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International Journal of Pharmaceutics 184 (1999) 207–217
international journal of pharmaceutics

An investigation into interactions between polyacrylic polymers and a non-ionic surfactant: an emulsion preformulation study

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Received 21 October 1998; received in revised form 1 March 1999; accepted 8 March 1999

Abstract

The aim of this study was to investigate possible interactions between a polymeric emulsifier and a non-ionic surfactant, with a view of achieving better understanding of emulsion stabilisation mechanisms. The polymeric emulsifier used was acrylates/C_{10-30} alkyl acrylate crosspolymer (Pemulen TR-2®), while Polyoxyethylene 20 sorbitan mono-oleate (Polysorbate 80) has been chosen as a model surfactant. Both materials were used within the concentration range relevant for their practical application. A 0.2%w/w aqueous dispersion of polymeric emulsifier, containing various amounts of surfactant (from 0.01 to 1.0% w/w) was used throughout the study. Interfacial aspects of the proposed polymer/surfactant interactions were analysed by means of surface tension measurements. Changes in the network structure of the test dispersions were quantified by continuous shear rheometry, supported by the texture analysis. To analyse the influence of hydrophobic alkyl groups present on the Pemulen TR-2® chains, an unmodified, hydrophilic polyacrylic acid polymer, Carbopol 934P®, was assessed under the same conditions. The results obtained by both surface tension and rheological studies have revealed large differences in behaviour of the two polymers in the presence of the model surfactant. Pemulen TR-2® was shown to desorb the surfactant from the surface, within the whole concentration range studied. Furthermore, an increase in viscosity and texture profile parameters with increasing Polysorbate 80 concentration up to 0.3% w/w was evident in the case of Pemulen TR-2® dispersions. This was followed by a decrease in the gel network strength at higher surfactant concentrations. On the other hand, Carbopol 934P® has shown no signs of surfactant desorption and only small changes in the network structure with the increasing concentration of surfactant. It is shown in this study that an interaction between a polymeric emulsifier Pemulen TR-2® and a non-ionic surfactant Polysorbate 80 does occur in their aqueous dispersion, and that it is: (a) hydrophobic in nature; (b) concentration-dependent; and (c) has an impact on the rheological properties of dispersion. © 1999 Elsevier Science B.V. All rights reserved.

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PII: S0378-5173(99)00097-6

Keywords: Polymeric emulsifier; o/w emulsion; Polyacrylic polymer/non-ionic surfactant interaction; Surface tension; Continuous shear measurements; Texture analysis

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1. Introduction

In most topical pharmaceutical emulsions primary emulsifiers are low molecular weight surfactants. Recently, the use of polymeric emulsifiers has been suggested as a non-irritant alternative to low molecular weight surfactants by a number of authors (e.g. Bremecker et al., 1992; Daniels and Barta, 1994; Rimpler, 1996). Due to their large molecules, polymeric emulsifiers do not penetrate into the skin, nor do they enhance an unwanted penetration of other formulation compounds. In addition, these materials have the advantage of: low usage level, excellent emulsion stability, simplified emulsion formation procedure and the possibility to formulate waterproof systems (Lochead et al., 1986; Hemker, 1990; Brisaert and Plaizier-Vercammen, 1997). Some of these polymers have been reported to form stable emulsions with oil droplets of 50–100 μm in diameter (Eccleston, 1997), which proves them useful as secondary emulsifiers in topical w/o/w emulsions. It is also stated in the literature (Bremecker et al., 1992) that an o/w emulsion based on such an emulsifier can provide a 'triggered release' of an active. These new opportunities make the studying of polymeric emulsifiers, their properties and interactions with other raw materials an interesting and indeed necessary step towards their extensive use in both pharmaceutical and cosmetic formulations.

Typical representatives of this novel class of o/w emulsifiers are Pemulens® (BF Goodrich, USA). They are the polymers of acrylic acid modified by long chain (C_{10}–C_{30}) alkyl acrylates and crosslinked with allylpenthaerythritol (Dittgen et al., 1997). The proposed mechanism of emulsion stabilisation by this novel class of emulsifiers is named electrosteric stabilisation (Lochead et al., 1986; Hemker, 1990), and represents a combined effect of electric repulsion and steric stabilisation. In the presence of an oil phase, hydrophobic alkyl chains anchor to the surface of oil droplets by hydrophobic interactions. At the same time, the long, hydrated and negatively charged hydrophilic chains form microgels around dispersed oil droplets and thus prevent their coalescence (Bremecker et al., 1992).

