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STUDY OF THE MICROSTRUCTURE OF OIL/WATER CREAMS WITH THERMAL AND RHEOLOGICAL METHODS

M. Kónya[1], *M. Sorrenti*[2], *F. Ferrari*[2], *S. Rossi*[2], *I. Csóka*[1], *C. Caramella*[2], *G. Bettinetti*[2] *and I. Erős*[1*]

[1]University of Szeged, Department of Pharmaceutical Technology, H-6720 Szeged, Eötvös u. 6., Hungary
[2]Department of Pharmaceutical Chemistry, University of Pavia, Italy

Abstract

Thermogravimetric and rheological investigations of oil/water (o/w) creams prepared with different types of surface-active agents (non-ionic, non-ionic POE-free, ionic) were carried out. Thermogravimetry was aimed at the indirect study of the water bond mechanism in o/w creams and the influence of the composition, type and concentration of the mixed emulsifier on the binding of water incorporated in the structure (interlamellar, bulk) and on the binding proportions. The microstructural changes during application were studied with respect to the stability of the lamellar bilayer.

Keywords: creams, interlamellarly fixed water, mixed emulsifier, thermogravimetry

Introduction

The o/w creams are widely used in pharmacy and cosmetics for their therapeutic properties and as vehicles to deliver drugs and cosmetic agents to the skin. The formulator must design a dermatological product which has good physical and chemical stability, an attractive appearance and also provides an appropriate carrier system for the active agent. The system must be non-irritant to the skin, easily applied and removed from the skin. Thus, many formulations are complex, multi-component preparations containing a number of emulsifiers, polymers and other additives. The most important and at the same time the most contradictory group of additives are the surfactants.

An understanding of the surfactants, the effect elicited by them and the microstructure of such systems are essential in order to optimize the formulation and manufacture of existing products and in the design of new dermatological delivery systems [1].

The o/w type creams stabilised with mixed emulsifier are at least four-phase systems (Fig. 1), which phases are the following:

- crystalline/hydrophilic gel phase, composed of bilayers of surfactant and fatty amphiphile [2]. Water molecules are inserted between the bilayers, thus forming interlamellar water layer.

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* Author for correspondence: E-mail: eros@pharma.szote.u-szeged.hu

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- bulk water layer. Water molecules bound as bulk water are in equilibrium with the interlamellarly fixed water in the gel phase. Both phases form the continuous (external) phase of the system. It is assumed that interlamellarly fixed water molecules exhibit different physicochemical and biopharmaceutical properties than those of the bulk water phase [3].
- lipophilic gel phase. The excess of the fatty amphiphile, which is not part of the hydrophilic gel phase, builds up a matrix with lipophilic character.
- dispersed oil phase. This inner phase is mainly immobilized mechanically from the lipophilic gel phase [4].

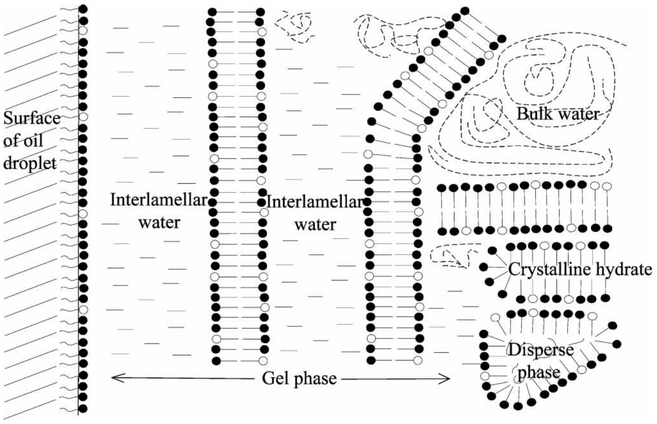

Fig. 1 Typical structure of o/w creams

The TG and DTG curves obtained from the thermogravimetric measurements are very informative in the examination of the above-described cream structure. The shape of the curves gives important information about the binding method of the incorporated water. The presence of the interlamellarly fixed water is indicated by further peak in the DTG curve, and by the inflection point of the TG curve. The ratio of the interlamellarly fixed water and bulk water can be calculated from the AUC of the DTG curve or by mass loss using the point of inflection of the TG curve [5, 6].

Thermoanalytical methods are becoming more and more widespread in pharmacy, especially in the case of solid dosage forms. These examination methods are less common in the case of semisolid preparations, creams.

