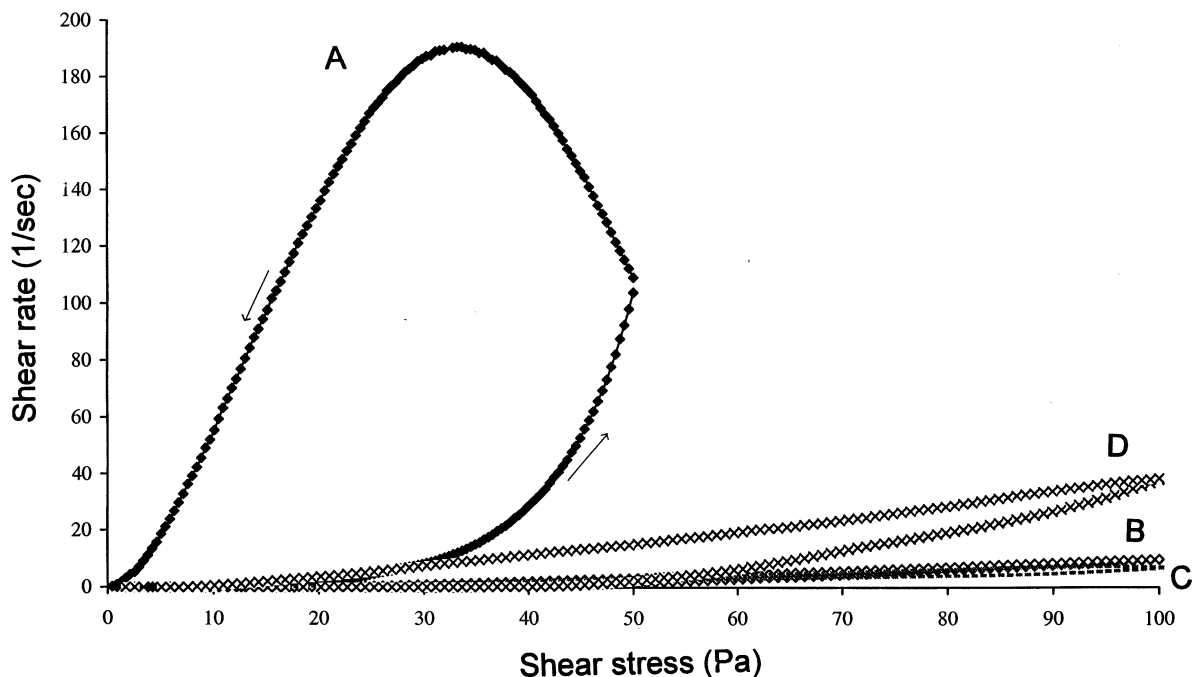


Fig. 4. Comparison of the rheological profiles of Aqueous Cream from manufacturers A–D.

By examining the effects of heating rate on the TGA profile, it is possible to delineate kinetic effects from phenomena which are a reflection of the equilibrium structure of the cream. Inspection of Fig. 2 indicates that while there are differences between the samples, the basic profiles remains similar, indicating that these profiles represent equilibrium rather than metastable structures. While one might expect surface water evaporation and caking effects (if indeed these are the responsible mechanisms) to alter with scanning rate, the proportion of water lost in these regions is small and hence, given the variability of the data, it is not possible to comment on their rate dependence.

3.2. Comparison of creams produced by manufacturers A–D

Batches of Aqueous Cream BP produced by manufacturers A–D were then tested using TGA and rheology, as shown in Figs. 3 and 4. Table 1 shows the percentage weight losses over four tem-

perature ranges; this method of presenting the numerical data has been selected as it allows direct comparison between samples while not necessitating the implied assumptions associated with integral measurements, as discussed earlier. It is, however, only semi-quantitative as the results will be influenced by the temperature range used; indeed, the coefficients of variation were in some cases greater than 20%, reflecting the difficulty associated with delineating the different peaks, i.e. a relatively small change in peak width or shape resulted in a large variation in the calcu-