It has been reported in the literature (Brisaert and Plaizier-Vercammen, 1997; Malpede and Fumagali, 1998) that some non-ionic surfactants in low concentrations (up to 0.5% w/w) may significantly increase emulsifying capacity of Pemulens® and similar polymeric emulsifiers. The combination of polymeric emulsifier and surfactant has been shown to improve physical stability of model emulsions, especially when polar oil phase were emulsified in water (Carlotti et al., 1995; Bobin et al., 1997; Malpede and Fumagali, 1998).

However, it is also known that polymer/surfactant interactions sometimes occur (Goddard, 1990) and that they may in turn lead to decreased physical stability of an emulsion. It was Friberg (1997) who first proposed a general scenario for the prediction of stability profiles of emulsions that contain both hydrophobically modified polymer and low molecular weight surfactant. According to his theory, within the concentration range where polymer and surfactant interact, emulsion stabilisation may partly or completely fail, due to the polymer being removed from the interface and engaged in the formation of polymer/surfactant complexes. It is, therefore, of interest to achieve a better understanding of stabilisation mechanisms of different polymer/surfactant pairs, especially within the range of concentrations used in practice.

In this study, an anionic polymeric emulsifier Pemulen TR-2® NF (acrylates/C_{10}–C_{30} alkyl acrylate crosspolymer) and a non-ionic surfactant Polysorbate 80 (polyoxyethylene 20 sorbitan mono-oleate) were used as a model pair, in the form of an aqueous dispersion. In parallel, another pair consisting of an anionic hydrophilic polymer Carbopol 934P® and Polysorbate 80 was evaluated under the same conditions as a 'blank probe'. Surface tension measurements were used to detect the influence of each polymer on the surface activity of Polysorbate 80. Changes in physical properties were investigated by two rheological techniques: continuous flow rheology and penetrometry (texture analysis). The results obtained were analysed in the light of existing fundamental models, which refer mainly to a charged surfactant and an uncharged polymer or a polymer of opposite charge (Carlsson, 1989; Goddard, 1990; Nystrom et al., 1995; Winnik and Regismond, 1996; Thuresson and Lindman, 1998).

2. Experimental section

2.1. Materials

A hydrophobically modified poly(acrylic acid) polymer Pemulen TR-2® NF (acrylates/C_{10}–C_{30} alkyl acrylate crosspolymer) and a corresponding hydrophilic polymer Carbopol 934P® (polyacrylic acid cross-linked with allyl sucrose, both manufacrured by BF Goodrich, USA) were used in fixed concentration of 0.2% w/w. The concentration of Polysorbate 80 (ICI, UK) varied as follows: 0.01, 0.03, 0.05, 0.07, 0.1, 0.2, 0.3, 0.5 and 1.0% w/w. Triethanolamine (98% pure, Merck, Germany) was used as a neutralisation base to adjust the pH value at 5.7 ± 0.2. Double distilled water was used for all experiments.

2.2. Preparation of polymer/surfactant mixtures

The polymer used was homogeneously dispersed in water solutions containing different amounts of Polysorbate 80 and allowed to hydrate for 24 h at the room temperature. Triethanolamine in the form of 10% w/w solution was added under slow agitation using laboratory mixer (Heidolph RZR 2020, Germany) to the pH value of 5.7 ± 0.2.

Samples were allowed to equilibrate for 48 h at the room temperature before testing. All measurements were carried out at 25 ± 1°C.

2.3. Surface tension measurements

Surface tension was determined with Digital tensiometer K-10 (A. Krüs, Germany). The water dispersion tested was placed in a 100 ml beaker and the Platinum–Iridium ring was positioned on the water/air interface. The system was then allowed to equilibrate for 30 min at 25 ± 1°C, before the ring was pulled up from the liquid surface. The surface tension values were recorded automatically, with at least three measurements performed for each sample. The coefficient of variation obtained was less than 3% for pure Polysorbate 80 solutions and less than 5% for polymer/surfactant dispersions. It is possible that an increased viscosity in the case of the polymer/surfactant dispersions may account for this higher data variation. This fact has already been reported in the literature on other systems (Carlsson, 1989).