The number of emulsifiers has considerably increased recently. The use of thermogravimetry may help to select the emulsifier which suits the application purpose the best, and also to get to know the structure of the o/w cream prepared with the given emulsifier. It becomes possible to determine the mechanism of water binding and the quantitative proportions of water bound in different ways (interlamellarly fixed water, bulk water), and also to monitor the changes occurring during storage. Results of thermogravimetric investigations reflect changes of structure and confirm the changes of rheological indices observed during storage. The joint use of thermogravimetry and rheology also makes it possible to model the microstructural changes during application.

The purpose of this article is to present the role of thermogravimetry in examining various types of emulsifiers and the structure of o/w creams prepared with them according to the above-mentioned viewpoints.

Experimental

Materials

Non-ionic and ionic surfactants combined with fatty amphiphilic moiety were used as mixed emulsifiers.

Non-ionic polyoxyethylene (POE)-free surfactants used: Tegin (glyceryl stearate SE – Goldschmidt AG), Tego Care PS (methyl glucose sesquistearate – Goldschmidt AG), Tego Care 450 (polyglyceryl-3-methylglucose distearate – Goldschmidt AG).

Non-ionic POE-type surfactant: Tween20 (polyoxyethylene (20) sorbitan monolaurate). Ionic type surfactants: Eucarol AGE/EC (alkylpolyglucoside citrate – Cesalpinia Chemicals, Lamberti Spa.), Eucarol AGE/ET (alkylpolyglucoside tartrate – Cesalpinia Chemicals, Lamberti Spa.).

The fatty amphiphile was cetostearyl alcohol, following concentrations were employed: 2% surfactant, 8% fatty alcohol; 3% surfactant, 12% fatty alcohol; 4% surfactant, 16% fatty alcohol. The lipophilic phase of creams was isopropyl myristate.

Methyl-parahydroxy benzoate (0.08 mass/mass%) and propyl-parahydroxy benzoate (0.02 mass/mass%) served as microbiological preservatives.

The 60 mass/mass% of the cream was represented by distilled water.

Cetostearyl alcohol, isopropyl myristate, methyl-parahydroxy benzoate, propyl-parahydroxy benzoate and distilled water were of Ph. Eur. 4. degree.

Methods

The creams were subjected to rheological and thermal tests. Measurements were performed 1 day, 2, 4 and 8 weeks after preparation.

TG measurements

Thermogravimetric measurements were performed with a Mettler TG50 thermobalance (Mettler Toledo, Switzerland) and with a Derivatograph-C (MOM, Hungary) simultaneous device [7–9]. From the different heating rates used (1, 5, 10°C min^{-1}), the +5°C min^{-1} one was chosen, temperature was increased from +25 to 150°C. The mass of samples were 2–5 mg, and 50±0.5 mg, depending on the device used. Each analysis was done at least twice.

Rheological measurements

A Bohlin CS Rheometer (Bohlin Inst. Div., Metrics Group Ltd., United Kingdom), and Haake RS1 Rheometer (ThermoHaake, Germany) were used to measure the rheological properties of creams. Rotational and oscillational measurements were performed. The temperature of the sample was 25.0±0.1°C. The tests were done at least in triplicate.

Results

Influencing effect of mixed emulsifier

The proportion of the above-described phases in coherent emulsion depends on the composition of the so-called mixed emulsifier. Mixed emulsifier is frequently used in o/w systems, it is the combination of an ionic or non-ionic surfactant with fatty amphiphiles such as fatty alcohols, acids or monoglycerides. The proportion of the emulsifier and the amphiphile usually varies between 1:2 and 1:20 [10]. Phase separation processes can be eliminated by their use, and they provide good stability for the product. Therefore by choosing the proper ratio of these additives, the water bound mechanism and consequently the structure of the external phase can be modified. The influence of the composition is presented by DTG curves in order to visualise this phenomenon better (Fig. 2.). It can be seen that the quantity of interlamellarly fixed water decreases and that of bulk water increases with the increase of the proportion of the amphiphile.