Table 1

Percentage weight loss values over specified temperature ranges for creams A–D

Sample	Temperature range (°C)			
	24–60	60–85	85–115	115–135
A	9.53	26.25	27.81	3.99
B	8.85	13.38	27.70	12.02
C	9.35	43.65	12.03	<1
D	9.50	30.39	22.60	4.92

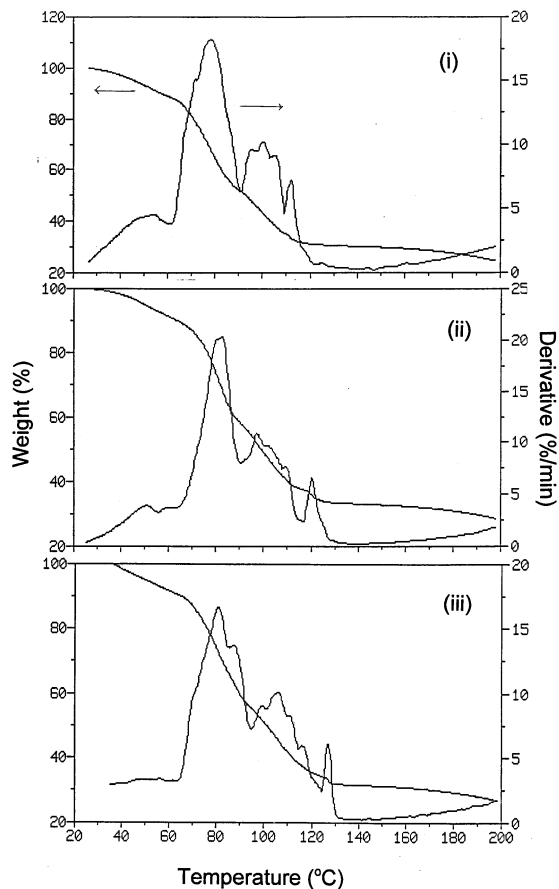


Fig. 5. Thermogravimetric analysis profiles of three batches of cream (i–iii) produced by manufacturer D performed at 10°C/min.

lated weight loss. It should be noted that the total % water losses over the temperature range under study are slightly lower than the expected figure of 69%, possibly due to evaporation on storage and measurement or residual water persisting at temperatures higher than those used in this study. It is, however, reasonable to assume that the observed losses correspond to the aqueous component of the system, although it is appreciated that loss of some volatile non-aqueous material is possible.

The TGA profiles, taken at 10°C/min, show considerable variations in the weight loss behaviour for creams obtained from the different manufacturers, over and above the variability of

the raw data. The levels of 'free surface' water between the four systems are similar in each case, while larger variations are seen in the bulk water fraction. In particular, cream B shows a lower proportion of water in this state while C and D show the highest. In the 85–115°C 'bound' region, cream C shows a lower proportion than the other three creams which yield similar values. The highest temperature fraction, however, shows a larger value for cream B, implying that this material shows the greatest tendency to 'cake' or entrap water on dehydration.

The rheological profiles of the four creams are shown in Fig. 4. The cream from manufacturer A gave lower overall viscosity values (seen by the higher values of shear rate at each shear stress) and the greatest hysteresis area. Interestingly, this batch showed a TGA loss profile which was intermediate within the observed range for the four systems. This implies that there is not a simple relationship between the water binding and the stress scan rheological behaviour. One might initially expect such a relationship to exist, as the lamellar structure is believed to be strongly associated with the viscoelastic properties of the creams. While the methodology used here only allows assessment of the viscosity of the systems, rather than the storage and loss moduli, the lack of correlation between the TGA data and the consistency of the creams, as assessed by the stress scans and visual observation, is nevertheless surprising. However, the TGA profiles reveal only the total amount of water in the lamellar and bulk states, hence there is still a great propensity for variation in, for example, lamellar distribution and rigidity within the system. In addition, factors such as the purity of the cetostearyl alcohol may have a profound effect on the rheology of the cream which may not necessarily be mirrored by a difference in the proportion of water in the bound and lamellar states.

