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THERMAL STABILITY OF PREDNISONE DRUG AND TABLETS

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Abstract

TG and DSC data were used to determine the thermal parameters of prednisone drug and tablets. Two formulations of prednisone 20 mg were analysed in the form of tablets. The TG curves of prednisone drug and tablets A and B displayed six, eight and seven thermal decomposition processes, respectively. Analysis of the DSC data pointed to chemical interactions between prednisone drug and the excipients of tablets A and B, suggested by alterations in the melting temperature of prednisone. The analysis revealed that prednisone drug is more stable than tablets A and B.

Keywords: DSC-photovisual, pharmaceutical equivalence, polymorphism, prednisone

Introduction

The synthetic glucocorticoid prednisone is prescribed for the treatment of a wide variety of diseases in consequence of its anti-inflammatory and immunosuppressant activities [1].

Thermal analytical techniques have been used to characterize the behaviour of samples as a function of temperature. These methods include DSC, DTA and TG. DSC has been applied extensively to identify polymorphism in drugs. A polymorph is a solid crystalline phase of a given compound, resulting from the possibility of at least two different arrangements of the molecules in the solid state [3].

A preformulation study is a phase in the development process in which the physical, chemical and mechanical properties of a drug are characterized, in order to develop stable, safe and effective dosage forms [2, 3].

In the present work, TG and DSC coupled to a photovisual system were used to determine the thermal parameters of prednisone drug and tablets in a comparison of different formulations.

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Methodology

Tablets A and B containing 20 mg prednisone, prednisone drug and binary mixtures were analysed. Tablet A was manufactured in the LTF/UFPB, and standard tablet B was acquired from a local drugstore. Tablet A had the following composition: prednisone 13.3; starch 46.7; lactose 30.0; PVP 2.0; talc 3.3; explocel 3.0 and magnesium stearate 1.7 %. Its final mass was 150 mg.

The non-isothermal and isothermal TG curves were obtained with a Shimadzu model TGA-50H thermobalance under an atmosphere of air at a flow rate of 20 ml min^{-1}, at a heating rate of 10°C min^{-1} up to 900°C. The sample mass used was about 8 mg. The isothermal TG curves were measured at 180, 200, 220 and 240°C during 240 min. The rate constants of the thermal decomposition reaction were determined from the TG data by using the Arrhenius expressions.

The DSC curves were obtained with a Shimadzu model DSC-50 calorimeter coupled to a photovisual system, in the temperature range 25–500°C, under an atmosphere of nitrogen at a flow rate of 50 ml min^{-1}. The excipients and binary mixtures were analysed at a heating rate of 10°C min^{-1}, to observe qualitative interactions. Tablets A and B were analysed at a heating rate of 5°C min^{-1} and the prednisone drug at rates of 2, 5, 10 and 20°C min^{-1}. The sample mass used was about 2 mg. The melting point was determined with the Tasys software of Shimadzu, which allows purity and melting point determination.

The DSC apparatus was calibrated via the melting point of indium at heating rates of 2, 5, 10 and 20°C min^{-1}, under the same conditions as for the samples. DSC and TG data were obtained from triplicate DSC and TG curves.

Results and discussion

The TG curves showed that, with the exception of talc, the excipients start to decompose at temperatures about 20°C lower than that of prednisone. Prednisone begins to decompose at about 230°C. It is clear from the TG curves that talc does not influence the decomposition of prednisone. The other excipients interact with prednisone, decreasing its stability.

Graphical analysis demonstrated that the best statistical parameters for prednisone drug (r=0.9980; sd=$5 \cdot 10^{-4}$), tablet A (r=0.9920; sd=$7 \cdot 10^{-4}$) and tablet B (r=0.9932; sd=$6 \cdot 10^{-4}$) were obtained for the 1/mass *vs*. time fit, indicating that the decomposition obeys second-order kinetics.

The rate constants are in agreement with the classical Arrhenius kinetics and revealed that prednisone drug is more stable than tablets A and B. The rate constants confirmed that a small degree of incompatibility was promoted by some excipients in the prednisone formulations; however, it was not enough to decrease their stability (Table 1).

Table 1 Rate constants of thermal decompositions of prednisone drug and tablets

Temperature/°C	Rate constant, k/s^{-1}		
	Prednisone		
	Drug	Tablet A	Tablet B
180	–	$6.03 \cdot 10^{-6}$	$5.58 \cdot 10^{-6}$
200	$2.84 \cdot 10^{-6}$	$2.22 \cdot 10^{-5}$	$4.30 \cdot 10^{-5}$
220	$2.28 \cdot 10^{-5}$	$1.39 \cdot 10^{-4}$	$1.65 \cdot 10^{-4}$
240	$1.38 \cdot 10^{-4}$	$2.90 \cdot 10^{-4}$	$3.09 \cdot 10^{-2}$

The DSC curve of prednisone drug at a heating rate at 10°C min^{-1} contained an endothermic peak corresponding to the melting point at 239°C, which is higher than the range reported in the literature: 233–235°C [4]. The reference substance (indium) and prednisone were therefore submitted to heating at different rates: 2, 5, 10 and 20°C min^{-1} (Table 2). Indium did not exhibit an appreciable variation in melting point with change of the heating rate. However, prednisone displayed significant differences in melting point at the different heating rates, which influenced the curve shape. As concern suitable choice of heating rate, it was found that the melting point of prednisone could be determined correctly only at a heating rate of about 5°C min^{-1}. At the other heating rates applied, the melting points observed differed from the USP melting temperature interval for prednisone, probably indicating the presence of polymorphs in the sample.

