

## POLYMER-PLASTICIZER INTERACTIONS: COMPARISON OF EXPERIMENTAL DATA WITH THEORETICAL RESULTS

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In the course of the formulation of coated dosage forms, selection of the suitable composition of the coating system is essential as regards dosage form. Since the systems applied for coating are multicomponent, it is highly important to quantitatively evaluate the possible interactions between the components. These interactions determine the physico-chemical stability of the formulated dosage form, the drug release process and the formulation parameters, as well. In the present study molar refraction values of polymer dispersions were determined for the quantitative estimation of polymer-plasticizer interactions. Dynamic surface tension measurements, differential scanning calorimetry and X-ray diffraction studies were applied to analyse the possible interactions between the polymer and the selected plasticizer.

The results indicate that the calculation of molar refraction values of polymer dispersions containing plasticizer offers useful means for the determination of the optimum concentration of the selected plasticizer.

**Keywords:** Eudragit aqueous dispersion; polymer-plasticizer interaction; molar refraction; X-ray diffraction; minimum film-forming temperature

### Introduction

Acrylate polymers and their derivatives, collectively known as Eudragit polymers, were the first synthetic polymers used in pharmaceutical coatings as aqueous polymeric dispersions. The physical properties of film-coating dispersions can potentially exert an influence at many stages during the film coating process [1-3]. The coating formulations usually contain many additives in addition to the polymer, therefore it is highly important to prove and quantitatively evaluate the possible interactions between the components. Among the additives that are incorporated into aqueous polymeric dispersions, the plasticizer is the most critical component that dictates proper film formation and quality of the resulting film. Incorporation of a plasticizer is recommended for Eudragit RL/RS 30D formulations due to the high glass transition temperature values of the polymers [4, 5]. For successful formation of an aqueous latex film, the minimum film-forming temperature (MFT) must be determined, since this is the lowest temperature at which a polymer emulsion forms a continuous film. The MFT of polymer emulsions have been studied by several authors [4, 6-7]. The Eudragit RS/RL 30D types possess a minimum film-forming temperature of approximately 50 and 40 °C respectively

and require the addition of between 10 and 20 %w/w of plasticizer to bring the minimum film-forming temperature down to a usable value [5].

The aim of the present study was to quantify the extent of interaction between the selected polymer and plasticizer and to confirm the obtained results with other physico-chemical — dynamic surface tension, differential scanning calorimetry, X-ray diffraction — methods. The selected methods characterize the film-forming properties of polymer systems which are of importance from the aspect of the coating process.

### Experimental

#### Materials

Eudragit RL 30 D (Röhm Pharma, Germany) aqueous film dispersions and sebacic acid dibutyl ester (dibutyl sebacate (DBS), Sigma) selected as plasticizer.

### 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 equilibration at 25-40°C for 1 hour. The temperature was continuously increased in the course of measurements to determine the minimum film formation temperature (MFT) of polymer dispersions. Measuring parameters were the following: Minimum number of cycles: 5; Minimum measuring time: 10 min; Speed up: 1 mm/min. The high standard deviations in the surface tension values within the measuring cycles referred to the film formation. The lowest temperature at the film formation started was defined as MFT.

### Film Preparation

Approximately 10 g Eudragit RL30D dispersions containing dibutyl sebacate of different concentrations were poured on a glass plate and dried in a sealed container above copper sulphate and stored at room temperature for 1 week. The obtained casted films were used for DSC and X-ray analysis.

### Determination of the Glass Transition Temperature of Casted Polymer Films by Differential Scanning Calorimetry

Approximately 2-5 mg polymer samples were sealed in closed aluminium pans and transferred to the DSC-cell of Perkin-Elmer DSC 4 instrument. After a primary cooling to -30°C, the samples were heated to 150°C and the glass transition temperature was determined using peak-analysis from the first derivative of the measured heat flow. The heating and cooling rates were always 20°C/min.

### X-Ray Diffraction (XRD) Measurements

XRD patterns of casted Eudragit films were taken with a computer-controlled Diffractometer (Philips Analytical X-Ray, type: PW1840). The measuring parameters were the following: Tube anode: Cu, Generator tension: 30 kV, Generator current: 30 mA, Wavelength Alpha1: 1.54056, Wavelength Alpha2: 1.54439, Intensity ratio (alpha2/alpha1): 0.500.

### Determination of the Refractive Index of Polymer Dispersions

The refractive indexes of various Eudragit dispersions

without and in the presence of plasticizer were determined at  $24 \pm 1^\circ\text{C}$  applying Abbe Refractometer. Preceding the measurements each sample was thoroughly stirred. In spite of the fact that the examined samples were polymer latex dispersions, the sample preparation and the determination of the refractive index were reproducible without any problem.

### Calculation of the Molar Refraction by the Lorenz-Lorenz Equation

The following equation was used for the determination of molar refraction values (R):

$$R = \frac{M}{d} \frac{n^2 - 1}{n^2 + 2} \quad (1)$$

where  $n$  is the determined refractive index,  $M$  is the molecular weight and  $d$  is the density of the examined material [8]. The molar refraction is an additive property. Due to the additive characteristic of molar refraction, the molar refraction of Eudragit dispersions containing dibutyl sebacate can be calculated by adding up the molar refraction values of each component of the system. The difference between the measured and the calculated molar refraction values of the examined polymer-plasticizer systems could refer to the nature and extent of polymer-plasticizer interaction.