3.3. Comparison of different batches of aqueous cream from manufacturer D

In order to gain an impression of whether the differences observed between the various creams is a result of interbatch, rather than intermanufac-

Table 2
Percentage weight loss values over specified temperature ranges for three batches of cream D

Sample	Temperature range (°C)			
	24–60	60–85	85–115	115–135
(i)	9.50	30.39	22.60	4.92
(ii)	8.31	29.17	26.84	4.39
(iii)	8.26	37.71	16.49	5.15

turer variation, two further batches of cream D were obtained and analysed under the same conditions as above. Fig. 5 shows the TGA profiles for the three batches, while Table 2 gives the weight losses over specific temperature ranges. The three profiles are relatively similar in each case. Examination of the rheological profiles (Fig. 6), however, indicates that batch (iii) shows a lower apparent viscosity than the other two, although the magnitude of this variation was not as great as was seen between the different manufacturers batches. Over and above the practical im-

lications of this observation, it also raises further questions regarding the relationship between the TGA profiles and the stress scan rheological behaviour.

4. Conclusions

The study has demonstrated that the physical properties of commercial creams may vary considerably, both in terms of water binding and viscosity, either as a result of different manufacturing procedures or interbatch variation. In addition, the study did not show a clear correlation between the viscosity, as measured by stress scans, and water binding, which is arguably surprising in view of the well established association between internal structuring and the rheological properties of these systems. However, this discrepancy does not in any way invalidate the use of TGA as a quality control tool for creams; indeed, the ability to make an assessment of the different binding states of water is extremely helpful in understand-

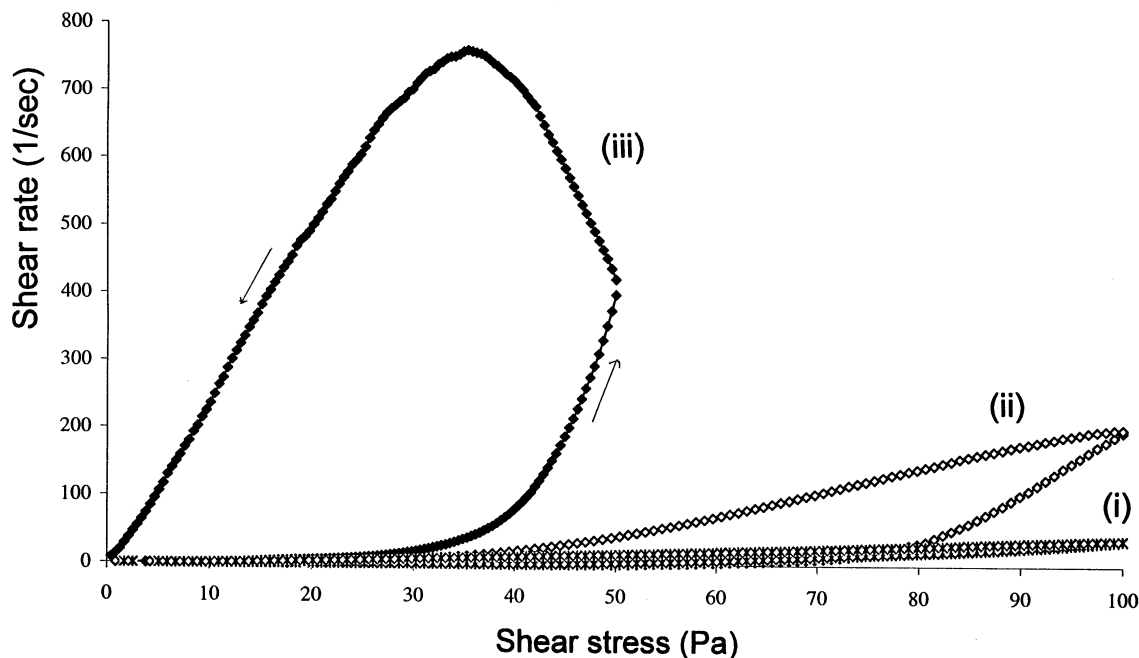


Fig. 6. Comparison of the rheological profiles of three batches (i–iii) of Aqueous Cream produced by manufacturer D.

ing the microstructure of cream systems. It is nevertheless of use to know the limits of the correlation between water binding and stress scan rheological performance for these systems.

