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Effect of plasticizer on the dynamic surface tension and the free volume of Eudragit systems

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Abstract

The purpose of the present study was to determine the changes of dynamic surface tension of aqueous Eudragit dispersions quantitatively and compare these data with the free volume of the free films formed from several dispersions of different dibutyl sebacate (DBS) concentrations. Eudragit L 30D and Eudragit RL 30D aqueous colloidal polymer dispersions and their cast free films were examined. The concentration of DBS varied in the dispersions from 0 to 20%. The dynamic surface tension of the dispersions were measured by the Du Nouy ring method while the free volume of cast films were determined by positron annihilation spectroscopy. The obtained results show that dynamic surface tension measurements indicate the white point (WP) of Eudragit dispersions by a significant standard deviation increase. This may suggest the applicability of dynamic surface tension measurements for the determination of the WP of polymeric dispersions. A decrease in the WP temperature of Eudragit dispersions with an increasing plasticizer concentration was observed up to the DBS concentration of 10% w/w. Above this concentration neither the WP of the polymer dispersion nor the free volume of the free films of the polymer were changed remarkably. © 2002 Elsevier Science B.V. All rights reserved.

Keywords: Dynamic surface tension; Aqueous Eudragit dispersions; White point; Free volume; Positron lifetime spectroscopy

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1. Introduction

Acrylate polymers and their derivatives, collectively known as Eudragit polymers, were the first synthetic polymers used in pharmaceutical coatings. To form films on the surfaces of pharmaceutic materials they are usually applied as aqueous polymeric dispersions. The physical properties of film-forming dispersions can potentially exert an influence at many stages during the coating process (Lehmann and Dreher, 1973; Ghebre-Sellassie et al., 1997). These stages include delivery to and droplet production at the atomizing device,

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travel to the tablet surface or multiparticulate core, and the wetting, spreading, penetration, evaporation, and adhesion of the atomized formulation at the substrate surface (Rácz, 1989; Aulton et al., 1997). Among the additives that are incorporated into the film-forming aqueous polymeric dispersions, the plasticizer is the most critical component. It governs the film formation and the quality of the resulting film. Incorporation of a plasticizer is recommended for polymer coating formulations due to the high glass transition temperatures of polymers (Fukumori et al., 1988). Eudragit L 30D, a relatively soft polymer, can be applied in the form of a latex under mild working conditions, with the addition of 10–20% plasticizer even at room temperature and usually good film formation can be expected (Lehmann, 1997). The plasticizer effect could generally be described using simplified forms of the Gordon–Taylor/Kelley-Bueche relationships derived from the free volume theory of polymers (Gordon and Taylor, 1952; Kelley and Bueche, 1961). The role of the free volume is explained by an increasing need for space caused by chain segment mobility which develops above the T_g (Lippold and Pagés, 2001). To study the effects of the plasticizer on the free volume positron lifetime spectroscopy might support a great benefit. It is frequently used to determine the size distribution of free volume holes in polymers. The measurements are based on the interaction of the free volume holes and the so called *ortho*-positronium atom. This ‘atom’ is a bound state of an electron and a positron and reacts to the changes of the free volume very sensitively. For a recent review on *ortho*-positronium in molecular materials see (Süvegh et al., 1999).

The aim of the present study has been the determination of the white point (WP) of different Eudragit colloidal polymer dispersions by dynamic surface tension measurements in the presence of various dibutyl sebacate plasticizer concentrations. Also the effects of the plasticizer on the free volume of free films formed from the dispersions has been in the scope of the work.

2. Materials and methods

2.1. Materials

Eudragit L 30 D, Eudragit RL 30 D (Röhm Pharma) aqueous colloidal polymer dispersions and sebacic acid dibutyl ester (dibutyl sebacate, Sigma) plasticizer were selected for the study. All materials were used as received, without any further purification.

2.2. Preparation of aqueous Eudragit dispersions

Eudragit L 30 D and Eudragit RL 30 D aqueous dispersions were applied as we received from the Röhm Pharma. Different dibutyl sebacate (DBS) was added to the dispersions in 5, 10 and 20% w/w concentrations under constant stirring at 100 rpm for 2 h. After 2-h stirring the obtained dispersions were homogeneous and their were used for further experiments.

