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COATING POLYMER-PLASTICIZER INTERACTION IN RELATION TO THE ENTHALPY RELAXATION OF POLYMER

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Abstract

In the course of the formulation of coated dosage forms, the selection of the suitable composition of the coating system is of great importance in respect of the final dosage form. Since the applied coating systems are multicomponent, the possible interactions between the components determine the physico-chemical stability of the formulated dosage form, the drug release process, as well as the formulation parameters. In the present study, the influence of the applied plasticizer, dibutyl sebacate on the enthalpy relaxation of casted Eudragit L 30D films was determined as a function of the plasticizer concentration. The enthalpy relaxation was recorded by DSC during the applied isothermal recovery process of Eudragit films. The obtained results indicate that enthalpy relaxation can be measured by DSC at 20 mass/mass% dibutyl sebacate concentration, which refers to the increased molecular mobility consequently to the effect of the interaction between the polymer and plasticizer.

Keywords: dibutyl sebacate, enthalpy relaxation, Eudragit L 30D, interaction

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, 2]. 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 [3]. For a plasticizer to be effective, it must be able to diffuse into and interact with the polymer and have minimal or no tendency for migration or exudation from the polymer. If a plasticizer does not remain in the film, then changes in the chemical and/or physical-mechanical properties of the polymeric material could result. In vitro dissolution studies with cast films of Eudragits have demonstrated that

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water-soluble plasticizers were leached more readily from the film when the level of hydrophilic polymer in the film was increased [4]. Therefore the selection of a plasticizer by the pharmaceutical scientist for a film-coating formulation is a very important decision in order to develop and optimize the stability and drug release properties of a pharmaceutical dosage form. The plasticizers can affect the long term performance of amorphous polymers in pharmaceutical dosage forms due to a reduction of glass transition temperature (T_g). It can be considered as that temperature at which the hard glassy form of an amorphous or largely amorphous polymer changes to a softer, more rubbery consistency [5, 6]. The T_g influences many physical properties of coating polymers including: elasticity, adhesion, viscosity, solvent release and permeability [7]. It has been repeatedly proved that the ageing of amorphous polymers is controlled by the type and the rate of their characteristic molecular motion. Volume relaxation and enthalpy relaxation are two phenomena of the physical ageing process, which describe the time dependent changes of an amorphous polymer held at temperatures below its T_g. By use of differential scanning calorimetry (DSC) the structural relaxation in amorphous polymers can be investigated with a high reproducibility. In some practical applications, including operational lifetime prediction, characterization of enthalpy relaxation by DSC has proved useful. These measurements are often referred to as ‘aging experiments’. It can be readily appreciated that whilst these molecular motions in the glassy region below T_g are relatively slow in normal experimental terms they can still have a profound influence over the life-time of a typical pharmaceutical product which is usually of the order of a few years. The failure to recognise the effects of these time-scale differences on the behaviour of amorphous systems may explain why many accelerated stability tests performed in the laboratory provide unrealistic predictions of the stability of pharmaceutical dosage forms stored under ambient conditions for much longer periods of time [6]. During a DSC experiment a polymer sample is subjected to thermal history, starting at a temperature above the glass transition temperature, involving periods of heating and cooling at constant rates as well as isothermal stages and finishing at a temperature in the glassy state. The obtained heat capacity (C_p, J g^{-1} K^{-1}) *vs.* temperature (T) curve depends on the thermal history of the sample and contains information about structural relaxation, which occurred both in the process prior to the thermal analysis and during the measuring scan itself [8].

Authors previously calculated the molar refraction values of polymer dispersions containing plasticizer to quantitatively characterize the polymer-plasticizer interaction and to determine the optimum concentration of the selected plasticizer [9].

The purpose of this work was to study the influence of dibutyl sebacate on the enthalpy relaxation of casted Eudragit films and to get information from the thermal history of the sample for the extent of polymer-plasticizer interaction.

Experimental

Materials and methods

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

Film preparation

Approximately 10 g Eudragit L 30D dispersions containing dibutyl sebacate of different concentrations (0, 5, 10 and 20 mass/mass%) were poured on a glass Petri dishes (diameter=10 cm) and dried in a sealed container above copper sulphate and stored at room temperature for 1 week. 2–5 mg of the obtained cast films were used for DSC analysis.

Thermal analysis

The glass transition temperature (T_g) and the enthalpy relaxation of the films were determined using a differential scanning calorimeter (DSC 2920, TA Instruments, New Castle, DE, USA) equipped with a liquid nitrogen cooling accessory. Prior to the analysis, the aluminium pans were weighed, sealed and transferred to the DSC-cell.