2.4. Continuous flow measurements

A shear-rate controlled viscometer Model DV-III V 3.1.RV (Brookfield, Germany) with the cylindrical measuring system (spindle SC4-31) was used. Continuous flow tests were performed by increasing a shear rate from 0.07 to 5 s^{-1} and decreasing it back to 0.07 s^{-1}, each stage taking 30 s. Five runs were carried out on each sample, with the coefficient of variation being less than 15%.

Using the Rheocalc software program provided with the equipment, the results obtained were fitted in the Cesson equation:

$$\sqrt{\tau} = \sqrt{\tau_0} + \sqrt{\eta}D$$

where τ is the shear stress at given shear rate, τ_0 is the yield stress value (shear stress at zero shear rate), η is the plastic viscosity and D is the shear rate.

For further rheological analysis, the yield values (τ_0) and the viscosity values at shear rates of 0.07 and 5 s^{-1} (taken from the ascending curve) were selected.

2.5. Texture analysis (penetration studies)

For the penetration tests a TA-XT2 Texture

Analyzer (Stable Micro Systems, Surrey, UK) was employed. The probe used was a plastic cylinder with a diameter of 13 mm. The pre-test speed of the probe was set up at 5 mm/s, the test speed (penetration and withdrawal) at 1 mm/s, and the probe depth at 5 mm. The maximum penetration resistance force (+ peak) and the work performed (+ area) along with withdrawal parameters (− peak and − area) have been obtained by plotting data in the force versus distance co-ordinate system, using the software provided with the equipment. The penetration studies were performed with at least five repeats for each sample, with the coefficient of variation being less than 5%.

3. Results

3.1. Surface tension measurements

The surface tension data of the test dispersions are presented in Fig. 1. It is evident from the constant surface tension curve for the pure surfactant that the concentration range of Polysorbate 80 used in this study was above its critical micellar concentration (CMC). This is in accordance with the litrature data (Hüttenrauch et al., 1988), which report its CMC to be around 0.01% w/w.

It is also evident that the two polymers have exhibited different behaviour in the presence of Polysorbate 80. Hydrophobically modified polymer (Pemulen TR-2®) in the concentration of 0.2% w/w has produced a distinctly different surface tension curve from the pure Polysorbate 80 (Fig. 1). The departure from the 'baseline' was especially pronounced in the concentration range from 0.01 to 0.3% w/w (with the surface tension values being increased for 10–12.5 mN/m). As the concentration of Polysorbate 80 further increased, the surface tension values subsequently decreased, approaching the value for the pure surfactant, but not reaching it within the concentration range studied. This kind of surface behaviour is regarded as an evidence for the polymer/surfactant interaction, i.e. the desorption of the surfactant from the surface (Carlsson, 1989; Goddard, 1990; Friberg, 1997). On the contrary, the surface ten-

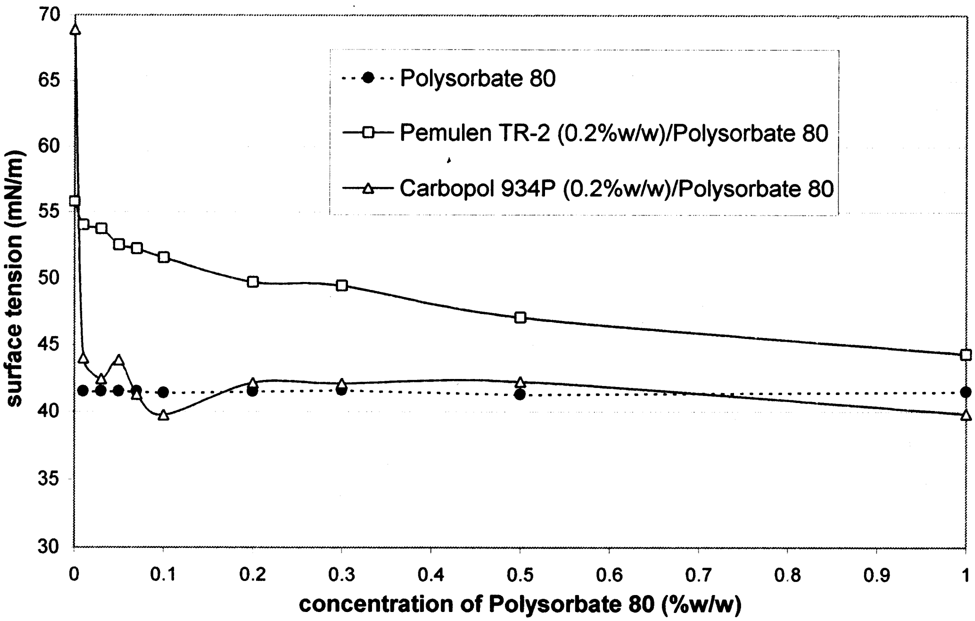

Fig. 1. Variation of the surface tension with the Polysorbate 80 concentration for the pure surfactant (dotted line) and the two polymer/surfactant dispersions (solid lines).