2.3. Dynamic surface tension measurements

The dynamic surface tension of different Eudragit dispersions was determined by the Du Nouy ring method using a computer-controlled and programmable tensiometer (KSV Sigma 70, RBM-R. Braumann GmbH, Germany) after an equilibration at 25–40 °C for 1 h. The temperature was continuously increased in the course of measurements to determine the WP temperature. Measuring parameters were as follows; minimum number of cycles, 5; minimum measuring time, 10 min; speed up, 1 mm/min.

2.4. The white point

According to the ISO definition (ISO 2115, 1996) the WP is the temperature limit below which an opaque mass, and above which a transparent film, is formed. The WP is normally some degrees below the minimum film-forming temperature (MFT), between these temperatures film formation is more or less questionable.

In the present work, the appearance of an exceptionally high standard deviation of the surface tension is referred to as the WP. For explanatory details see the discussion section below.

2.5. Film preparation

Approximately 10 g from each dispersion were poured on a glass Petri dish (diameter = 10 cm) and dried in a sealed container above copper sulfate and stored at room temperature for 1 week. The obtained cast films were used for positron lifetime measurements.

2.6. The basics of positron lifetime spectroscopy

The positron is the antiparticle of the electron and, thus, all of its characteristic physical parameters (e.g. its mass, the absolute value of its charge and spin) are equal with those of the electron. It is as stable a particle in a vacuum, as an electron but the two particles annihilate each other, forming gamma photons, when they meet. When positrons are injected into a material, the annihilation is inevitable and quite fast. Its actual rate, λ depends on, roughly speaking, the electron and positron densities:

$$\lambda = C\int \rho_{+}\rho_{-}\,\mathrm{d}V, \tag{1}$$

where C is a constant, ρ_{+} and ρ_{-} are the positron and electron densities, respectively. In positron lifetime spectroscopy, lone positrons are injected into the samples separately, so, the annihilation rate is determined by the electron density at the place of the positron. The mean lifetime of positrons ($\tau = 1/\lambda$) varies from 100 ps to 100 ns depending on the material and the positron state.

In the case of polymers the most important positron state is the so called *ortho*-positronium atom. It is a bound state of an electron and a positron, i.e. a light hydrogen atom in which the proton is replaced by a positron. Although this exotic atom lives relatively long in a vacuum (141 ns), in materials the surrounding electrons moderate this lifetime significantly. The measurable lifetime is determined by equations similar to Eq. (1) and usually it is only 1–3 ns.

The most fortunate thing with positron lifetime spectroscopy is that both positrons and positronium atoms tend to be localized in free volumes. Moreover, they scan the local electron density, i.e. when localized, the electron density at the free volume holes. The actual positronium lifetime is proportional with the free volume size (Deng and Jean, 1993):

$$\tau = \frac{1}{2}\left[1 - \frac{R}{R+\Delta R} + \frac{1}{2\pi}\sin\left(\frac{2\pi R}{R+\Delta R}\right)\right]^{-1} \tag{2}$$

where τ is the positronium lifetime, R is the radius of the free volume hole, and ΔR is a constant.

The calibration of Eq. (2) is a really hard task to do because the original free volume model contains serious simplifications (Domján et al., 1997) sometimes providing erraneous void sizes (Süvegh et al., 2000). Consequently, the free volume sizes obtained from Eq. (2) must be handled with special care. On the other hand, the qualitative suggestions of Eq. (2) are quite reliable, i.e. a longer lifetime always means larger free volume holes in the material.

Having a proper equipment, one can measure the decay curve of positrons. This lifetime spectrum, $S(t)$ is most similar to radioactive decay curves and usually assumed to be a single sum of several exponentials:

$$S(t) = \sum_{i=1}^{n} A_i\lambda_i \exp(-\lambda_i t) \tag{3}$$

where A_i is the intensity of the ith positron state and the number of states, n is usually not more than four. For polymers $n = 3$ is the normal assumption and the longest one of them is associated with the annihilation of *ortho*-positronium atoms.

