Journal of Thermal Analysis and Calorimetry, Vol. 94 (2008) 1, 271–274

THERMOANALYTICAL AND MICROSCOPICAL INVESTIGATION OF THE MICROSTRUCTURE OF EMULSIONS CONTAINING POLYMERIC EMULSIFIER

Mária Szűcs[1], *Patrizia Vaghi*[2], *Giuseppina Sandri*[3], *M. Cristina Bonferoni*[3], *Carla M. Caramella*[3], *Piroska Szabó-Révész*[1] *and I. Erős*[1*]

[1]University of Szeged, Faculty of Pharmacy, Department of Pharmaceutical Technology, Eötvös u. 6., 6720 Szeged, Hungary
[2]University of Pavia, Centro Grandi Strumenti, Via Bassi 21, 27100 Pavia, Italy
[3]University of Pavia, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, Viale Taramelli 12, 27100 Pavia, Italy

Polymeric emulsifiers provide exceptional stability to oil-in-water, water-in-oil or multiple emulsions by their steric stabilization. Pemulens as polymeric emulsifiers are able to stabilize *o/w* type emulsions because their short lipophilic part integrates into the oil droplets while their long hydrophilic part forms a micro gel around the droplet. In our present study the microstructure and integration of the polymeric emulsifier at the water–oil interface was investigated with thermogravimetric and microscopical methods. It was established that depending on the amount of both of the polymeric emulsifier and added coemulsifier the microstructure of the system changes.

Keywords: *confocal laser scanning microscopy, gel-emulsion, microstructure, polymeric emulsifier, thermogravimetry*

Introduction

An emulsion is a heterogeneous disperse system of two immiscible liquids (by convention described as oil and water), one of which is dispersed as fine droplets uniformly throughout the other [1]. They are not stable thermodynamically, several processes are known to lead to the destruction of their structure, such as: flocculation, creaming, sedimentation, coalescence, phase inversion and Ostwald ripening. Therefore one of the most important tasks is to ensure the kinetic stability of these systems. In addition to stability, other requirements also have to be satisfied by emulsions used in cosmetic and pharmaceutical industries, as appropriate consistence and safety of ingredients [2].

Emulsifiers are used both to advance emulsification and to ensure stability during storage and application. Polymeric emulsifiers appeared at the end of the last century. They provide exceptional stability to oil-in-water, water-in-oil or multiple emulsions by their steric stabilization. Some of these polymeric emulsifiers have been designed to act both as primary emulsifiers and viscosity enhancing agents. Pemulens (CTFA/INCI designation: Acrylate/C10-C30 alkyl-acrylate cross polymer) belong to this group. One of their most important properties resides in their affectiveness in stabilizing *o/w* type emulsions even for very low Pemulen concentrations (0.1–0.4 mass/mass%). The short lypophilic part of Pemulens is integrated into the oil droplets while the long hydrophilic part of the molecules forms a micro gel around the droplet so this micro gel stabilizes the dispersed phase [3].

Thermal analysis is becoming increasingly important in the structure examination of pharmaceutical dosage forms. Recently, in addition to the research of solid dosage forms [4–7], it has also been used successfully in the investigation of liquid and semi-solid systems. Thermoanalytical measurements allow investigating the microstructure of emulsions, creams and other semi-solid systems. Several papers about the structure of various semi-solid pharmaceutical preparations and cosmetic products (e.g. creams and liquid crystals) have been published in literature [8–12]. The majority of the investigations focus the attention on the binding of water: free, bound or interlamellar water is distinguished [13–17]. In the case of Pemulens free and bound (micro gel) water can similarly be identified and quantified with thermogravimetric measurements.

