Drug Development and Industrial Pharmacy, 33:141–146, 2007

ISSN: 0363-9045 print / 1520-5762 online
DOI: 10.1080/03639040600815061

Study of the Effect of Stirring on Foam Formation from Various Aqueous Acrylic Dispersions

János Bajdik, Gábor Lebák, Piroska Szabó-Révész and Klára Pintye-Hódi
Department of Pharmaceutical Technology, University of Szeged, Szeged, Hungary

Ottó Berkesi
Institute of Physical Chemistry, University of Szeged, Szeged, Hungary

ABSTRACT Acrylic polymers in aqueous dispersions are very often used to prepare coating suspensions which contain insoluble particles. The mixing of the pigment suspension and the polymer dispersion is a very important step in the preparation of the liquid. The stirring can cause precipitation of the polymer and foam formation. Foam formation from different Eudragit dispersions was evaluated in this study. A high-speed mixer was applied and the foam and liquid phases formed were separated. The changes in concentration of the polymer in the two phases were studied by FT-IR with a horizontal attenuated total reflection (HATR) accessory. The presence of shape-holding foam can be detected at very different rates of stirring. The most intensive foam formation was detected for Eudragit FS 30 D. The Eudragit RL 30 D dispersion was the least sensitive to high-speed mixing. The relative content of the polymer in the foam was higher than that in the liquid. This is indicated by the accumulation of surface-active agent on the surface of the bubbles formed in the foam. This phenomenon differed considerably for the various dispersions. An exact knowledge of the foam formation from aqueous acrylic dispersions is very important in order to determine the parameters of mixing and the quantity of antifoaming agent.

KEYWORDS Aqueous acrylic dispersions, Foam formation, FT-IR, Stirring

INTRODUCTION

Film-forming polymers in aqueous dispersions are increasingly used during the production of solid dosage forms for various purposes. Dispersions of acrylic acid derivatives are applied to prepare coated products (Bajdik et al., 2004; Siepmann et al., 2005; Zelkó et al., 2002) and matrices (Genç et al., 1999; Minghetti et al., 1999; Tsai et al., 1998). Films prepared from these liquids dissolve in the stomach or in the intestines, and permeable films ensure drug release by means of diffusion (Rowe et al., 2003). Various water-insoluble additives are applied for different reasons in these aqueous dispersions for the preparation of polymer films. They can modify the properties of the film formed (Felton & McGinity, 2002; Petereit & Weisbrod, 1999) and thus their

Address correspondence to Professor Klára Pintye-Hódi, H-6720 Szeged, Eötvös u. 6, Hungary; Tel: +36/62545576; Fax: +36/62545571; E-mail: klara.hodi@pharm.u-szeged.hu

homogeneous distribution is indispensable. It is recommended to add an insoluble glidant (e.g., talc, magnesium stearate, and so on) to the suspension to avoid sticking (Nimkulrat et al., 2004). Insoluble pigments (e.g., iron oxide, titanium dioxide, and so on) are also applied to ensure the appropriate appearance of the coated product (Plumb et al., 2002).

High-speed stirrers have been marketed in order to increase the efficiency of stirring of liquids, but their application is not recommended in the case of certain aqueous polymer dispersions (Lehmann, 1999). The suggested mixing order for the preparation of a coating suspension is very important. According to the Eudragit prospectus (Degussa AG, Pharma Polymers, Darmstadt, Germany), the separate homogenization of glidants, pigments, plasticizers, and other excipients is the first step and this pigment suspension must be gently mixed with the acrylic dispersion. High-speed mixing can cause precipitation of the polymers, which can not be redispersed. Another problem that can arise during high-speed mixing is foam formation. An antifoaming agent can be applied to avoid the formation of small bubbles in the liquid, because foam formation in the coating liquids is likely to cause unevenness in the film, thereby modifying its protective function (Cole, 1995). Foam formation from such polymer dispersions has not been evaluated exactly and the definition of "gentle mixing" is not clear-cut.