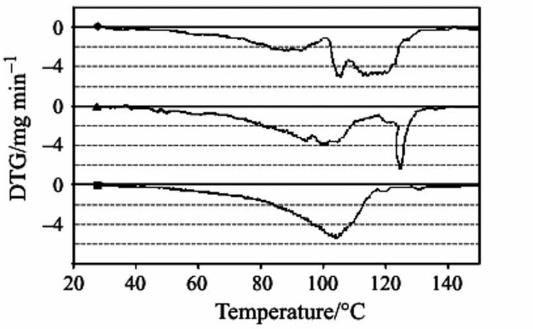

Fig. 2 Influence of the composition of mixed emulsifier, DTG curves of creams prepared with Eucarol AGE/EC, the ratio of surfactant and amphiphile 1:4, 1:6, 1:12

However, the phase ratios and the final consistency of the system are influenced not only by the composition of the mixed emulsifier but also by its quantity. As the quantity of the mixed emulsifier increases, the amount of the water inserted between the bilayers increases at the expense of bulk water. Figure 3a and b show how the distribution of the incorporated water changes in the structure, in the case of an emulsifier content of 2 and 3%. While with 2%, only bulk water is present in the system, but increasing it to 3% water is incorporated among the bilayers, too.

Microstructural change during storage

Non-ionic, POE-containing emulsifier

The thermogravimetric results of creams prepared with mixed emulsifier containing non-ionic polyoxyethylene-chain surfactant clearly showed the changes in the manner of water binding during storage, as well as the relationship between the structural change and the composition. This is presented in Fig. 4a, b in the case of samples prepared with

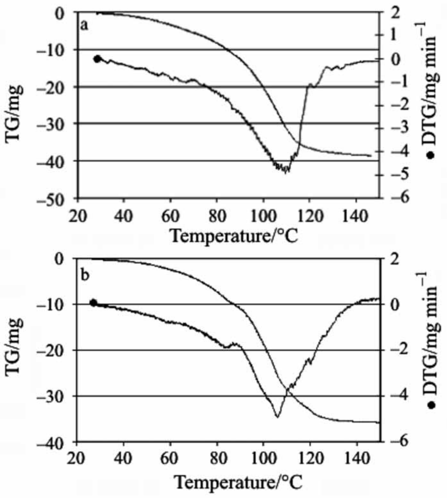

Fig. 3 Influence of the quantity of mixed emulsifier, TG and DTG curves (●) of creams prepared with Eucarol AGE/EC; a – 2 mass/mass% and b – 3 mass/mass%

Tween 20. One day after preparation no inflection point was observed in the TG-curve and only one peak was observed in the DTG curve between 25 and 90°C. However, after the 4th week an inflection point at approximately 85°C and a second peak appeared which showed the presence of interlamellarly fixed water between 85 and 120°C. The quantitative proportion of water fixed in the structure in various ways can be calculated from the mass loss, shown in Table 1. The characteristic increase of interlamellarly fixed water at the expense of bulk water can be observed during 2 months storage.

This phenomenon can be explained by considering the mechanism by which the non-ionic gel phase forms. In the case of a cream prepared with a non-ionic, POE-chain-

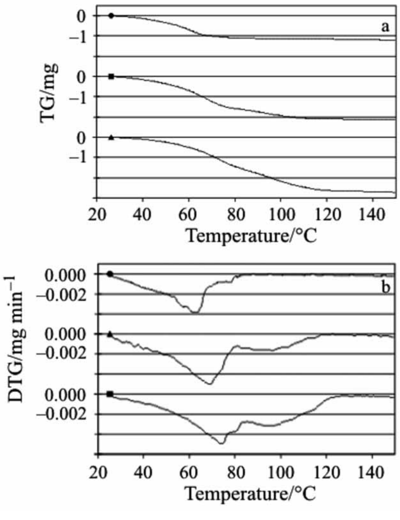

Fig. 4 a – TG curves and b – DTG curves of cream prepared with Tween 20 2 mass/mass%, after preparation, after 4 weeks, after 8 weeks

containing emulsifier a major change takes place in consistency after preparation. The reason for this is the slow hydration of the POE-chains at the high temperature of preparation, thus the gel phase is only formed partially when the coherent emulsion is cooled. On storage, the increased solubility of POE-chains permits additional gel phase to form, although this is now very slow because of the crystalline nature of the chains. As hydration proceeds and gel phase forms, the consistency of the system is increased [11, 12].