The medium long lifetime component of lifetime spectra is associated with positrons that are not able to form positronium atoms in the polymer but, instead, annihilate directly with the electrons of the polymeric chains. The lifetime of these positrons is determined, roughly speaking, by the average electron density in the material. Consequently, in a material without serious chemical reactions taking place, the changes of this lifetime indicate the changes of free volume, as well, as *ortho*-positronium lifetimes.

2.7. Positron lifetime measurements

Positron lifetime measurements were performed with a conventional fast–fast coincidence system

(MacKenzie, 1983). The system was constructed from standard ORTEC electronic units and the detectors from BaF_2 scintillation crystals and XP2020Q photomultiplier tubes. The time resolution of the system was about 200 ps. The spectrum evaluation was done by the RESOLUTION computer code (Kirkegaard et al., 1981).

Three lifetime components were found in every spectrum but among these lifetimes the most important was the longest one.

All of the measurements were performed to room temperature and normal pressure.

3. Results and discussion

Tables 1 and 2 summarize the dynamic surface tension values for the different Eudragit L 30 D and Eudragit RL 30 D dispersions measured at several temperatures. In general, the applied plasticizer decreased the surface tension value of the dispersions, due to its interfacial structure modifying effect. The WP, which could be observed visually, was also appeared in every dispersion, regardless to the presence of the plasticizer. The plasticizer, however, decreased the WP temperature significantly.

The most remarkable feature of the tables is the surprisingly high standard deviation of tension data at the WP. In every case, this high standard deviation occurred consequently at the temperature where the dispersion formed a discontinuous opaque white mass, i.e. at the WP. The explanation for this coincidence is hidden in the combined effects of the measuring method and the discontinuity of the material. The Du Nouy ring method involves a repeated sinking of the ring in the dispersion and, as expected on the basis of statistical thermodynamics, not always the same molecules contact with the ring in the repeated measurements. This is exactly the cause of repetition, i.e. the resulted 'averaging' eliminates most of the effects of random fluctuations. In discontinuous materials these fluctuations are naturally larger, so, the standard deviation of the measured surface tension have to be definitely higher than in 'homogeneous' dispersions. The most important consequence of the discussed coincidence is that, in the future, surface tension measurements might replace the dubious observation with the naked-eye method in the determination of the WP temperature.

The presence of DBS in Eudragit dispersions caused a decrease in the WP temperature. Additionally, positron lifetime spectroscopy measurements indicated the parallel increase of the average size of free volume holes in the prepared free films. Figs. 1 and 2 illustrate that, along with the increase of DBS concentrations, both positron and *ortho*-positronium lifetimes increase. Both curves show saturation at around 10% w/w DBS concentration and above this concentration the free volume does not change significantly. The observed free volume increase might as well explain the decrease of the WP temperature. As the dibutyl sebacate concentration increases, its plasticization effect changes the originally compact structure of polymer molecules in the dispersion. The new structure implies larger free volume holes, as shown by the observed positron life-

Table 1
Dynamic surface tension values (mN/m ± S.D.) of Eudragit L 30 D dispersions containing dibutyl sebacate measured at different temperatures

Temperature (°C)	Dibutyl sebacate concentration		
	5% w/w δ (mN/m) ± S.D.	10% w/w δ (mN/m) ± S.D.	20% w/w δ (mN/m) ± S.D.
25.0	42.26 ± 0.31	38.56 ± 0.76	34.23 ± 0.72
27.5	41.81 ± 0.43	37.67 ± 0.90	33.19 ± 0.69
30.0	40.94 ± 0.96	35.57 ± 0.97	33.15 ± 0.68
32.5	40.54 ± 0.87	31.95 ± 8.13	29.42 ± 12.27
34.5	38.81 ± 2.15	–	–

Table 2
Dynamic surface tension values (mN/m ± S.D.) of Eudragit RL 30 D dispersions containing dibutyl sebacate measured at different temperatures