The main objective of our project was to establish parameters that can be applied for the stirring of aqueous dispersions. These parameters are not known in the literature, and in general, the settings are empirical. The effects of the conditions (the mixing volume, the dimensions of the mixing tank, the type of mixing apparatus, the stirring time, the stirring rate, and so on) must be evaluated. Although the high-speed mixers are not often applied for polymer dispersion, the first step in our work was to study the effects caused in the liquid by high-speed stirring of aqueous dispersions of polymers with various properties. This information can be of use to determine the applicable mechanical stress. Only foam formation and the changes in polymer concentration in the resulting foam and liquid were examined in this work. It is known that surfactant polymers can be expected to be enriched on the surface of the bubbles in the foam (Aulton, 2002). Modeling of this phenomenon with a method of measuring the quantity of polymer enriched on the surface of the bubbles is necessary. FT-IR measurement with a horizontal attenuated total reflection (HATR) accessory was applied to determine the changes in the relative quantity of the polymer in the bulk phase and the foam, in order to assess and so the enrichment at the air–liquid interface.

Such information can be very important for producers to eliminate a number of problems that can arise during the preparation of coating fluids containing solid pigments, more intensive mixing being necessary for an even distribution. Knowledge of foam formation from aqueous dispersions provides essential information relating to the optimal composition (the quantity of antifoaming agent) and the technology of preparation of coating suspensions.

MATERIALS AND METHODS

Materials

Eudragit RL 30 D, L 30 D-55, FS 30 D, and RS 30 D (Röhm GmbH & Co. KG, Darmstadt, Germany) polymers were used. These dispersions contain different additives, which can influence the behavior of the fluids during stirring.

Additives used were Eudragit RL 30 D (0.25% sorbic acid and 0.1% sodium hydroxide), Eudragit L 30 D-55 (0.7% sodium laurylsulfate and 2.3% Polysorbate 80 on solid substance), Eudragit FS 30 D (0.3% sodium laurilsulfate and 1.2% polysorbate 80 on solid substance), Eudragit RS 30 D (0.25% sorbic acid and 0.1% sodium hydroxide).

A total of 100 g of dispersion was stirred in a glass beaker with a diameter of 6 cm. No other additives were used during stirring, and thus the effect of the stirring on the dispersions could be examined directly.

Stirring

The liquids were stirred in a high-speed Ultra Turrax (IKA Ultra-Turrax T25 basic, IKA-Werke GmbH & Co. Kg, Staufen, Germany). The rotation rates examined were 6500, 9500, 13,500, 17,500, 21,500, and 24,000 rpm. With the exception of the stirring rate, all the parameters were kept constant during stirring.

Examination Methods

Prepared aqueous coating suspensions should be used within 24 hr, so the liquids were examined 24 hr after stirring. The samples were stored in a hermetically closed glass container until measurement. The polymer contents of the liquids and the foams produced were monitored with a FT-IR (AVATAR 330 FT-IR, Thermo Nicolet Corp., Madison) apparatus, with a HATR method. Multi-bounce HATR with a standard zinc selenide crystal involved the following features: angle of incidence 45° and depth of penetration 2 μm at 1000 cm^{-1}. The peak at 1720–1730 cm^{-1} was chosen as the basis for comparison. The carbonyl group in the acrylic acid structure in all the polymers examined can be assigned to peak. The direction in the change in polymer concentration could be inferred from the change in the relative intensity of angle deformation characteristic of water and from that of the C=O stretching vibration characteristic of the polymer.

RESULTS AND DISCUSSION

All the samples were stirred for 5 min. Foam formation was observed in every liquid, but it appeared at different stirring rate. Foam formation was considered to occur when the coherent layer formed had a thickness which could be definitely separated from the liquid phase during measurement. Foam formation appeared at 21,500 rpm in the case of Eudragit RL, 17,500 rpm for Eudragit L and RS, and 9500 for Eudragit FS. The maximum stirring rate for Eudragit FS was 13,500 rpm. The liquid phase could then hardly be detected.

There were differences in the characteristics of the FT-IR spectra of the liquid and the foam of Eudragit RL (Figs. 1 and 2). The relative intensity of the peak characteristic of the polymer was higher for the foam than for the corresponding fluid. The FT-IR spectra of the liquids were identical within the margin of error, and hence the composition of the liquid can be regarded as constant. There was a similar finding for the foams.