Table 2 Melting point, T_m, and heat of fusion, ΔH_f^0, of indium and prednisone drug at different heating rates

Heating rate/ °C min^{-1}	Indium		Prednisone	
	T_m/°C	ΔH_f^0/J g^{-1}	T_m/°C	ΔH_f^0/J g^{-1}
2	155.28	28.08	228.45	105.55
5	155.78	28.49	233.09	83.11
10	156.60	27.91	239.30	100.07
20	157.48	28.25	245.47	98.91

Figure 1 depicts DSC curves of prednisone and the excipients; different phase transitions can be observed. Talc did not display a phase transition. The DSC curves were analysed with the aid of Shimadzu Tasys software.

The DSC curves of the binary mixtures revealed interactions between the drug and the excipients lactose, starch, PVP and magnesium stearate. Only a weak melting peak was determined for the mixture of prednisone with talc, due to the thermal conductance of talc. Tablets A and B reflected the behaviour of lactose, because they did not present the melting point characteristic of prednisone at 233–235°C (Fig. 2).

Figure 3 presents pictures and DSC/TG curves of prednisone drug. The melting process is not accompanied by a mass loss in the TG curve (Fig. 3). The DSC curve of tablet A revealed several phase transitions (Fig. 4). The first phase transition corre-

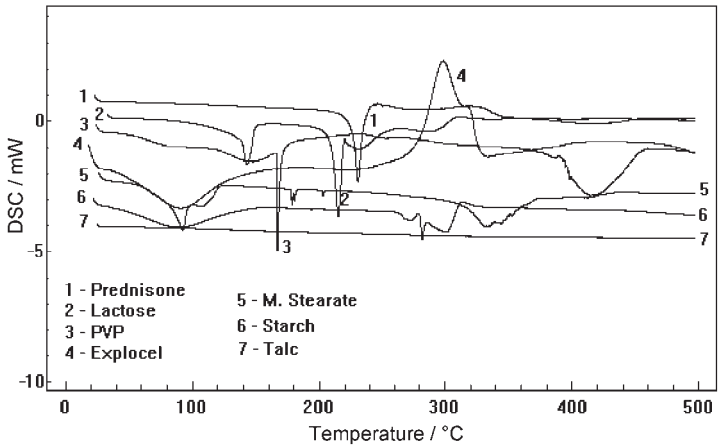

Fig. 1 DSC curves of prednisone drug and excipients

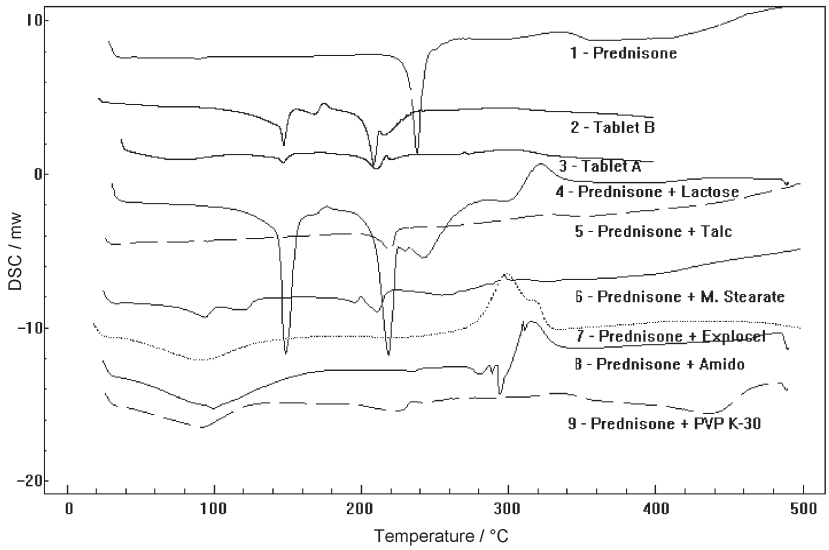

Fig. 2 DSC curves of prednisone and its binary mixtures

sponds to water loss, in agreement with the TG curve, while the second, third and fourth phase transitions, without mass loss in the TG curve, may be due to chemical or physical interactions between the drug and the excipients. Tablet B underwent various phase transitions (DSC curve) with mass loss (TG curve) (Fig. 5) below the melting point of prednisone, indicating strong interactions between the drug and the excipients. The DSC-photovisual studies visualized meanful differences in thermal behaviour between the two tablets, demonstrating that the two formulations are not pharmaceutically equivalent.

