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THERMOANALYTICAL BEHAVIOUR OF SOME COATING FREE FILMS

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Differential scanning calorimetry (DSC) was used in the investigation of the behaviour of coating free films. The films were produced from two film-forming polymers which are chemically different but equally used for producing controlled-release dosage forms: Eudragit NE 30 D (synthetically produced polymethacrylate copolymer) and LustreClear product (mixture containing natural and semi-synthetic components: microcrystalline cellulose, hydroxy-ethyl cellulose, carrageenan and polyethylene glycol). During their comparative analysis the characteristic parameters of the DSC curves obtained with dynamic measurement method were used and their changes as a function of storage conditions and storage time were observed. It was found that the thermoanalytical behaviour of the examined methacrylate-based Eudragit NE and cellulose-based LustreClear films was different. The specific enthalpy change of Eudragit NE fresh films was very little, but it increased considerably during storage. The specific enthalpy change of LustreClear films was much greater but its value shows only a slight further increase during storage. The results obtained help to choose the proper temperature for coating and drying.

Keywords: *carrageenan, DSC, Eudragit NE 30 D, free films, LustreClear, methacrylate copolymer, microcrystalline cellulose, storage conditions*

Introduction

Drug release from dosage forms can be influenced in several ways, and the examination of thermal behaviour is frequently justified [1, 2]. Film coating has been widely used in controlled-release dosage forms [3, 4], this is a widespread method for protection, retardation and identification.

The long-term stability of these controlled-release dosage forms is one of the major concerns of pharmaceutical scientists. Film coats are used widely [4, 5], but their thermoanalytical behaviour is known little [6], considerably more research has been focused on the thermal behaviour of active agents [7, 8].

The development of purely water-based Eudragit dispersions back in 1972 represented a major improvement in processing conditions and opened up many new applications. These dispersions were obtained by emulsion polymerization. In process, the polymer is precipitated from the monomer units emulsified in water in the form of water-insoluble, submicroscopic latex particles ranging from 0.01 to 1 μm in diameter. The resultant polymer dispersions have high solids contents of 30 to 40%, are very low in viscosity and easy to process.

These materials can be used for the preparation of matrix tablets, controlled-release buccal patches, controlled-release floating pellets, topical delivery systems and combination colonic drug delivery systems. The stability of such coating materials under very different circumstances therefore is very important.

The Eudragit NE 30 D polymer is not soluble in the gastrointestinal tract, but is permeable for different active agents. Eudragit NE 30 D aqueous dispersion is a commonly used coating material, which contains methacrylate copolymers as film-forming agent and nonoxynol 100 as an endogenous emulsifier with a melting point of 58–59°C.

It is known that this endogenous surfactant can crystallize during storage, which can alter the dissolution profile of the active agent: the crystallization of the emulsifier increases the number of holes on surface of film [9–11].

Although a temperature of 5–25°C is prescribed by the manufacturer for the storage of the dispersion, in the case of the final product it may happen that the film-coated product is exposed to different conditions (higher temperature) during storage or transport. The changes influence the mechanical strength of the diffusion film, its permeability, penetrability for the liquid, swelling in the digestive juices, which all have an effect on the value of drug release, so the study of storage conditions is especially important.

Cellulose derivatives, semi-synthetic and other natural substances belong to another group. Cellulose derivatives only soften at higher temperatures, their films are less sticky, but also porous, and therefore they are more likely to need a copious amount of plasticizer. Moreover, cellulose esters are more prone to hydrolysis, which changes their solubility properties.

LustreClear microcrystalline cellulose (MCC)/ carrageenan-based coating system is used as an aque-

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ous, clear-film coating on tablets and other solid-dosage forms. LustreClear uses a breakthrough technology based on the unique combination of microcrystalline cellulose (MCC) and carrageenan (a natural hydrocolloid) [12].

The aim of our work was to perform the comparative thermoanalytical examination of the films prepared from the two different polymers, with special respect to studying the effect exerted by the plasticizers used in them and by the storage conditions. The results obtained during the examination of free films are suggestive of the behaviour of the coating of the solid dosage forms during storage, which is of decisive importance with respect to drug release.