A difference was also detected between the FT-IR spectra of the fluid and foam of Eudragit L (Figs. 3 and 4), this difference being more relevant than for Eudragit RL. The relative polymer level was higher for the foam. A higher stirring rate caused a decrease in the relative level in the liquid. The examination of the foams revealed the highest polymer enrichment at a rotation rate of 24,000 rpm, the enrichment in the foam at lower stirring rates occurring to slighter extents. This means that, at a higher stirring rate, the concentration of the polymer compared to water is higher on the surface of the foam than at a lower

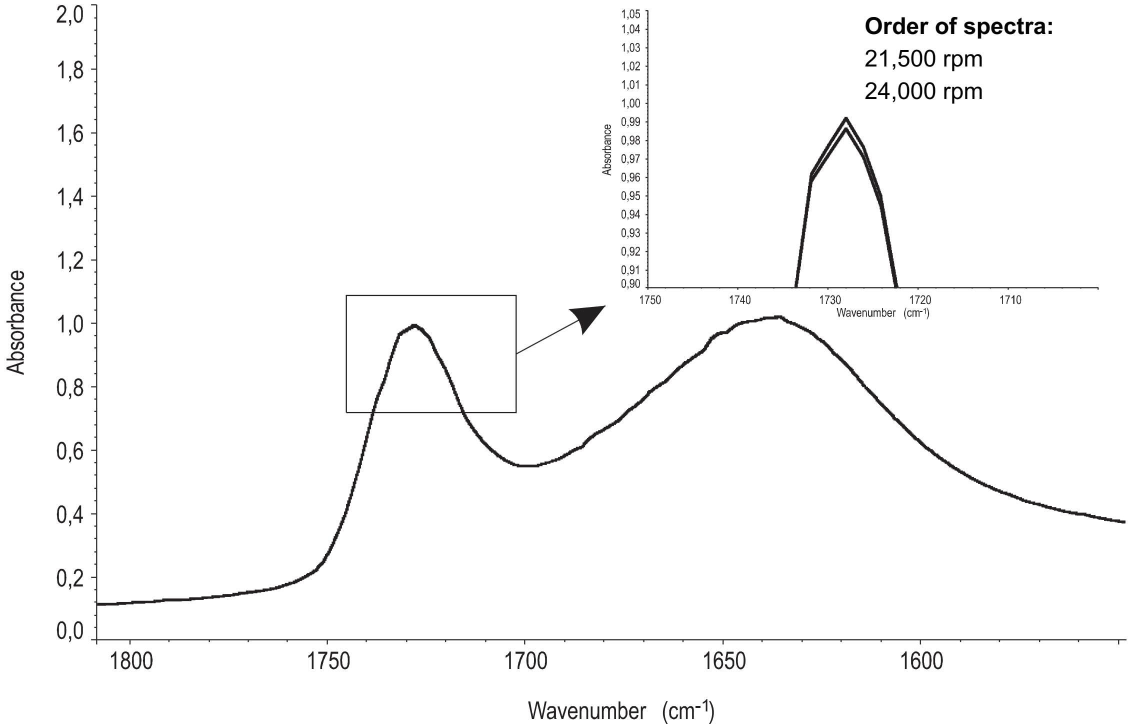

FIGURE 1 FT-IR Spectra of Liquids of Eudragit RL Stirred at Different Rates.