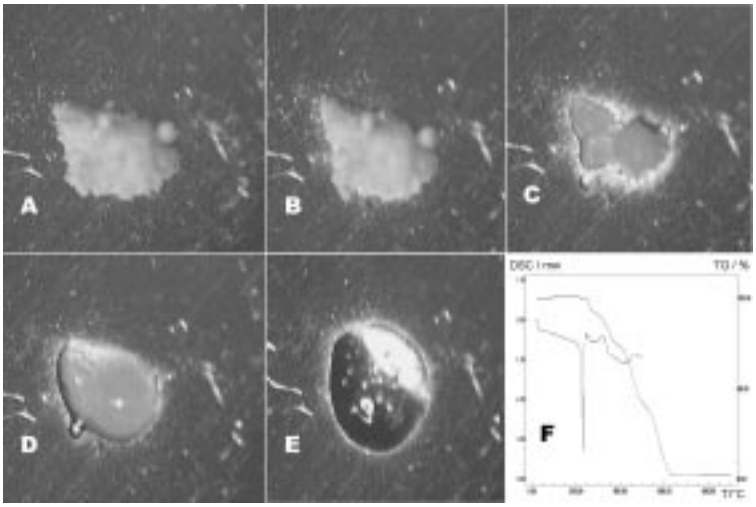

Fig. 3 DSC-photovisual pictures of prednisone drug (**A** – 19; **B** – 220; **C** – 233; **D** – 235 and **E** – 242°C) and **F** – thermoanalytical curves

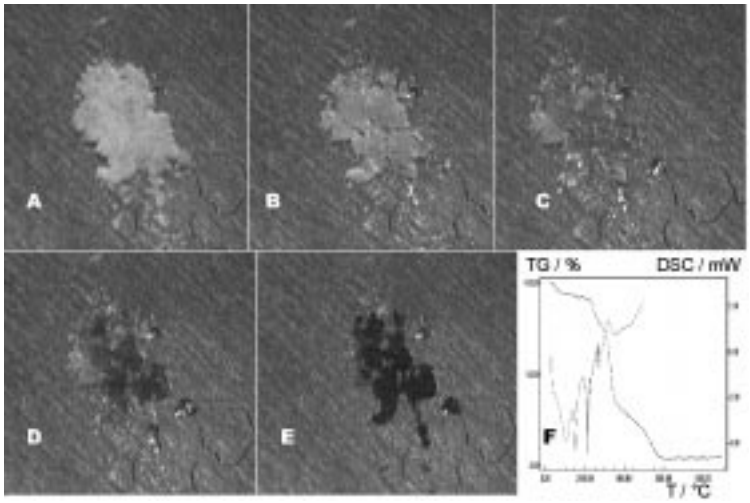

Fig. 4 DSC-photovisual pictures of tablet A (**A** – 21; **B** – 210; **C** – 220; **D** – 233 and **E** – 267°C) and **F** – thermoanalytical curves

The observations of chemical or physical interactions between the drug and the excipients in tablets A and B revealed that DSC coupled to the photovisual system is a good tool for the study of such systems.

The rate constants obtained from the isothermal TG data for the drug and tablets A and B provided evidence of differences between the formulations. The rate constants (Table 1) indicated the following sequence of thermal stability:

prednisone drug>tablet A>tablet B.

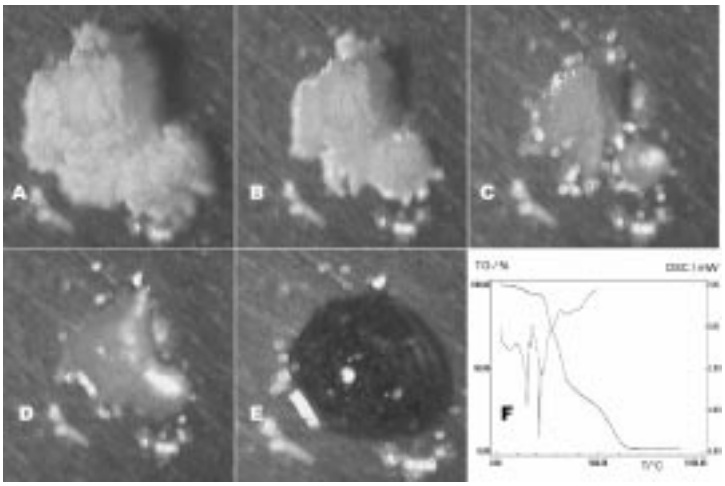

Fig. 5 DSC-photovisual pictures of tablet B (**A** – 27; **B** – 200; **C** – 204; **D** – 206 and **E** – 226°C) and **F** – thermoanalytical curves

Conclusions

The kinetic and DSC-photovisual studies allowed an assessment of the pharmaceutical equivalence of two prednisone formulations.

References

1 H. Blume, S. A. Quereshi, S. L. Ali and I. J. McGilveray, Drug Development and Industrial Pharmacy, 21 (1995) 925.
2 H. C. Ansel, N. G. Popovich and L. V. Allen Jr., Pharmaceutical Dosage Forms and Drug Delivery Systems, Williams & Wilkins, 1995.
3 Remington, The Science and Practice of Pharmacy, 19th ed., Faston, PA, Mac Publ. Co., 1995.
4 The Merck Index, 12th ed., Whitehouse Station, 1996.