Table 1
Viscosity values (η) at the two shear rates (0.07 and 5 s^{-1}) for the Pemulen TR-2®/Polysorbate 80 and the Carbopol 934P®/Polysorbate 80 aqueous dispersions

Concentration of Polysorbate 80 (% w/w)	Pemulen TR-2 (0.2% w/w)/Polysorbate 80 water dispersions		Carbopol 934P (0.2% w/w)/Polysorbate 80 water dispersions	
	η at 0.07 s^{-1} (Pas)	η at 5 s^{-1} (Pas)	η at 0.07 s^{-1} (Pas)	η at 5^{-1} (Pas)
0	35.2	1.911	27.50	1.704
0.01	41.6	2.019	25.60	1.589
0.03	44.8	2.062	27.73	1.740
0.05	49.6	2.148	27.30	1.697
0.07	65.6	2.212	25.10	1.546
0.1	88.0	2.513	27.20	1.654
0.2	100.8	2.853	27.00	1.632
0.3	104.0	3.114	27.00	1.600
0.5	51.2	2.427	25.50	1.525
1.0	33.6	1.740	24.50	1.310

sion of Polysorbate 80 has been only marginally changed in the presence of Carbopol 934P® (Fig. 1).

3.2. Continuous shear measurements

Viscosity values obtained at the lower and higher shear rates (η at 0.07 and 5 s^{-1}) and the yield stress values (τ_0) of the polymer/surfactant dispersions are presented in Table 1 and Fig. 2, respectively. The rheological parameters obtained have revealed different behaviour of the two polymer/surfactant pairs, which mirrored the surface tension data. Dispersions of Pemulen TR-2® in the presence of Polysorbate 80 have shown an increase in the viscosity and yield stress values, with the maximum being achieved at the surfactant concentration of 0.3% w/w, followed by a sharp decrease (Table 1 and Fig. 2). The addition of Polysorbate 80 has increased the viscosity values at 0.07 s^{-1} and the yield values by a factor of approximately 3, while viscosity at shear rate 5 s^{-1} was increased by a factor of around 1.6.

Under the same conditions, dispersions of Carbopol 934P® and Polysorbate 80 have exhibited no significant changes in rheological parameters with increasing concentration of surfactant (Table 1 and Fig. 2). The viscosities and yield values do not differ significantly until a relatively high surfactant concentration of 0.1% w/w was achieved, at which point a slight decrease was evident.

3.3. Texture analysis (penetration studies)

The results of penetrometry tests are shown in Tables 2 and 3 and Fig. 3. In penetrometry studies, the values of positive and negative areas are associated with the cohesion work of the sample and the work of adhesion to the probe, respectively (Tamburic et al., 1996). The general rank order of both cohesiveness and ahesiveness of the Pemulen TR-2®/Polysorbate 80 dispersions correlates well with their viscosity and yield stress values (Tables 1 and 2, Figs. 2 and 3). The samples have shown the evidence of gel network strengthening with increasing concentration of Polysorbate 80, reaching the maximum at 0.3% w/w, and then decreased.

The Carbopol 934 P®/Polysorbate 80 dispersions have revealed the same trend as already obtained by rheological measurements, i.e. no apparent changes in the network structure. In order to assess the relationship between rheological and penetrometry data, the case of Pemulen TR-2®/Polysorbate 80 mixture was chosen and the yield stress values were plotted versus the maximum cohesion force (+peak) and cohesion work (+area) values (Fig. 4). The regression coefficients obtained (0.961 and 0.940, respectively) indicate a reasonably good correlation between the sets of data acquired by different instruments.

