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X-Ray diffraction, differential scanning calorimetry and thermogravimetry combined with infrared analysis of freeze-dried prednisolone hemisuccinate

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In this study, the thermal behaviour of freeze-dried prednisolone hemisuccinate (Prednisolut®) was investigated by means of X-ray scattering, differential scanning calorimetry (DSC) and fourier transformation infra-red analysis (FT-IR).

1. Introduction

The use of glucocorticoids like prednisolone and prednisolone esters as prodrugs has often been described [1, 2]. These drug substances often exist in several crystal and amorphous forms, including solvates. The present form is important with regard to the physical and chemical stability [3, 4]. The study of the crystallinity of prednisolone has confirmed polymorphic forms [4, 5]. The thermal behaviour of prednisolone, prednisolone acetate and prednisolone meta-sulfobenzoate was investigated [4], and the crystal form has been defined as polymorphic and pseudo-polymorphic forms. From the pharmacopeias, USP and PhEur, it is known that prednisolone as well as the esters of prednisolone decompose at higher temperatures [6, 7]. However, nothing is known so far about the decomposition products. The objective of this work was to investigate the thermal behaviour of freeze-dried prednisolone hemisuccinate (Prednisolut®).

2. Investigations, results and discussion

Three analytical techniques, X-ray scattering, differential scanning calorimetry (DSC) and combined thermogravimetry (TG)/fourier transformation infra-red analysis (FT-IR) were used to characterize pharmaceutical product studied. The TG/FT-IR was used to clearly interpret the DSC thermograms and to differentiate reversible changes from irreversible changes (volatilization, decomposition, chemical reactions). This method should provide an uneqivocal identification of the phenomena revealed by DSC [8–10].
The X-ray scattering experiments suggest the existence of an amorphous form of freeze-dried prednisolone hemisuccinate. Diffraction patterns are shown in Fig. 1.
The DSC thermogram shows four peaks representing water loss (98.4 °C) and three peaks (181.3 °C, 229.5 °C, 346.0 °C) evaluated as a result of chemical reactions as described below. The glass transition temperature for the freeze-dried amorphous prednisolone hemisuccinate (Prednisolut®) was found to be 148.9 °C (Fig. 2).

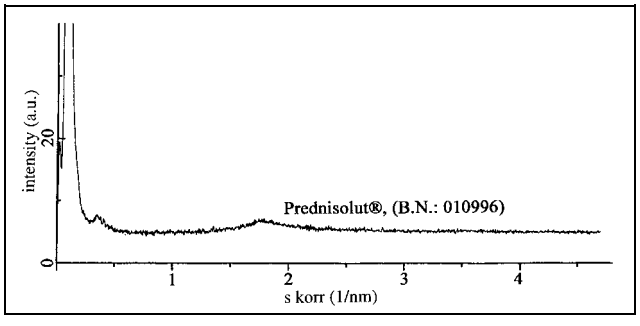

Fig. 1: X-ray diffraction pattern of Prednisolut® (B. N.: 010996)

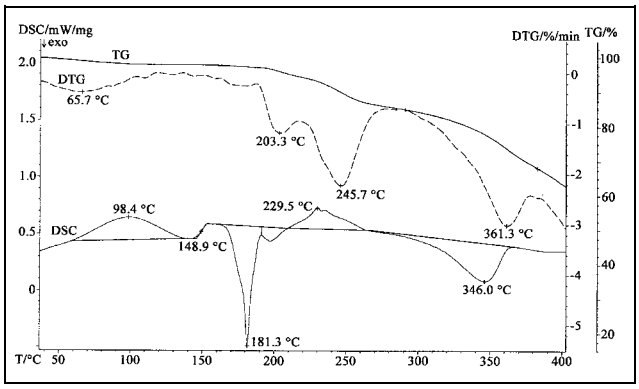

Fig. 2: DSC thermogram and TG analysis of Prednisolut® (B. N.: 010996)

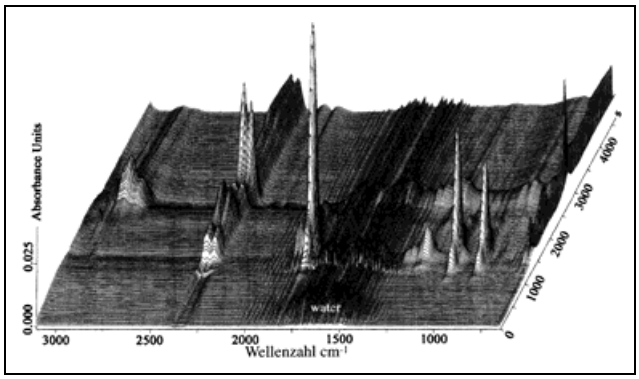

Fig. 3: TG/FT-IR data set of Prednisolut® (B. N.: 010996)