Table 1 Quantity of bulk water and interlamellarly fixed water in creams based on non-ionic POE-type emulsifier (Tween 20, 2 mass/mass%), (mean values, *SD*, *n*=3)

Mechanism of water binding	TG/%					
	1st day		4th week		8th week	
	Mean value	*SD*	Mean value	*SD*	Mean value	*SD*
Bulk water	58.11	3.2	44.25	0.24	37.61	0.78
Interlamellarly fixed water	–	–	14.15	0.56	24.09	0.82

Non-ionic emulsifier without POE-chain

The TG results of creams prepared with POE-free non-ionic emulsifiers invariably showed that water is bound only as bulk water. No changes were observed in the course of the curves (Fig. 5) or in the mass decrease data during the entire period of investigation. In each case 60% of the examined quantity was removed from the system until 120°C corresponding to the incorporated water amount.

This phenomenon is caused by the factors forming and influencing the structure, as there are no hydrated POE-chains in the composition.

Ionic emulsifier

The thermogravimetric curves of creams formulated with ionic mixed emulsifier clearly revealed that the gel structure was formed right after the first day, water was present in interlamellar form and as bulk water. It can be seen from Fig. 6 that the mass loss took place in two stages at approximately 80 and 110°C.

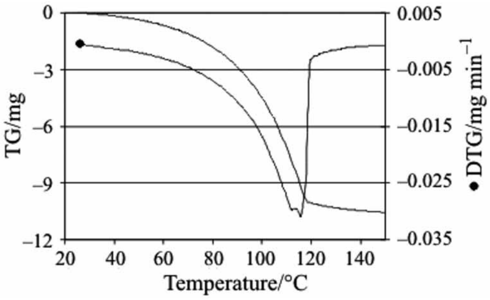

Fig. 5 Typical TG and DTG curve of creams prepared with non-ionic POE-free emulsifier (Tego Care PS)

The proportion of the two types of water did not change decisively during 2 months storage. This is explained by the fact that the coherent emulsions prepared with ionic emulsifier reach their final consistencies within a few hours. Electrostatic hydration is rapid both above and below the gel-liquid crystalline transition temperature. Thus the phase equilibrium is formed soon after preparation, and microstructural changes are negligible during storage [13].

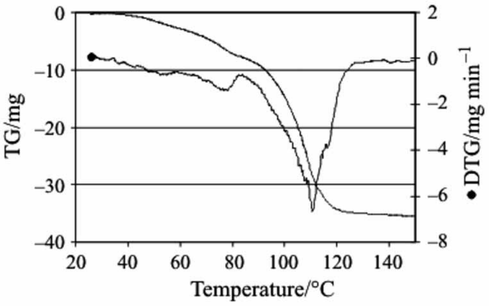

Fig. 6 Typical TG and DTG curve of creams prepared with ionic emulsifier (Eucarol AGE/ET)

Table 2 Quantity of bulk water and interlamellarly fixed water in creams based on ionic emulsifier (Eucarol AGE/ET, 2 mass/mass%), (mean values, *SD*, *n*=3)

Mechanism of water binding	TG/%					
	1st day		4th week		8th week	
	Mean value	*SD*	Mean value	*SD*	Mean value	*SD*
Bulk water	20.74	0.58	15.71	0.46	15.34	0.07
Interlamellarly fixed water	50.15	0.32	54.62	0.36	56.07	0.62

Furthermore, it could be observed that ionic emulsifiers are able to bind considerably more water among the bilayers than non-ionic emulsifiers (Table 2). At the same time the evaluation of the mass loss data revealed that - only in the case of the ionic system - 70% of the examined quantity of the sample was removed up to ±150°C. This can be explained by the fact that the emulsifiers were already aqueous solutions.

Rheological results

The above-presented thermogravimetric results harmonize with the rheological parameters (yield point, thixotropic area, viscoelastic behaviour) during storage.

The appearance of the interlamellarly bond water resulted in the following changes in the rheological behaviour. Higher yield values were measured, when the water was fixed mainly as bulk water. These values were five times higher, than that of systems formed by ionic and POE-type non-ionic emulsifiers (Fig. 7).