Acknowledgements

The authors would like to thank the Wellcome Trust for financial support for Dr Tamburic.

References

- Barry, B.W., 1974. Rheology of pharmaceutical and cosmetic semisolids. In: Bean, H.S., Beckett, A.H., Carless, J.E. (Eds.), *Advances in Pharmaceutical Science*. Academic Press, London, pp. 1–72.
- Eccleston, G.M., 1977. Structure and rheology of cetomacrogol creams: the influence of alcohol chain length and homologue composition. *J. Pharm. Pharmacol.* 29, 157–162.
- Eccleston, G.M., 1984. Properties of fatty alcohol mixed emulsifiers and emulsifying waxes. In: Florence, A.T. (Ed.), *Materials Used in Pharmaceutical Formulation, Critical Reports on Applied Chemistry*, vol. 6. Blackwell, Oxford, pp. 125–156.
- Goggin, P., Craig, D.Q.M., Gregory, D., 1994. Emulsion production monitoring by dielectric spectroscopy. *Pharm. Res.* 11, S244.
- Gstirner, F.D., Kotttemberg, D., Maas, A., 1969. Gel structure of hydrous emulsifying ointment. *Arch. Pharm.* 302, 340–353.
- Junginger, H.E., 1983. Hydrophile Gelstrukturen in O/W Cremes. *Dtsch. Apoth. Ztg.* 133, 1988–1992.
- Junginger, H.E., Akkermans, A.A.M.D., Heering, W., 1984. Ratio of interlamellarly fixed water to bulk water in O/W creams. *J. Soc. Cosmet. Chem.* 35, 45–57.
- Junginger, H.E., 1984. Colloidal structure of O/W creams. *Pharm. Weekblad Sci. Ed.* 6, 141–149.
- Kallioninen, S., Helenius, K., Yliruusi, J., 1994. Physical characteristics of some emulsion creams in which the length of ethylene oxide chain of emulsifier varies. *Pharmazie* 49, 750–756.
- Kallioninen, S., Helenius, K., Yliruusi, J., 1995. Structure of non-ionic emulsion creams studied by thermoanalytical methods. *Pharmazie* 50, 478.
- Louden, J.D., Patel, H.K., Rowe, R.C., 1985. A preliminary examination of the structure of gels and emulsions containing cetostearyl alcohol and cetrimide using laser Raman spectroscopy. *Int. J. Pharm. Sci.* 25, 179–190.
- Mueller-Goyman, C.C., Frank, S.G., 1986. Interaction of lidocaine and lidocaine-HCl with the liquid crystal structure of topical preparations. *Int. J. Pharm.* 29, 147–159.
- Rowe, R.C., Bray, D., 1987. Water distribution in creams prepared using cetostearyl alcohol and cetrimide. *J. Pharm. Pharmacol.* 39, 642–643.
- Rowe, R.C., Dissado, L.A., Zaidi, S.H., Hill, R.M., 1988. The characterisation of heterogeneous gels by a dielectric technique: 2. Formulation and structural considerations. *J. Colloid Interface Sci.* 122, 354–366.
- Rowe, R.C., Patel, H.K., 1985. Reflectance measurements on gels and emulsions containing cetrimide and cetostearyl alcohol: a preliminary investigation. *J. Pharm. Pharmacol.* 37, 222–225.
- Tamburic, S., Craig, D.Q.M., Vuleta, G., Milic, J., 1996. A comparison of electrical and rheological techniques for the characterisation of creams. *Int. J. Pharm.* 137, 243–248.