Experimental

Materials

Coating materials

Eudragit NE 30 D (Degussa-Röhm, D), and LustreClear® (FMC Biopolymer, USA) products were used for the studies.

The Eudragit NE 30 D product is an aqueous dispersion with nonoxynol 100 serving as an endogenous emulsifier and at the same time plasticizer [13].

LustreClear is a powdered product which contains Carrageenan (film-forming), hydroxyethyl cellulose (secondary film-forming), polyethylene glycol (plasticizer) and microcrystalline cellulose (dispersion aid) in the form of a physical powder mix.

As both materials contain a plasticizing component, there is no need for adding further plasticizer in the course of the production of coating films.

Composition of coating aqueous dispersions were:

Eudragit® NE 30 D

Eudragit NE 30 D	75.24 g
Dimeticon E	5.80 g
Colloidal silica, anhydrous	0.44 g
Ethanol	18.68 g
Talc	3.34 g
Distilled water	86.74 g

LustreClear®

LustreClear	27.0 g
Distilled water	273.0 g

Methods

Production of free films

The films were produced with spraying. The dispersion was sprayed on a rotating teflon surface (Eudragit NE 30 D) or on a rotating glass plate (LustreClear). The spraying conditions were the following: the nozzle diameter was 0.8 mm, the pressure of the spraying air was 0.8 bar, and the temperature of the drying air was 25–30°C (Eudragit NE) or 30–35°C (LustreClear). The different films had approximately the same thickness.

Storage conditions

The free films were examined after drying at room temperature for 24 h (fresh), then they were stored under various conditions: in an exsiccator (at 25°C 35 RH%) or hygrostat (at 25 and 40°C with a relative humidity content of 60 and 75%, respectively).

Examination of thermal behaviour

The thermoanalytical examinations were carried out with the Mettler Toledo 821^e instrument with a dynamic method in the interval of 0–100°C, at a heating rate of 2°C min^{-1}. Small pieces of free films (about 10 mg) were weighed and put into the sample pans. The data were calculated from the average of three parallel measurements and were evaluated with STAR^e 6.01 Software.

Indium and zinc were used for calibration. To check the temperature and heat flow accuracy of a DSC modules indium (for the low temperature) and zinc (for the high temperature) were selected.

Results and discussion

Examination of fresh films

Figure 1 shows the thermal behaviour of spray-dried free films. Eudragit NE 30 D films show a smaller endothermic peak at a peak temperature of 53.04°C, indicating the presence of nonoxynol 100, which is used also as a plasticizer in the film-forming liquid disper-