Emulsions can be visualized with confocal laser scanning microscopy either with the fluorescent dyeing of the disperse phase (or more rarely of the dispersion medium) or with the use of fluorescence-labelled surfactants [18–22]. In the present study our aim is to determine the location of the polymer with the second method. When rhodamin B is used as a fluorophore, H bonds and electrostatic interactions arise between the latter and the carboxyl group of the polymer as the structure of the rhodamine B is similar to a tertiary

* Author for correspondence: eros@pharm.u-szeged.hu

1388–6150/$20.00

Akadémiai Kiadó, Budapest, Hungary
Springer, Dordrecht, The Netherlands

amine [23], as a consequence, the concentration of the dye will be higher where the polymer concentration is also higher.

Our aims were the following: 1) to perform thermogravimetric and microscopical examinations in order to learn about the microstructure of the gel emulsions as so far, such examinations have not been encountered in the literature of pharmaceutical technology yet; 2) to determine the binding of the water in the system; 3) to describe the changes arising in the microstructure due to the effect of the coemulsifier.

Experimental

Materials and emulsions preparation

The polymeric emulsifier was acrylate/C10-C30 alkyl-acrylate cross polymers (Noveon, Pemulen TR2). Coemulsifier was PEO-PPO-PEO triblock polymer (Synperonic PE/L 101; S101, Uniqema, UK). The oil phase was Miglyol 812 (Sasol, Germany) and the aqueous phase was purified water (Ph. Hg. VIII.) containing 0.01 mass/mass% methyl paraben (Ph. Hg. VIII.). The neutralizing agent was trolamine (Ph. Hg. VIII.). The fluorescent dye was rhodamine B (Fluka, Italy). The polymeric emulsifier was added to purified water containing trolamine and a preservative agent, than they were stored at room temperature for 24 h (pH was 5–5.5). The oil (containing suspended rhodamine B) was added to this gel by drop wise while the sample was being stirred with mixer (MLW ER-1, 800 rpk, 20 min). In the samples containing coemulsifiers, the coemulsifier was added to the oil phase. In the first series, the polymer concentration was changed under constant water oil ratio (80:20) and in the second one the secondary emulsifier was varied under constant polymer water oil ratio. The samples were made in mass/mass% concentration.

Methods

Thermogravimetric investigation

The measurements were carried out using MOM Derivatograph-C (MOM, Hungary) instrument. Samples were weighed (40–50 mg) in platinum pans (No. 4). The reference was a pan containing aluminium oxide. The samples were heated from 25 to 200°C at 10°C min^{-1}. TG (mass loss% *vs*. temperature) and DTG (derivative TG) curves were plotted. Each study was repeated three times.

Confocal laser scanning microscopy

Image acquisition was performed by Confocal Microscope System Leica TCS SP2 (Leica Microsystems Heidelberg GmbH, Germany) interfaced with a Leica DMIRBE inverted microscope and using a 40×1.25 N.A. oil immersion objective. The excitation source was a Green Helio-Neon (λ_{ex}=543 nm) laser, the fluorescence emission of rhodamine B was recorded between 580 and 630 nm.

Results and discussion

Our basic assumption was that the polymer, due to its surfactant nature migrates toward the interface; consequently its concentration will decrease in regions far from the oil droplets. If this concentration difference is considerable, two aqueous phases are obtained, which can be separated well with thermogravimetric investigations. When the quantity of the polymer is increased, two processes can be expected to occur: 1) the interface becomes saturated so the excess polymer will not appear in the boundary layer any more, therefore it will reduce the concentration difference between the interface and the more distant areas. 2) The increased polymer concentration will result in a greater number of interactions between the chains, which in turn over a certain concentration will inhibit the orientation of the polymers towards the interface to some extent. As a consequence, the differentiation of the gel structure can be expected to disappear with increasing polymer content. Figure 1 clearly shows that in the case of a low polymer content two peaks can be separated well in the DTG curve, one peak corresponds to free water at about 100°C, the other to micro gel (bound) water at about 140°C. When the quantity of the polymer is increased, the two peaks disappear as expected, and only one peak can be observed instead. This is confirmed by pictures made with confocal microscopy. In the case of a low concentration (Fig. 2) a sharp contour is dyed by rhodamin around the droplet, indicat-