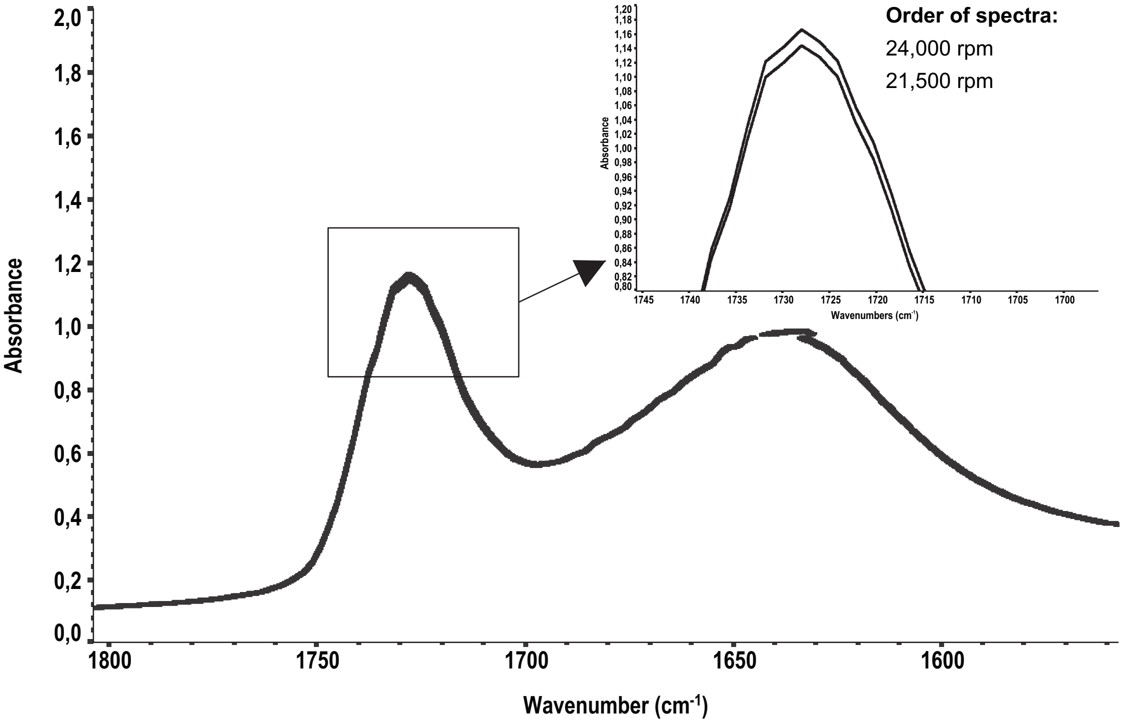

FIGURE 2 FT-IR Spectra of Foams of Eudragit RL Stirred at Different Rates.

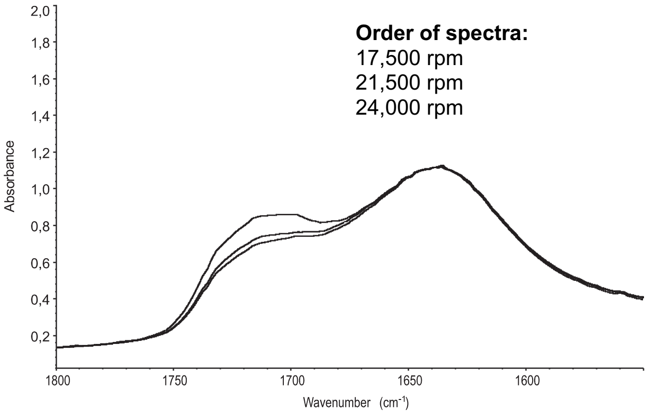

FIGURE 3 FT-IR Spectra of Liquids of Eudragit L Stirred at Different Rates.

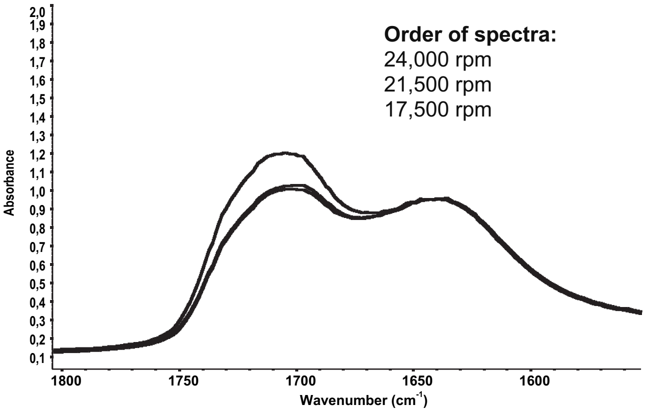

FIGURE 4 FT-IR Spectra of Foams of Eudragit L Stirred at Different Rates.

stirring rate, i.e., the surface of the bubble is more saturated.

The examination of the samples obtained during the stirring of Eudragit FS demonstrated a decreasing quantity of polymer in the liquid with increase in stirring rate, and a relatively higher concentration in the foam. Furthermore, the greatest quantity of polymer in the foam was not found at the highest stirring rate (Fig. 5).

A similar finding was made for the foam of Eudragit RS, where the greatest polymer quantity in the foam did not occur at the highest stirring rate. The explanation for this is that smaller bubbles are formed in response to a higher rate, a larger surface area of which cannot be saturated by the polymer, so that a lower relative concentration is measured. The difference between the characteristics of the spectra of the fluids and foams was also very outstanding (Figs. 6 and 7). A decrease in peak height was observed for the liquids stirred at higher rate, but this phenomenon was not relevant.