4. Discussion

The phenomenon of polymer/surfactant interaction in aqueous medium has been the focus of intensive fundamental and applied research. Studies have been carried out on many different systems, with varying properties of both polymer and surfactant. However, most of them deal with either a charged surfactant and an uncharged polymer or a charged surfactant and a polymer of opposite charges (Carlsson, 1989; Winnik and Regismond, 1996), and are rarely applicable to pharmaceutical formulations.

It is recognised that the main driving force of the above interactions is the association of ionic surfactant molecules with the hydrophobic regions of dispersed polymer molecules, with the aim to increase surfactant micelle stability (Chen and Dickinson, 1995; Winnik and Regismond, 1996). Nonionic surfactant micelles, on the other hand, are relatively stable structures and, in general, their stability would not increase upon association to a polymer. However, if the polymer had binding sites that are sufficiently hydrophobic, an extra attractive force would be available and the possibility for binding to non-ionic surfactants would increase markedly (Thuresson and Lindman, 1998).

The main aim of this study was to detect whether or not this happens in the aqueous dispersion of the chosen anionic polymeric emulsifier and a non-ionic surfactant. It has been clearly shown by the surface tension results (Fig. 1) that the hydrophobically modified polyacrylic polymer Pemulen TR-2® interacts with the Polysorbate 80 within the whole concentration range studied, as opposed to the hydrophilic polymer of the similar structure, Carbopol 934P®. The possibility of extensive hydrogen bonding has been ruled out on the basis of Carbopol 934P® non-reactivity. Therefore, it is the hydrophobic association that causes the effects detected by the surface tension and rheological tests.

Recently, a comprehensive model of the interaction between hydrophobically modified polymers and a surfactant, based on the surface tension measurements, was presented by Friberg (1997) and analysed in the connection with emul-

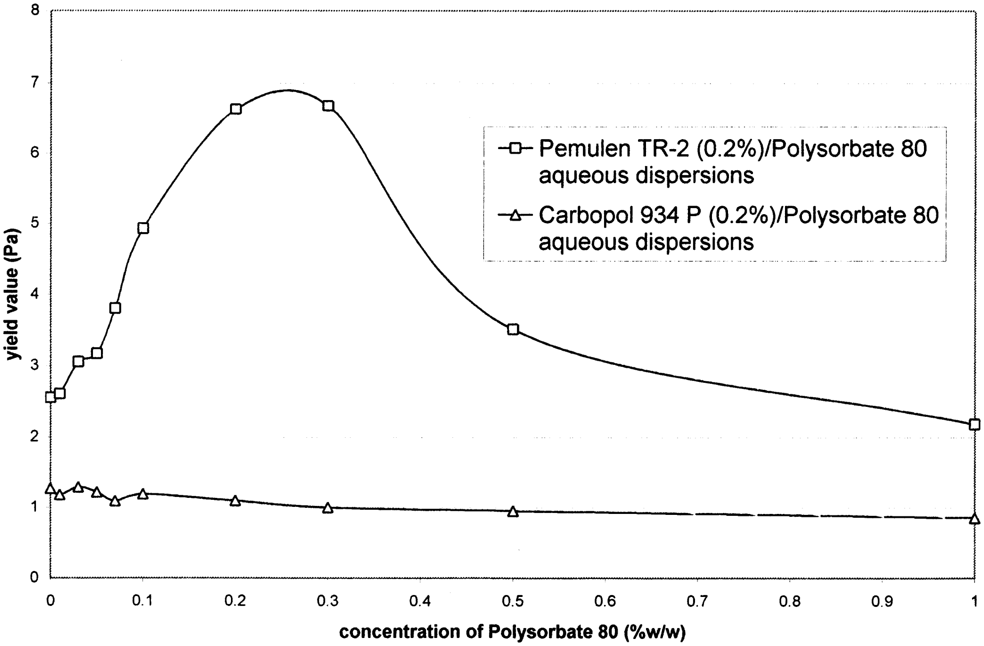

Fig. 2. Yield stress values for Pemulen TR-2® and Carbopol 934P® aqueous dispersions (pH 5.7 ± 0.2) in the presence of varying concentrations of Polysorbate 80.

