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THERMAL STABILITY OF METRONIDAZOLE DRUG AND TABLETS

Nadábia A. B. de Souza [1], *Ana C. D. Medeiros* [1,2], *Ana F. O. Santos*[1] *and R. O. Macêdo*[1*]

[1]Unidade de Desenvolvimento e Ensaios de Medicamentos/Laboratório de Tecnologia Farmacêutica-Universidade Federal da Paraíba-Campus I-João Pessoa, Paraíba ZIP 58059-900, Brasil
[2]Universidade Estadual da Paraíba, Campina Grande, Paraíba, Brazil

Abstract

TG and DSC data were used to determine the thermal parameters of metronidazole drug and tablets. Three tablets A, B and C were analysed. The TG curves of metronidazole drug and tablets A and B displayed five and C four thermal decomposition processes, respectively. Analysis of the DSC data pointed to chemical interactions between metronidazole drug and the excipients of tablets, suggested by alterations in the melting point of metronidazole. The rate constants obtained from the isothermal TG data presents following sequence of the thermal stability: tablet A>tablet C>metronidazole drug>tablet B.

Keywords: DSC-photovisual, metronidazole, pharmaceutical equivalence

Introduction

The metronidazole drug is an active adversely wide spectra of parasite and bacterium anaerobics. The drug also has potent amebicid and trichomonicid power [1].

The thermal analysis is extensively used to describe analytical techniques that study sample behaviour as a function of temperature. Macêdo *et al*. [2–15] showed applications of different thermal analysis techniques in pharmaceutical technology, including DSC Photovisual, an excellent technique for chemical interactions studies between drug substance and excipients.

In the present work, TG, DTA and DSC coupled to a photovisual system were used to determine the thermal parameters of metronidazole drug and tablets.

Methodology

Metronidazole drug and tablets A, B, C containing 250 mg metronidazole, were analysed. Tablet A was manufactured in the LTF/UFPB, standard and generic, tablets B and C, respectively, were acquired from a local drugstore. Tablet A had the following composition: metronidazole 59.53%, starch 13.02%, avicel 101 17.02%, croscarmelose sodium 2.01%, PVP 5.43%, magnesium stearate 0.97% and talc 1.93%.

* Author for correspondence: E-mail: ruimacedo@ltf.ufpb.br

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Akadémiai Kiadó, Budapest

The non-isothermal and isothermal TG curves were obtained with a Shimadzu thermobalance model TGA-50H under an atmosphere of air at a flow rate of 20 mL min^{-1}, at a heating rate of 10 K min^{-1} up to 1.173 K. The sample mass used was about 8 mg. The isothermal TG curves were measured at 413, 423, 433, 443 and 453 K during 240 min. The rate constants of the thermal decomposition reaction were determined from the TG data 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 298–773 K, under an atmosphere of nitrogen at a flow rate 50 mL min^{-1}. The sample mass used was about 2 mg. The melting point was determined with Tasys software of Shimadzu.

Results and discussion

The DSC curve of metronidazole drug at a heating rate at 10 K min^{-1} presented an endothermic peak corresponding to the melting point at 435 K is higher than the range reported in the literature 431–433 K. The United States Pharmacopeia XXIV [1] show the melting range at 432–435 K. Thus, the melting point observed was admitted.

Figure 1 shows DSC curves of metronidazole drug and the tablets where different phase transitions can be observed. Tablets B and C showed endothermic peak at 434 K. While tablet A displayed an endothermic peak at 430 K that to suggesting interactions between metronidazole drug and excipients confirmed by melting point characteristic of metronidazole. Some new exotherm peaks can be observed in the case of the tablets referring to decomposition processes and phases transition confirmed by the DSC-photovisual.