The differences in behavior of the stirred dispersions cannot be explained in terms of the additives in the dispersion, because the larger amount of surfactant

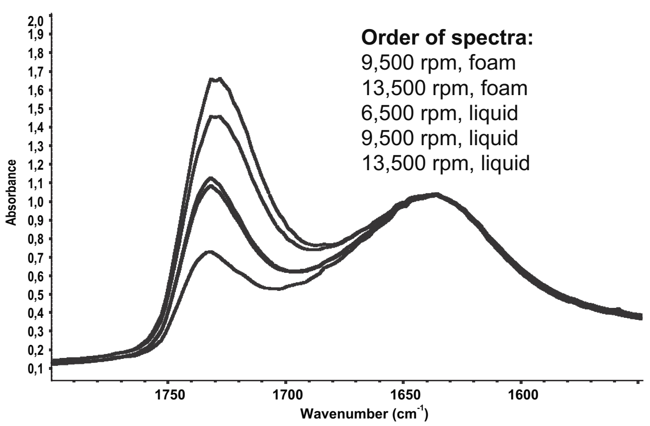

FIGURE 5 FT-IR Spectra of Foam and Liquid of Eudragit FS Stirred at Different Rates.

in Eudragit L 30 D-55 did not induce a higher degree of foam formation than that for Eudragit FS 30 D, which contains the same tensides, but in lower concentration. Accordingly, it can be stated that the properties of the film forming agent are more relevant in this case.

CONCLUSIONS

The FT-IR method with the HATR accessory was applied to determine the compositions of the liquid and foam phases. It was established that the various aqueous dispersions reacted differently to various stirring rates. Foam formation from the polymer dispersion and the properties of the bubbles formed are influenced considerably by the material properties of the dispersion. Eudragit FS proved the most sensitive as it exhibited intensive foam formation even at a lower stirring rate. Eudragit RL was found to be the least sensitive as foam formation occurred at a higher stirring rate and the polymer concentration in the boundary surface of the resulting bubbles could be considered constant, independently of the stirring rate. Since the relative concentration of the solid was very different in the foam, foam formation and separation of the foam can change the properties of the film obtained. Such examinations of polymer dispersions can be important to establish the exact mixing conditions and to choose the appropriate additives.

ACKNOWLEDGMENT

This work was supported by Hungarian Scientific Research Fund (OTKA) grants T-043025 and F-049310.

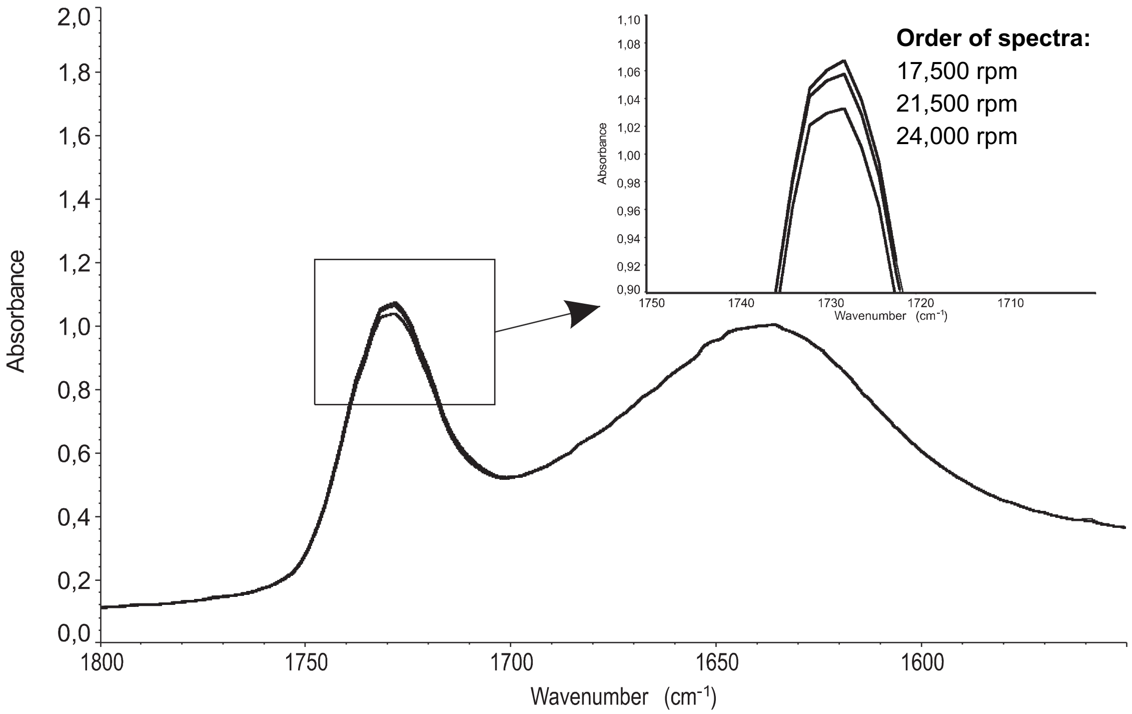

FIGURE 6 FT-IR Spectra of Liquids of Eudragit RS Stirred at Different Rates.