Temperature (°C)	Dibutyl sebacate concentration		
	5% w/w δ (mN/m) ± S.D.	10% w/w δ (mN/m) ± S.D.	20% w/w δ (mN/m) ± S.D.
25.0	41.86 ± 0.31	38.73 ± 0.87	37.95 ± 0.72
27.5	40.81 ± 0.43	37.67 ± 0.90	36.34 ± 0.59
30.0	39.94 ± 0.96	35.57 ± 0.97	33.15 ± 0.58
32.5	39.54 ± 0.87	31.95 ± 2.99	29.42 ± 2.36
34.5	37.93 ± 2.34	–	–

times. These larger holes allow more space for molecular movements and, thus, molecular groups and side chains possess larger mobility. It is assumed that this latter phenomenon leads to the decrease of the WP temperature and, moreover, enables film formation at a lower temperature.

A further similarity between free volume and surface tension measurements is provided by the saturation behavior of the respective observables. Above 10% w/w platicizer concentration no significant changes were observed in any case. Neither the WP temperature, nor the free volume changed above 10% w/w DBS. The saturation is, most probably, due to the immiscibility of the plasticizer with the polymer at higher concentrations. In previous works, the authors provided several distinct proofs for the immiscibility. It was, e.g. shown that a peak appears in X-ray diffraction patterns of cast Eudragit films above 10% w/w DBS concentration, referring to the separated plasticizer (Orbán et al., 2001). Also a remarkable enthalpy relaxation was measured at 20% w/w DBS concentration in free films of Eudragit (Zelkó et al., 2002) at the glass transition temperature, due to the enhanced molecular mobility of Eudragit.

4. Conclusions

Since, in the case of pharmaceuticals, usually the whole coating operation comes to a standstill if the coating dispersion takes the form of an opaque white mass, an accurate determination of the WP temperature has a decisive impact from the point of formulation. In the solvation of this serious technical problem dynamic surface tension measurements might be a great benefit. In the present study, the sudden increase of the standard deviation of surface tension values always coincided with the optically observable WP temperature.

The increasing plasticizer concentration decreased the WP temperature of dispersions and, parallely, increased the free volume of free films up to 10% w/w concentrations. The increased free volume allowed more space for molecular movements, thus the enhanced molecular mobility could be an underlying factor in chemical and physical instability of the Eudragit film coatings containing more than 10% w/w DBS.

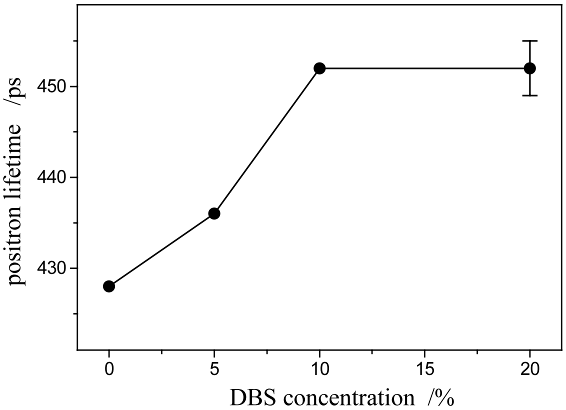

Fig. 1. The lifetime of positrons in free Eudragit films as a function of DBS concentration. Note that this lifetime component is proportional with the average electron density of the material and, consequently, also with the average free volume size.

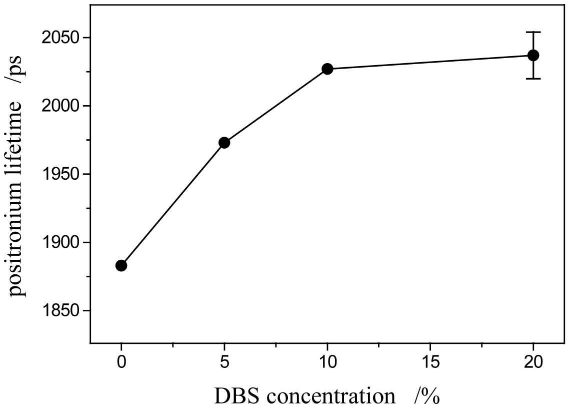

Fig. 2. The lifetime of *ortho*-positronium atoms vs. DBS concentration. The connection between this lifetime and the size of free volume holes is given by Eq. (1).