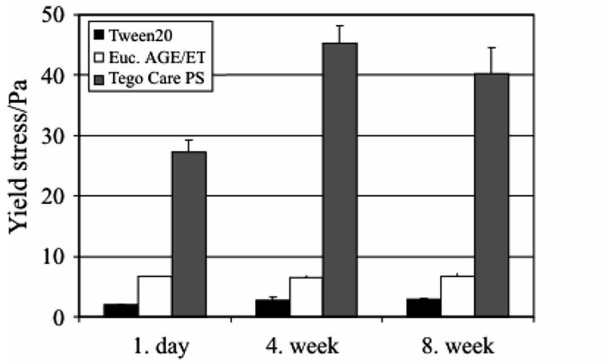

Fig. 7 Yield values of creams prepared with Tween 20, Eucarol AGE/ET, Tego Care PS 3 mass/mass%

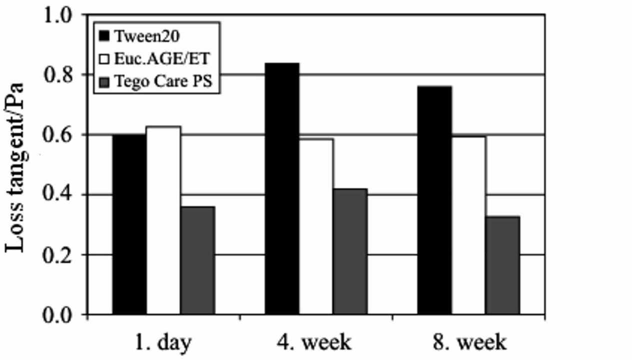

Fig. 8 Viscoelastic behaviour of creams prepared with Tween 20, Eucarol AGE/ET, Tego Care PS 3 mass/mass%

The viscoelastic behaviour changed as follow: the bulk water containing systems were more elastic, while the other type had a viscous character dominating. POE-type emulsifiers containing systems had an increase in their loss tangent value parallel with the formation of interlamellarly fixed water during storage (Fig. 8).

Microstructural changes during use

The presence of the two types of water and their quantitative relationship is important during the design and formulation of creams. The penetration ability of the incorporated active agent through the skin layers is influenced by water fixed in the lamellar structure. Bulk water ensures better hydration, and the quantity of loosely bond water increases the rate of drug release and exerts a certain cooling effect.

The composition of the cream changes as a result of shearing forces of application. As researchers' opinions differ to what extent the stability of the lamella is influenced by this change, we examined it in the case of our studied systems with thermogravimetric and rheological methods. The results obtained are illustrated in

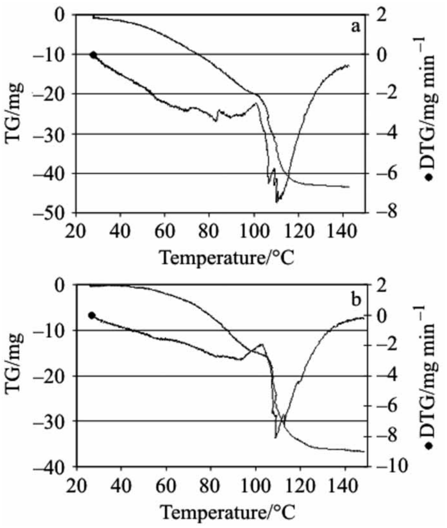

Fig. 9 TG and DTG curve of cream based on Eucarol AGE/EC 4 mass/mass%
a – after preparation and b – after stress application

Fig. 9a, b in the case of samples prepared with Eucarol AGE/EC 4%, after shearing simulating application (shear rate 150 s^{-1}, 20 s, 35°C).

It can be seen that with these parameters the shape of the curve is characteristic of the given sample and we found that the proportion of the phases did not change considerably. (This fact points ahead to the biopharmaceutical examinations in progress.)

Conclusions

Thermogravimetric data revealed that the composition and the concentration of the mixed emulsifier system and within this, the type of surfactant altered the water binding mechanism in o/w creams. Interlamellarly fixed water was present in case of POE-type nonionic emulsifiers and ionic ones. The difference between these was, that there was an immediate interlamellarly fixed water appearance and in a higher ratio, than that of POE-type nonionics. POE-free nonionic emulsifier were able to form bulk water only.

Rheological measurements showed also significant differences caused by the different water bond mechanism resulting from the use of different emulsifiers. The systems were easily differentiated by their yield value and the viscoelastic behaviour.

Thermogravimetric and rheological data harmonize not only in the quantitative characterisation of water bond mechanism, but also gave information on time needed for its development. The appearance of interlamellarly fixed water in case of POE-type non-ionic emulsifier containing system was detected both with thermogravimetric and rheological data.

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