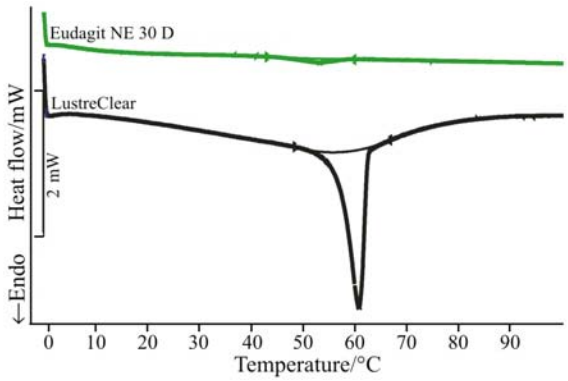

Fig. 1 DSC curves of Eudagit NE 30 D and LustreClear fresh films

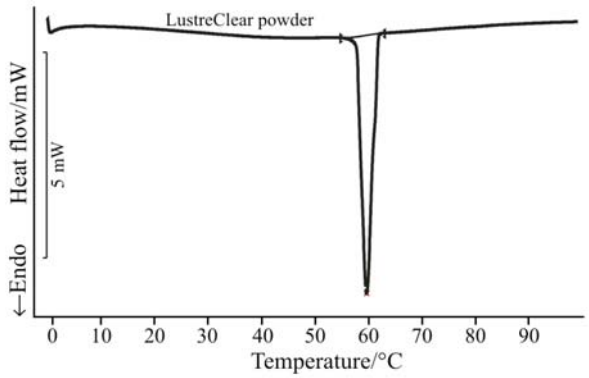

Fig. 2 DSC curves of LustreClear powder

sion and is not built in the structure of the film [13]. In the case of LustreClear films the intensive endothermic peak appears at a peak temperature of 59.87°C, which corresponds to the melting point of polyethylene glycol, used as a plasticizer in the LustreClear powder. The same peak can be measured during the examination of LustreClear film-forming powder, which is presented in Fig. 2, as this is the only material in the composition which can be expected to have a marked endothermic peak.

The thermoanalytical properties of fresh Eudragit NE 30 D and LustreClear films and the LustreClear powder are summarized in Table 1. The comparison of the data reveals that the parameters describing the endothermic peaks show little difference with the exception of specific enthalpy change, which is orders of magnitude smaller in the case of the Eudragit NE film.

Effect of storage on Eudragit NE 30 D films

From among the curves obtained during the thermoanalytical examinations the fresh, 1-week, 2-week and 4-week curves of Eudragit NE 30 D film stored in an exsiccator are presented in Fig. 3.

It is clear that the endothermic peak measurable at about 52°C is very small after preparation, but during storage it becomes more and more intensive because of the recrystallisation of nonoxynol. This value of specific enthalpy (ΔH) change increases considerably, with the exception of storage at 40°C/75 RH%. This change was the most pronounced in the case of films stored in the exsiccator. In the case of films stored at 40°C/75 RH%, a greater quantity of adsorbed humidity is built in among the structural elements of the film preventing the crystallization of water-soluble nonoxynol 100, so compared to the fresh sample the value of specific enthalpy does not change even during storage. As the mass of the films did not change considerably during storage, in this case the small enthalpy change can be explained only by the fact that humidity is incorporated among the macromolecules to a greater extent, thus it is present primarily as bound water and not as a solvent. In this way nonoxynol cannot undergo extensive crystallization. Similarly, the enthalpy increase measured during storage indicates the role of bound and unbound water and at the same time the crystallization of nonoxynol.

The thermoanalytical data summarised in Tables 2–4 reveal that the other parameters remained practically unchanged.

Effect of storage on LustreClear films

It is obvious from the data of the thermoanalytical properties of the LustreClear film that the area under the endothermic peak is much greater but its value shows only a slight further increase during storage (Fig. 4). PEG, used as a plasticizer in LustreClear films in pharmaceutical industry, cannot be built in completely into the film over a certain concentration, it forms a separate phase, as a result of which an endothermic peak appears in the DSC curve at about 60°C.

On the basis of the summary of results in Tables 5–7 it can be stated that an increase can be measured in the change of specific enthalpy during storage in the exsiccator, but the values of the other parameters characterising the peak remain practically unchanged in this case, too.

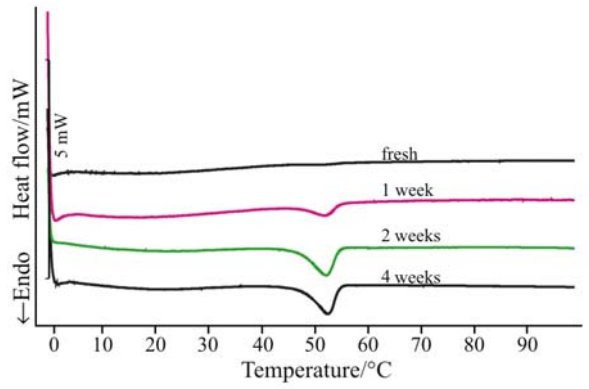

Fig. 3 DSC curves of Eudagit NE 30 D films (storage: exsiccator)