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References

Aulton, M.E., Twitchell, A.M., Hogen, J.E., 1997. Physical properties of HPMC solutions and their role in the film coating process and the quality of the coated product. In: McGinity, J.W. (Ed.), Aqueous Polymeric Coatings for Pharmaceutical Dosage Forms. Marcel Dekker, New York.

Deng, Q., Jean, Y.C., 1993. Free-volume distributions of an epoxy polymer probed by positron annihilation. Macromolecules 26, 30–35.

Domján, A., Süvegh, K., Vértes, A., 1997. o-Ps in solid materials: perturbation theory calculations. Mater. Sci. Forum 255, 251–253.

Fukumori, Y., Yamaoka, Y., Ichikawa, H., Takeuchi, Y., Fukuda, T., Osako, Y., 1988. Coating of pharmaceutical powders by fluidized bed process. IV. Softening temperature of acrylic polymers and its relation to film-formation in aqueous coating. Chem. Pharm. Bull. 36, 427–493.

Ghebre-Sellassie, I., Nesbitt, R.U., Wang, J., 1997. Eudragit aqueous dispersions as pharmaceutical controlled release coatings. In: McGinity, J.W. (Ed.), Aqueous Polymeric Coatings for Pharmaceutical Dosage Forms. Marcel Dekker, New York, pp. 267–286.

Gordon, M., Taylor, J.S., 1952. Ideal co-polymers and the second order transitions of synthetic rubbers. I. Non-crystalline copolymers. J. Appl. Chem. 2, 493–500.

ISO 2115, 1996. International Organization for Standardization, Geneva, Switzerland.

Kelley, F.N., Bueche, F., 1961. Viscosity and glass temperature relations for polymer diluent systems. J. Polym. Sci. 50, 549–556.

Kirkegaard, P., Eldrup, M., Mogensen, O.E., Pedersen, N.J., 1981. Program system for analyzing positron lifetime spectra and angular correlation curves. Comput. Phys. Commun. 23, 307–343.

Lehmann, K., 1997. Chemistry and application properties of polymethacrylate coating systems. In: McGinity, J.W. (Ed.), Aqueous Polymeric Coatings for Pharmaceutical Dosage Forms. Marcel Dekker, New York, pp. 101–176.

Lehmann, K., Dreher, D., 1973. The use of aqueous synthetic-polymer dispersions for coating pharmaceutical dosage forms. Drugs Germany 19, 126–136.

Lippold, B.C., Pagés, R.M., 2001. Film formation, reproducibility of production and curing with respect to release stability of functional coatings from aqueous polymer dispersions. Pharmazie 56, 5–17.

MacKenzie, I.K., 1983. Experimental methods of annihilation time and energy spectrometry. In: Brandt, W., Dupasquier, A. (Eds.), Positron Solid-State Physics. North-Holland, Amsterdam, p. 196.

Orbán, Á., Zelkó, R., Dredán, J., Marton, S., Rácz, I., 2001. Polymer–plasticizer interactions: comparison of experimental data with theoretical results. Hung. J. Ind. Chem. 29, 7–9.

Rácz, I., 1989. Drug Formulation. Wiley, New York.

Süvegh, K., Vértes, A., Hyodo, T., 1999. Positronium as a sensitive detector of changes in molecular structure. Adv. Mol. Struct. Res. 5, 313–357.

Süvegh, K., Klapper, M., Domján, A., Mullins, S., Vértes, A., 2000. Comparison of simulated and measured free volume distributions in polymers. Radiat. Phys. Chem. 58, 539–543.

Zelkó, R., Orbán, Á., Nagy, J., Csóka, G., Rácz, I., 2002. Coating polymer–plasticizer interaction in relation to the enthalpy relaxation of polymer. J. Therm. Anal. Calor. 68, 531–537.