Table 2
Penetrometry parameters for the Pemulen TR-2®/Polysorbate 80 aqueous dispersions

Concentration of Polysorbate 80 (%w/w)	Pemulen TR-2 (0.2% w/w)/Polysorbate 80 water dispersions		
	+Area (μJ)	−Peak (mN)	−Area (μJ)
0	842.9	107.7	704.4
0.01	900.3	104.9	714.0
0.03	873.8	104.9	710.0
0.05	927.7	106.8	723.9
0.07	949.2	105.9	731.4
0.1	952.9	108.6	757.1
0.2	1222.5	119.8	874.1
0.3	1291.9	125.4	877.9
0.5	998.2	105.9	714.5
1.0	850.3	91.0	583.2

sion stability. In the light of the proposed general model, it could be concluded that the polymer/surfactant pair investigated here does interact within the whole concentration range studied, showing, as a consequence, a distinctly different surface tension curve from the pure surfactant (Fig. 1). Furthermore, it could be speculated that the first part of the curve (up to 0.3% surfactant) corresponds with the region where polymer/surfactant micelles are formed. In this region, only a small amount of surfactant is present at the water/air interface because it is mostly engaged in the polymer/surfactant complex formation. It is assumed that polymer + polymer/surfactant complexes + surfactant monomers are present at this stage (Carlsson, 1989; Friberg, 1997).

The plateau region between 0.2 and 0.3% indicates that equilibrium has been reached, with the possibility of the highest interaction intensity between the two materials. From that point onwards, only a decrease in surface tension was observed, with the tendency of reaching the 'baseline' value at higher surfactant concentrations. This is in accordance with the proposed fundamental model (Carlsson, 1989; Friberg, 1997) that in the region following the plateau, the surface tension is being reduced, since the polymer becomes saturated by surfactant and a larger number of surfactant molecules are made available for the adsorption at the interface. Fig. 1 clearly shows that it takes more that 1.0% Polysorbate 80 to completely saturate 0.2% Pemulen TR-2® and to return to its 'baseline' value. This finding is important from the formulation point of view, since it is highly possible that emulsion stabilisation would fail if these two materials were used within the concentration range of the polymer/surfactant complex formation (Friberg, 1997).

In the case of Carbopol 934P®/Polysorbate 80 surface tension plot (Fig. 1), it is evident that such an interaction does not take place. The difference in surface activity between the two polyacrylic acid polymers is also clearly shown, with the starting value (0% surfactant in dispersion) for Carbopol 934P® being much higher than for Pemulen TR-2®.

The results obtained by continuous shear measurements for Pemulen TR-2®/Polysorbate 80 dispersions have supported the preliminary conclusions derived from the results of surface tension tests. Within the high interaction region, the viscosity and yield stress values have increased to the maximum (at the surfactant concentration of 0.3% w/w) and than decreased. Such behaviour has been attributed to the interactions of the surfactant micelles with the polymer alkyl chains (Nystrom et al., 1995; Petit et al., 1995; Thuresson and Lindman, 1998). The surfactant micelles solubilise alkyl chains which belong to the polymer macromolecules and so increase the cross-linking of the system, which is then quantified by increased rheological parameters.

The subsequent decrease in viscosity, on the other hand, is attributed to the disruption of some inter-polymer bonds as the stoichiometry between micelles and polymer hydrophobic tails changes, i.e. when the polymer hydrophobic sites become saturated with surfactant micelle. Shearing of micelles between the polymer chains is no longer a necessity and consequently, the connectivity of the system drops and the viscosity decreases (Nystrom et al., 1995; Petit et al., 1995; Thuresson and Lindman, 1998). However, the changes in viscosity and yield values are not so pronounced in the case of Pemulen TR-2®/Polysorbate 80 dispersions, since the polymer itself is already cross-linked. It is important to stress that in the case of a linear polymer/surfactant pair, rheological changes would be much more dramatic.

Previous investigation on the rheological profiles of polyacrylic acid hydrogels has shown that the yield values obtained were in good correlation with the storage modulus, which is known to be a reflection of the polymer network connectivity (Tamburic et al., 1998). Practical implication of this correlation lies in that the elastic properties of some samples may be fairly well estimated on the basis of the yield values obtained from continuous flow measurements. Assuming that the rank order of yield values obtained for the Pemulen TR-2®/Polysorbate 80 pair (Table 1) corresponds with the respective network's connectivity, then the above molecular considerations on the reversible cross-linking within the system do acquire further credibility.