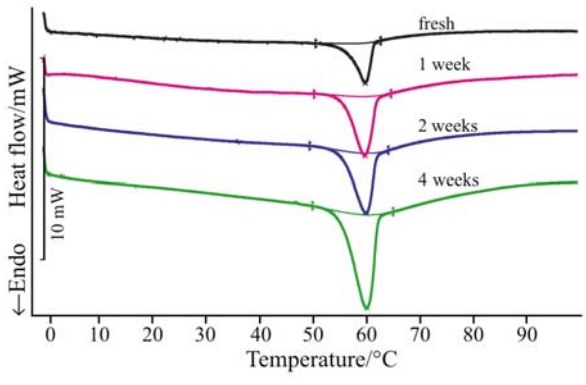

Fig. 4 DSC curves of LustreClear films (storage: exsiccator)

Table 1 Fresh free films and LustreClear powder

	Fresh free films		Powder
	Eudragit NE 30 D	LustreClear	LustreClear
ΔH/J g^{-1}	0.64	42.02	67.23
Peak/°C	53.04	59.87	59.96
Onset/°C	48.41	56.73	58.29
Endset/°C	56.75	61.59	62.32

Table 2 Storage of Eudragit NE 30 D films: exsiccator (25°C/35 RH%)

	1 week	2 weeks	4 weeks
ΔH/J g^{-1}	1.72	5.25	7.00
Peak/°C	52.57	52.85	53.16
Onset/°C	48.07	47.76	48.55
Endset/°C	55.29	55.27	55.30

Table 3 Storage of Eudragit NE 30 D films: 25°C/60 RH%

	1 week	2 weeks	4 weeks
ΔH/J g^{-1}	6.18	6.46	7.23
Peak/°C	52.70	53.00	52.89
Onset/°C	47.65	48.26	48.37
Endset/°C	55.26	56.02	55.82

Table 4 Storage of Eudragit NE 30 D films: 40°C/75 RH%

	1 week	2 weeks	4 weeks
ΔH/J g^{-1}	0.69	0.90	1.03
Peak/°C	57.61	57.90	58.50
Onset/°C	54.22	54.40	55.57
Endset/°C	59.96	60.40	60.37

Table 5 Storage of LustreClear films: exsiccator (25°C/35 RH%)

	1 week	2 weeks	4 weeks
ΔH/J g^{-1}	41.94	46.50	46.66
Peak/°C	59.85	58.97	59.48
Onset/°C	56.45	55.61	55.93
Endset/°C	61.36	60.97	61.51

Table 6 Storage of LustreClear films: 25°C/60 RH%

	1 week	2 weeks	4 weeks
ΔH/J g^{-1}	48.86	45.38	45.68
Peak/°C	59.62	59.24	59.66
Onset/°C	54.99	55.83	55.95
Endset/°C	61.34	61.30	62.23

Table 7 Storage of LustreClear films: 40°C/75 RH%

	1 week	2 weeks	4 weeks
ΔH/J g^{-1}	52.98	50.65	51.58
Peak/°C	59.86	59.99	60.07
Onset/°C	55.99	55.74	55.61
Endset/°C	62.11	62.03	62.30

In the case of films stored at 40°C/75 RH% the greater quantity of adsorbed humidity is built in among the structural elements of the film and thus prevents PEG from building in the structure, and a more gradual crystallization of PEG takes place during storage compared to the fresh sample, which results in the increase of the values of specific enthalpy.

Conclusions

The thermoanalytical behaviour of the examined methacrylate-based Eudragit NE and cellulose-based LustreClear films was different. The specific enthalpy change of Eudragit NE fresh films was very little.

In the case of Eudragit this value increased during storage, except for the films stored at 40°C/75 RH%.

In the case of LustreClear free films only the values of specific enthalpy change showed a difference compared to the fresh films. The other parameters remained practically unchanged during storage.

On the basis of the results it can be established that the thermoanalytical behaviour of films is influenced not only by storage time but also by temperature and humidity content. The results obtained help us to choose the proper temperature for coating and drying.

Concerning Eudragit NE 30 D films, the greatest change in the thermoanalytical parameters was observed in the case of storage in an exsiccator, that is in a space with low humidity, while the smallest change was recorded for samples stored at 75 RH%. However, lower humidity is more favourable for LustreClear films with respect to preventing structural changes in the film.

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