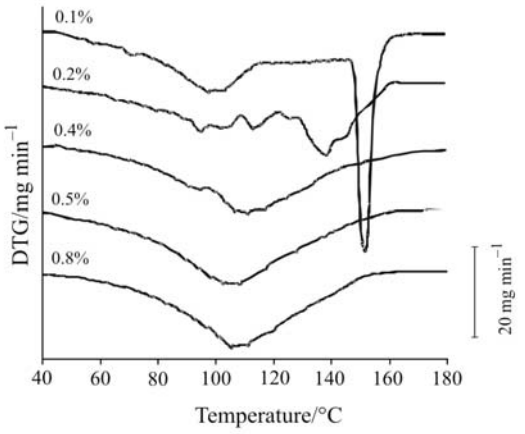

Fig. 1 DTG curves of emulsions with increasing polymeric emulsifier content

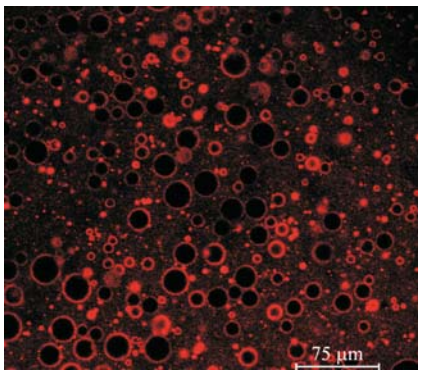

Fig. 2 CLSM picture of emulsion containing 0.1 mass/mass% polymeric emulsifier

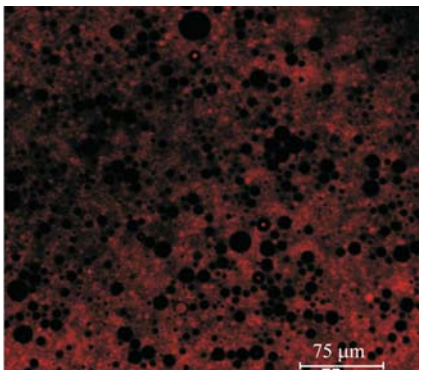

Fig. 3 CLSM picture of emulsion containing 0.8 mass/mass% polymeric emulsifier

ing a higher polymer concentration, while with higher concentrations the dye is of homogeneous distribution (Fig. 3).

If a coemulsifier is also used, changes in the microstructure can be assumed. The coemulsifier with its smaller molecules is also oriented on the interface, therefore in a higher concentration it can displace the polymeric emulsifier with greater molecules. As a result, the micro gel around the droplet will disappear. The two peaks of the DTG curve are shifted with an increasing coemulsifier concentration. The polymeric emulsifier is displaced from the interface and will gelate, thus the first peak will be shifted towards a higher temperature. At the same time the water on the interface will also evaporate from the system at a higher temperature. The quantity of water bound in different ways can be calculated from the step height of the TG curves. (In certain case large relative error can be seen in the water content determination which can be explained by the inhomogeneity of the macro-emulsion systems.) If the quantity of the micro gel water on the interface is examined with respect to the total quantity of water with increasing coemulsifier concentration it can be stated that the amount of the micro gel water gradually decreases and finally disappears as a homogeneous gel is created by the polymer in the aqueous phase (Table 1).

Table 1 Peaks of the DTG curves and the amount of the micro gel water of the emulsions containing coemulsifier

Coemulsifier concentration/ mass/mass%	DTG		Micro gel water/ mass/mass%
	1st peak/ °C	2nd peak/ °C	
0.001	108±4	131±2	36.8±6.0
0.01	113±2	138±4	24.0±3.0
0.10	113±1	145±4	25.4±9.5
0.50	119±4	150±6	16.4±7.8
1.00	133±4	–	–

Conclusions

Gel-emulsions containing Pemulens form a special (micro gel) structure. It was established that the increase of the polymeric emulsifier and coemulsifier concentration leads to the disappearance of the micro gel structure. In case of the polymeric emulsifier the probable reason is the saturated surface and/or the improved polymer–polymer interaction, while in case of the coemulsifer the reason is its stronger affinity to the interface. According to the previous statement instead of two peaks only one peak can be seen in the DTG curve which corresponds to the homogenous water phase. Parallel with the latter, fluorophore does not dye a sharp contour around the droplets but is distributed homogenously in the total amount of the water.