## Results and discussion

Table 1 summarizes the measured ( $R_m$ ) and the calculated ( $R_c$ ) molar refraction values of Eudragit RL 30D dispersions containing dibutyl sebacate of different concentrations. Since the molar refraction is an additive property, the molar refraction of Eudragit RL 30D coating dispersions was obtained by adding the molar refraction values of Eudragit RL 30D and that of the dibutyl sebacate. The obtained results show that along with the increase of dibutyl sebacate concentration, the differences between the measured and calculated molar refraction values also increased. At 20%w/w plasticizer concentration the calculated molar refraction difference is higher with a magnitude than that of the difference calculated at 10%w/w plasticizer concentration. The reason of this phenomena could be the immiscibility of dibutyl sebacate with Eudragit RL 30D at higher than 10%w/w concentrations.

Table 2 illustrates the minimum film formation temperature values of the same systems analysed by dynamic surface tension measurements. The results indicate that the increasing plasticizer concentration decreased the minimum film formation temperature, but above 10%w/w dibutyl sebacate concentration no significant MFT changes were seen. The obtained MFT values leveled out to constant value with the increasing DBS concentration which also refers to the immiscibility of the selected plasticizer in the polymer

Table 1 Measured ( $R_m$ ) and calculated ( $R_c$ ) molar refraction values of different Eudragit RL30D - dibutyl sebacate systems (average values,  $n=6$ ,  $RSD < 5\%$ )

Dibutyl sebacate concentration (%w/w)	$R_m$	$R_c$	$(R_m - R_c)/R_m$
0	6547.87	—	—
5	6554.61	6551.09	0.0001
10	6599.05	6560.43	0.006
20	6860.70	6568.23	0.043

Table 2 Minimum film-forming temperature values (MFT) of Eudragit RL30D dispersions containing dibutyl sebacate of different concentrations (average values,  $n=6$ ,  $\pm S.D.$ )

Dibutyl sebacate concentration (%w/w)	MFT ( $^{\circ}C$ )
0	$36.5 \pm 0.5$
5	$34.5 \pm 1.0$
10	$32.0 \pm 1.0$
20	$32.0 \pm 1.0$

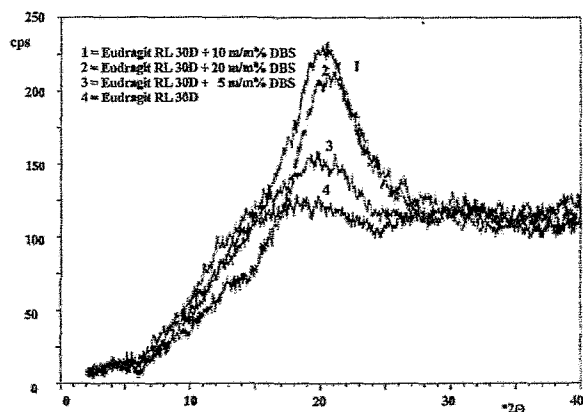


Fig. 1 X-ray Diffraction pattern of Eudragit RL 30D casted films containing dibutyl sebacate of different concentrations

dispersion above 10%w/w plasticizer concentration. The latter is in good compliance with the molar refraction results, calculated by the Lorenz-Lorenz relationship. Authors previous results indicate that not only the MFT values did not significantly change above 10%w/w plasticizer concentration but the glass transition values of casted polymer films, either [9]. The X-ray diffraction pattern of casted Eudragit films (Figure 1) shows that in the presence of 10 and 20 %w/w dibutyl sebacate concentration a peak appears indicating the separated plasticizer.

## Conclusions

Information can be obtained from the calculation of molar refraction values of Eudragit dispersions containing plasticizer concerning the extent of interaction between the polymer and the plasticizer. The theoretical results based on the calculation of molar refraction values of the selected polymer-plasticizer system were in good compliance with the results of applied physico-chemical methods that characterize the film-forming behaviour of polymers.

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## REFERENCES

1. LEHMANN K. and DREHER D.: *Drugs Made in Germany*, 1973 19, 126-136
2. MCGINITY J. W. (Ed): *Aqueous Polymeric Coatings for Pharmaceutical Dosage Forms*, Marcel Dekker, Inc., New York-Basel-Hong Kong, pp. 267-286, 1997
3. MUSKÓ Zs., PINTYE-HÓDI K., SZABÓ-RÉVÉSZ P., KÁSA P. JR., ERŐS I. and DEÁK D.: *Hung. J. Ind. Chem.*, 2000, 28, 111-115
4. FUKUMORI Y., YAMAOKA Y., ICHIKAWA H., TAKEUCHI Y., FUKUDA T., and OSAKO Y.: *Chem. Pharm. Bull.* 1988, 36, 427-493
5. COLE G., HOGAN J. and AULTON M.: *Pharmaceutical Coating Technology*, Taylor & Francis Ltd, T.J. Press Ltd, Padstow, p. 304, 415, 1995
6. BRODNYAN J. G. and KONEN T.: *J. Appl. Polym. Sci.* 1964, 8, 687-697
7. BERTHA S. L. and IKEDA R. M.: *J. Appl. Polym. Sci.* 1971, 15, 105-109
8. NEUMÜLLER O. A.: *Römpps Chemie-Lexikon*, Franckh'sche Verlagshandlung, Kosmos-Verlag, Stuttgart, 7. Auflage, IV. Vol., p. 74, 1977 (in Hungarian)
9. ORBÁN Á., ZELKÓ R., DREDÁN J., BALOGH E., MARTON S. and RÁCZ I.: *Investigation of Polymer-plasticizer Interactions in Relation to Drug Release from Film-coated Pellets*. Proceedings of the 3<sup>rd</sup> World Meeting APV/APGI, Berlin, 901-902, 2000