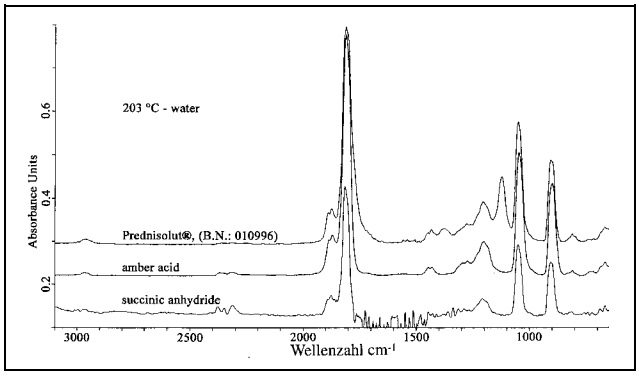

Fig. 4: IR data set of Prednisolut® (B. N.: 010996) versus IR data sets from spectral libary (amber acid, succinic anhydride) at 203 °C

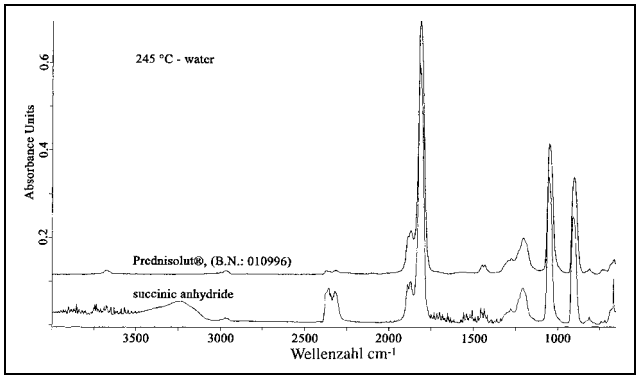

Fig. 5: IR data set of Prednisolut® (B. N.: 010996) versus IR data set from spectral libary (succinic anhydride) at 245 °C

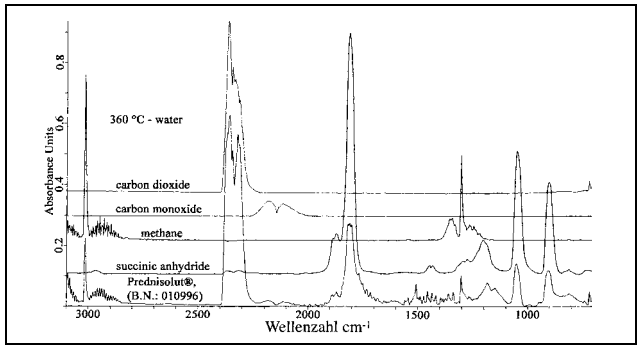

Fig. 6: IR data set of Prednisolut® (B. N.: 010996) versus IR data sets from spectral libary (methane, succinic anhydride, carbon dioxide, carbon monoxide) at 360 °C

The mass loss was additionally characterized by means of TG/FT-IR on the basis of IR spectra of the evolved gases. The temperature ranges for loss of water, carbon dioxide and volatile compounds were identified using selected regions of wavelength.

FT-IR detection of the evolved gases put out at 25–400 °C, shows water at 65 °C by the presence of 3 peaks (500 s, 1500 s, 2500 s) at 1300–1750 cm^{-1}.

To identify the unknown volatile compounds between 150–400 °C, the resultant spectra were compared with those found in a search of vapor-phase IR spectral libary. The following compounds were identified: amber acid, succinic anhydride (203 °C), succinic anhydride (245 °C) and methane, succinic anhydride, carbon dioxide, carbon monoxide (360 °C) [11].

The two selected analytical techniques – DSC and combined thermogravimetric and IR analysis – demonstrate the utility of these analytical methods in the determination of glass transitions, characterization of desolvation and degradation processes of freeze-dried prednisolone hemisuccinate (Prednisolut®) as well as in the study of polymorphic transformations and crystallizations.

The results afford an unequivocal identification of DCS peaks of freeze-dried prednisolone hemisuccinate (Prednisolut®), enabling the identification of the glass transition temperature and of irreversible changes.

3. Experimental

3.1. Instrumentation

Wide-angle X-ray scattering was performed using an URD 63 diffractometer. The source of radiation was the CuKalpha line with a wavelength of 1.5418 Å filtered with Ni.

DSC measurements were carried out using Netzsch DSC-200 and the software Netzsch SW/xx/56x.01. The heating rate was 10 K/min, and between 20 °C and 400 °C were applied. The characteristic onset, peak maximum and conclusion temperatures were determined.

For the TG/FT-IR measurement a Netzsch TG 209 system coupled with a Bruker Optik GmbH Vector 22 fourier transform (FT-IR) spectrophometer was used. Nitrogen was used as carrier gas (20 ml/min). The sample was subjected to 26–400 °C at 10 K/min. The freeze-dried sample mass was 4.310 mg. The recorded resolution of the IR spectra was 4 cm^{-1}. The spectra were differentiated by their IR absorption profiles of 650–5000 cm^{-1}. Experiments were run at a TG ramp of 10 K/min from ambient to 800 °C [11].

3.2. Materials and agents

Prednisolut® (B. N.: 010996) was obtained from Jenapharm GmbH & Co. KG. Nitrogen was obtained from Air Liquide, Böhlen.

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