In all experiments, the heating and cooling rate was set at 20°C min^{-1}. An 'expanded cooling/heating' procedure was used to determine the glass transition temperature and the enthalpy relaxation. The samples were subjected to thermal history including an isothermal stage at a temperature 15°C below the T_g (ageing temperature) for 30 min (ageing time). The temperature profile of this procedure enabled to quantify the molecular mobility of the polymer during the isothermal phase. The glass transition temperature was determined using peak-analysis from the first derivative of the measured heat flow during the last heating cycle (Figs 1–4). The enthalpy re-

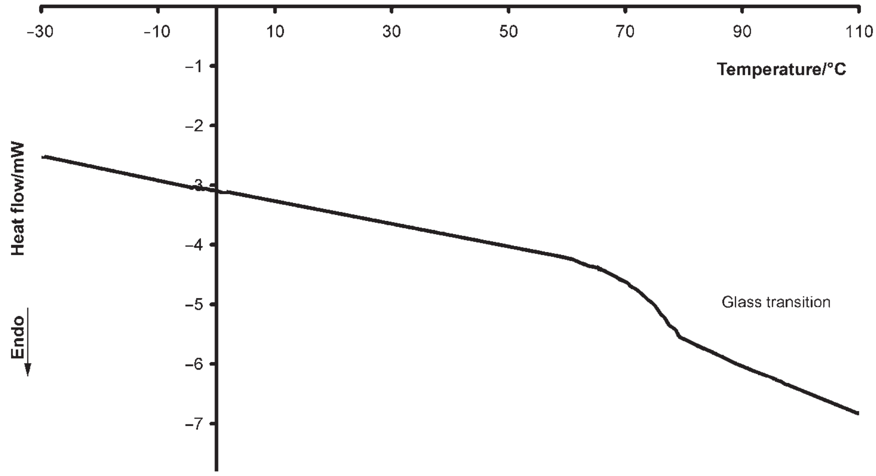

Fig. 1 DSC curve (recorded after the isothermal stage) of Eudragit L 30D film

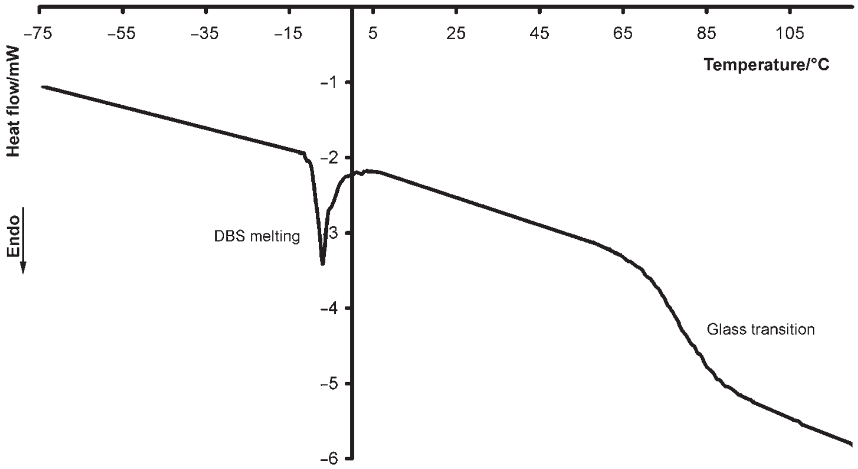

Fig. 2 DSC curve recorded after the isothermal stage of Eudragit L 30D film containing 5 mass/mass% dibutyl sebacate

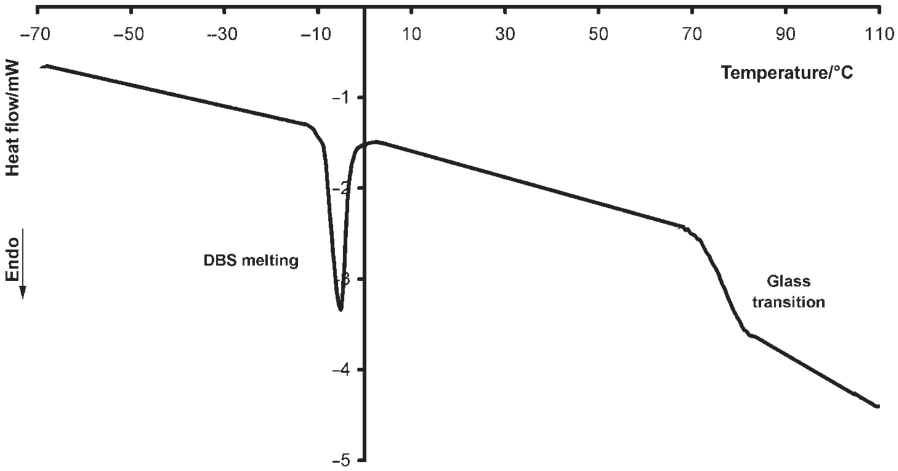

Fig. 3 DSC curve recorded after the isothermal stage of Eudragit L 30D film containing 10 mass/mass% dibutyl sebacate

laxation (ΔH_{∞}; mJ g^{-1}) was characterised by the area under the endothermic peak, associated with the glass transition phenomenon observed during this final cycle.