The existence of hydrophobic associations has been reported in the literature for another anionic polymer/non-ionic surfactant system, namely gum arabic/polyoxyethylene-oleyl ether (Brij 96), with the later present in the concentration range of up to 10% w/w (Attwood and Florence, 1983). The increase in viscosity of the system was attributed to an increased hydration of the gum/surfactant complex, with the water being trapped in the adsorbed polyoxyethylene layers. In the case of the polymer/surfactant pairs evaluated in this study, it is believed that the hydration mechanism does not play a major role in the observed rheological behaviour. Firstly, because the surfactant was present in much lower concentrations and secondly, because of the lack of change in the Carbopol 934P®/Polysorbate 80 rheological behaviour (Fig. 2). It is possible, however, that polyoxyethylene chains of Polysorbate 80, which are known to have high hydration properties (Eccleston, 1997), have caused minor dehydration of the Carbopol 934P® polymer chains at higher concentrations, and hence a slight decrease in viscosity.

It was one of the aims of this study to explore whether the changes in rheological behaviour of the test dispersions could be detected using the penetrometry studies. Texture analysis, a sophisticated form of penetrometry, has recently attracted an interest in the field of pharmaceutical

Table 3
Penetrometry parameters for the Carbopol 934P®/Polysorbate 80 aqueous dispersions

Concentration of Polysorbate 80 (%w/w)	Carbopol 934P (0.2%w/w)/Polysorbate 80 water dispersions		
	+Area (μJ)	−Peak (mN)	−Area (μJ)
0	722.8	105.9	648.8
0.01	767.1	101.2	639.4
0.03	799.4	91.9	571.9
0.05	751.9	88.2	537.5
0.07	751.9	90.1	566.8
0.1	742.3	89.1	579.1
0.2	741.8	82.2	488.7
0.3	683.9	87.7	538.8
0.5	661.2	80.8	487.3
1.0	758.1	79.9	472.4

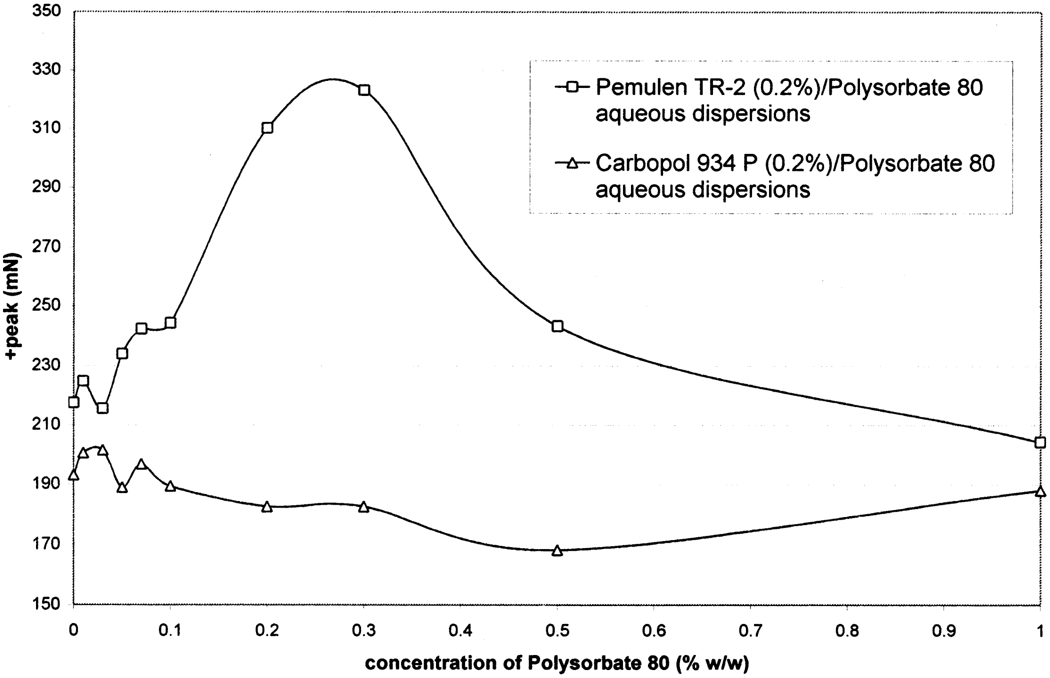

Fig. 3. Maximum penetration resistance force (+peak) for the Pemulen TR-2® and Carbopol 934P® aqueous dispersions in the presence of varying concentrations of Polysorbate 80.

gel characterisation, whereby a good correlation between a viscoelastic parameter (storage modulus) and the texture analysis parameters was found (Tamburic et al., 1996; Tamburic and Craig, 1997). In this study, too, reasonable good correlation between a continuous flow parameter (yield stress value) and the maximum resistance force and work was found (Fig. 4). The lack of an absolute correlation could be explained by the fact that penetrometry and rheological tests, although both the measure of 'consistency', characterise very different sample properties. The rheology essentially measures the response of the sample to shear, while the penetrometry largely indicates the response to pressure. The same rank order of the network structuring obtained by both techniques in this study, as well as a good linear correlation between different parameters, proves this simple technique very useful in the area of the polymer/surfactant interaction evaluation.