Acknowledgements

We thank Noveon, Inc. for the sample (Pemulen TR2).

References

1 G. M. Eccleston, Encyclopedia of Pharmaceutical Technology, J. Swarbrick and J. C. Boylan, Eds, 2th Edition, Vol. 2, Marcel Dekker, New York 2002.
2 M. M. Breuer, Encyclopedia of Emulsion Technology, P. Becher, Ed., 2th Edition, Marcel Dekker, New York 1985, Chapter 7.
3 B. F. Goodrich, The Science of Rheology: Pharmaceutically Applied, Technical Note, 1992.
4 J. L. Ford, Int. J. Pharm., 179 (1999) 209.
5 R. C. Mashru, V. B. Sutariya, M. G. Sankalia and P. Yagnakumar, J. Therm. Anal. Cal., 82 (2005) 167.
6 M. Bartolomei, P. Bertocchi, E. Antoniella and A. Rodomonte, J. Pharm. Biomed. Anal., 40 (2006) 1105.
7 K. M. Picker-Freyer, J. Therm. Anal. Cal., 85 (2006) 495.
8 U. T. Lashmar, J. P. Richardson and A. Erbod, Int. J. Pharm., 125 (1995) 315.
9 A. Kovács, I. Csóka, M. Kónya, E. Csányi, A. Fehér and I. Erős, J. Therm. Anal. Cal., 82 (2005) 491.

10 S. A. Vanapalli, J. Palanuwech and J. N. Coupland, Colloid Surf. A, 204 (2002) 227.
11 J. I. Uriguen, L. Bremer, V. Mathot and G. Groeninckx, Polymer, 45 (2004) 5961.
12 J. Bender, W. Michaelis and R. Schubert, J. Therm. Anal. Cal., 68 (2002) 603.
13 H. Junginger, Pharmazie, 39 (1984) 610.
14 S. Kallioninen, K. Helenius and J. Yliruusi, Pharmazie, 50 (1995) 478.
15 A. Fehér, E. Csányi, I. Csóka, A. Kovács and I. Erős, J. Therm. Anal. Cal., 82 (2005) 507.
16 V. L. Peramal, S. Tamburic and D. Q. M. Craig, Int. J. Pharm., 155 (1997) 91.
17 M. Kónya, M. Sorrenti, F. Ferrari, S. Rossi, I. Csóka, C. Caramella, G. Bettinetti and I. Erős, J. Therm. Anal. Cal., 73 (2003) 623.
18 S. Kerstens, C. Mugnier, B. S. Murray and E. Dickinson, Food Biophys., 1 (2006) 133.
19 S. Kerstens, B. S. Murray and E. Dickinson, J. Colloid Interface Sci., 296 (2006) 332.
20 I. Heertje, J. Nederlof, H. A. C. M. Hendrickx and E. H. Lucassen-Reynders, Food Struct., 9 (1990) 305.
21 I. Heertje, H. van Aalst, J. C. G. Blonk, A. Don, J. Nederlof and E. H. Lucassen-Reynders, Food Sci. Technol., 29 (1996) 217.
22 J. Brujic, S. F. Edwards, I. Hopkinson and H. A. Makse, Physica A, 327 (2003) 201.
23 Z. S. Guan, Y. Zhang, Q. Zhang and D. X. Li, J. Colloid Interface Sci., 302 (2006) 113.

Received: December 3, 2007
Accepted: March 10, 2008
OnlineFirst: June 25, 2008

DOI: 10.1007/s10973-007-8907-9