Expanded cooling/heating scan for the determination of the enthalpy relaxation was the following:

1. Cooling to –50°C, cooling rate: 20°C min^{-1}
2. Heating to T_g–15°C, heating rate: 20°C min^{-1}
3. Isothermal stage: T_g–15°C, period: 30 min
4. Cooling to –50°C, cooling rate: 20°C min^{-1}
5. Heating to 160°C, heating rate: 20°C min^{-1}

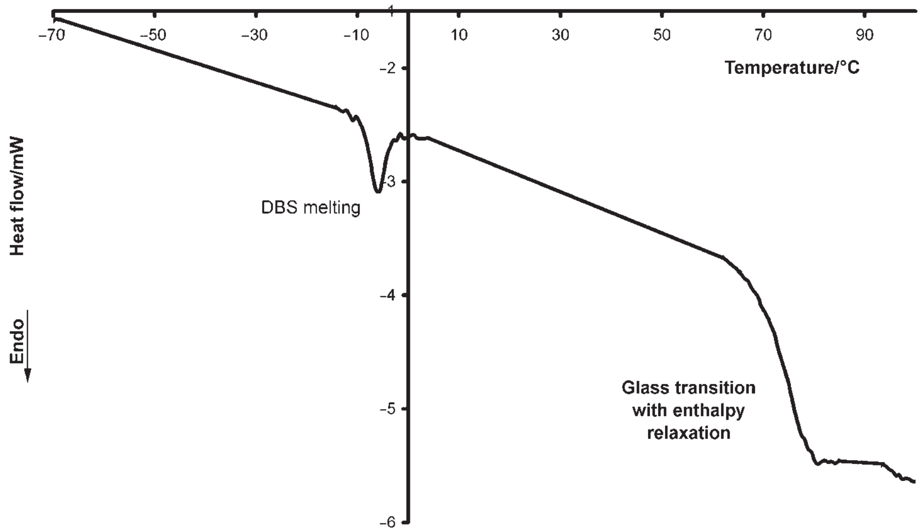

Fig. 4 DSC curve recorded after the isothermal stage of Eudragit L 30D film containing 20 mass/mass% dibutyl sebacate

Results and discussion

Figures 1–4 illustrate the measured heat flow during the final heating run after the samples were kept in isotherm conditions at temperature 15°C below T_g for 30 min and Table 1 summarizes the characteristic values of glass transition of different Eudragit samples. The results indicate that the presence of dibutyl sebacate did not remarkably alter the glass transition temperature of cast Eudragit L 30D polymer films. In the case of 20 mass/mass% plasticizer content relaxation endotherm was observed, under the given experimental conditions, at the glass transition (Table 1 and Fig. 4) which refers to the improved molecular mobility. It is assumed that as the dibutyl sebacate concentration increases there is an increase in the free volume of the polymer as thus the total volume occupied by a given number of molecules will increase. This will allow more movement of molecular groups and side chains. Table 2 summarizes the characteristic values of crystallization and melting of dibutyl sebacate. The obtained endotherm peaks (Figs 2–4) refer to the melting of the crystallized DBS in the course of the heating phase of the program. The melting peak of DBS measured at –5.6 (±1.5°C) and the calculated melting enthalpy was proportional to the plasticizer concentration in the polymer dispersion up to 10 mass/mass% concentration (Table 2), but above this value (20 mass/mass% concentration) it was not proportionally increased (Fig. 4, Table 2). The reason of this phenomenon could be the immiscibility of dibutyl sebacate with Eudragit L 30D at 20 mass/mass% concentration. The latter is in good compliance with the previous results [9] calculated by the molar refraction values on the basis of the Lorenz–Lorenz relationship [10].

Table 1 Characteristic values of glass transition of different Eudragit L 30D samples (average of two parallels)

Sample	Onset/ °C	Inflection/ °C	Endpoint/ °C	ΔC_p/ J g^{-1} K^{-1}	ΔH_∞/ J g^{-1}
Eudragit L 30D without plasticizer	68.7	75.5	82.6	0.31	–
Eudragit L 30D +5 mass/mass% DBS	67.7	76.9	88.4	0.45	–
Eudragit L 30D +10 mass/mass% DBS	69.8	77.0	82.1	0.41	–
Eudragit L 30D +20 mass/mass% DBS	67.2	74.2	77.9	0.44	0.50

Table 2 Characteristic values of the crystallisation and the melting of dibutyl sebacate (average of two parallels)

Sample	Crystallisation peak/°C	ΔH/ J g^{-1}	Melting peak/ °C	ΔH/ J g^{-1}
Eudragit L 30D +5 mass/mass% DBS	–20.4	1.8	–7.0	2.2
Eudragit L 30D +10 mass/mass% DBS	–19.7	3.7	–5.6	3.5
Eudragit L 30D +20 mass/mass% DBS	–21.1	0.7	–5.6	1.0

Conclusions

Interaction was observed between Eudragit L 30D and dibutyl sebacate and it was confirmed by the enthalpy relaxation values measured by differential scanning calorimetry at the glass transition temperature of cast Eudragit films commonly applied for film coating procedures. The enhanced molecular mobility of the coating polymer along with the immiscibility of the plasticizer at 20 mass/mass% dibutyl sebacate concentration, confirmed by DSC, could be an underlying factor in chemical and physical instability of the examined Eudragit film coatings.

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