5. Conclusion

In this study, the interfacial and rheological properties of two polymer/surfactant aqueous dispersions were investigated, with the aim to determine whether any interaction takes place and if so, to analyse its nature and possible effects to the emulsion formulation domain.

A hydrophobically modified polyacrylic polymer Pemulen TR-2® and a non-ionic surfactant Polysorbate 80 were used as a model pair and evaluated alongside the 'blank probe' consisting of the Crabopol 934P®/Polysorbate 80 pair. It was shown that an interaction between Pemulen TR-2® and Polysorbate 80 takes place throughout the concentration range studied, as opposed to Carbopol 934P® and the same surfactant. It was also shown that the interaction was hydrophobic in nature, concentration-dependent and had an effect on the rheological status of the dispersion.

It is now of interest to correlate the established interaction with the physical structure and stabil-

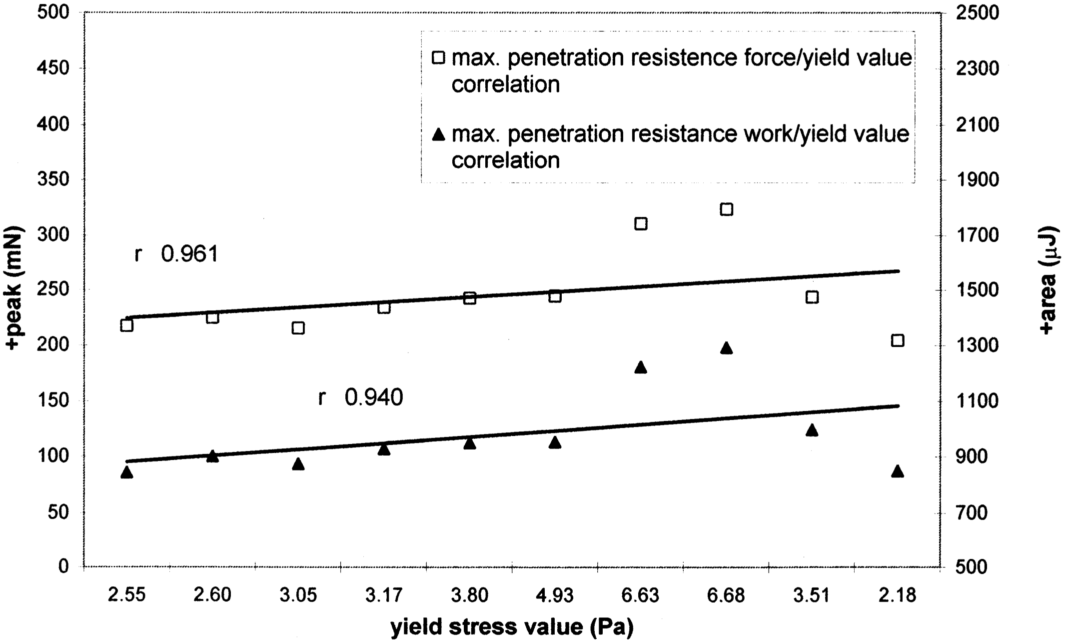

Fig. 4. Correlation between rheological parameter (yield stress value) and texture analysis parameters (maximal positive force and area) for the PemulenTR-2®/Polysorbate 80 aqueous dispersions.

ity profiles of emulsions stabilised with polymer/surfactant combinations. Further investigation is in progress.

Acknowledgements

The authors wish to thank Professor Istvan Erös and Dr.Ildiko Csoka from Department of Pharmaceutical Technology, Albert Szent-Györgyi Medical University in Szeged, Hungary for their support and assistance during rheological studies. The provision of Pemulen and Carbopol samples by BF Goodrich is also gratefully acknowledged.

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