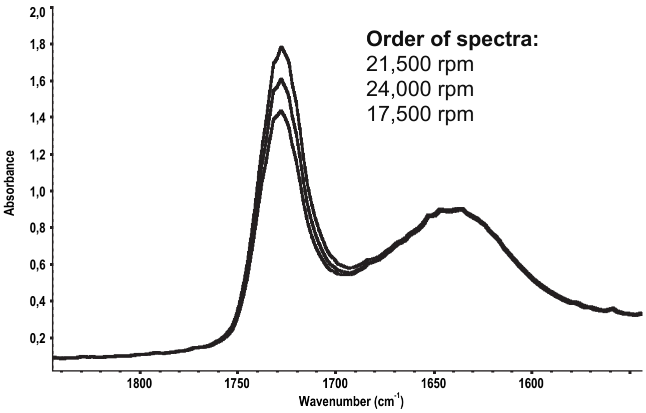

FIGURE 7 Spectra of Foams of Eudragit RS Stirred at Different Rates.

REFERENCES

Aulton, M. E. (2002). *Pharmaceutics The Science of Dosage Form Design*, Churchill Ltd: Livingstone.

Bajdik, J., Pintye-Hódi, K., Planinšek, O., Tüske, Zs., Tasic, L., Regdon jr., G., Srčič, S., & Erős, I. (2004). Surface treatment of indomethacin agglomerates with Eudragit. *Drug Dev. Ind. Pharm., 30*, 381–388.

Cole, G. (1995). *Pharmaceutical Coating Technology*, Taylor & Francis Ltd.: London.

Felton, L. A., & McGinity, J. W. (2002). Influence of insoluble excipients on film coating systems. *Drug. Dev. Ind. Pharm., 28*, 225–243.

Genç, L., Bilaç, H., & Güler, E. (1999). Studies on controlled release dimenhydrinate from matrix tablet formulations. *Pharm. Acta Helv., 74*, 43–49.

Lehmann, K. (1999). *Practical Course in Film Coating of Pharmaceutical Dosage Forms with Eudragit®*, Pharma Polymers: Darmstadt.

Minghetti, P., Cilurzo, F., Casiraghi, A., & Montanari, L. (1999). Application of viscometry and solubility parameters in miconazole patches development. *Int. J. Pharm., 190*, 91–101.

Nimkulrat, S., Suchiva, K., Phinyocheep P., & Puttipipatkhachorn S. (2004). Influence of selected surfactants on the tackiness of acrylic polymer films. *Int. J. Pharm., 287*, 27–37.

Petereit, H. U., & Weisbrod, W. (1999). Formulation and process considerations affecting the stability of solid dosage forms formulated with methacrylate copolymers. *Eur. J. Pharm. Biopharm., 47*, 15–25.

Plumb, A. P., Rowe, R. C., York, P., & Doherty, C. (2002). The effect of experimental design on the modeling of a tablet coating formulation using artificial neural networks. *Eur. J. Pharm. Sci., 16*, 281–288.

Rowe, R. C., Sheskey, P. J., & Weller, P. I. (2003). *Handbook of Pharmaceutical Excipients 4th Edition*, Pharmaceutical Press: London.

Siepmann, F., Siepmann, J., Walther, M., MacRae, R. J., & Bodmeier, R. (2005). Blends of aqueous polymer dispersions used for pellet coating: Importance of the particle size. *J. Control. Release, 105*, 226–239.

Tsai, T., San, Y. P., Ho, H. O., Wu J. S., & Sheu, M. T. (1998). Film-forming polymer-granulated excipients as the matrix materials for controlled release dosage forms. *J. Control. Release, 51*, 289–299.

Zelkó, R., Orbán, Á., Süvegh, K., Riedl, Z., & Rácz, I. (2002). Effect of plasticizer on the dynamic surface tension and the free volume of Eudragit systems. *Int. J. Pharm., 244*, 81–86.