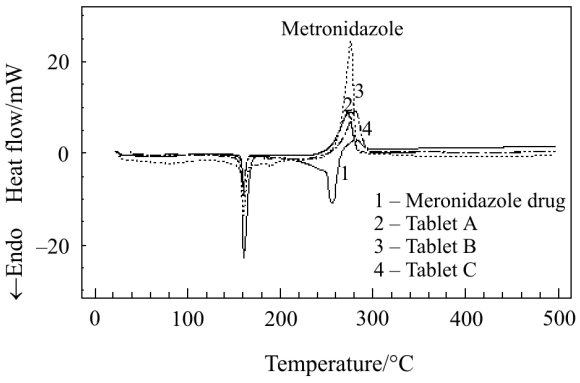

Fig. 1 DSC curves of tablets A, B, C and metronidazole drug

The DSC-photovisual studies showed meanful differences in thermal behaviour between the three tablets. DSC photovisual showed coloration changes with the increase of temperature, evidencing possible chemical or physical interactions between the drug and the excipients in tablets A, B and C.

Figure 2, picture A_1 to A_5 presented coloration and physical state change of the metronidazole drug: solid→liquid→gas with complete volatility of the sample. Fig-

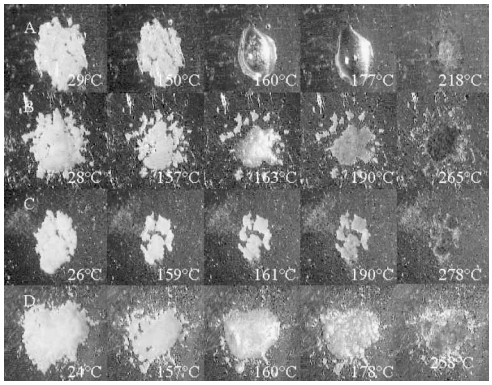

Fig. 2 DSC-photovisual pictures of metronidazole (A – drug, B – tablet A, C – tablet B and D – tablet C)

ure 2, picture B corresponding to the tablet A, differences in the coloration at 430 and 436 K, pictures B_2 and B_3. The thermal decomposition processes can be visualized in the pictures B_4 and B_5. The tablet B, Fig. 2, pictures C, evidenced stability of sample until 434 K, picture C_3. The coloration change occurred from 463 K, pictures C_4 and C_5. Tablet C presented similar behaviour with tablet A, Fig. 2, pictures B and C.

The TG curve for the metronidazole drug showed one thermal decomposition process, and had a mineral residue of 2.99%. Tablets A and B presented five thermal decomposition processes with a mineral residue of 3.88 and 0.22%, respectively. The TG curve for tablet C displayed four thermal decomposition processes, and had a mineral residue of 11.09% shown in the Fig. 3.

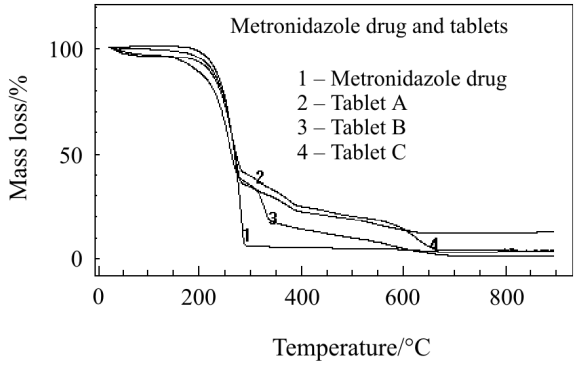

Fig. 3 The TG curves of drug and tablets A, B and C of the metronidazole

The rate constants obtained from the isothermal TG data for the drug and tablets A, B and C evidenced different behaviour among ones, Table 1. The rate constants were calculated from Arrhenius classical equation for first order kinetic indicating the following sequence of thermal stability: Tablet A>Tablet C>Metronidazole drug>Tablet B.

Table 1 Rate constants of thermal decomposition of metronidazole drug and tablets

Temperature/°C	Rate constant/s^{-1} Metronidazole			
	Drug	Tablet A	Tablet B	Tablet C
140	$3.04 \cdot 10^{-6}$	$1.03 \cdot 10^{-6}$	$4.16 \cdot 10^{-6}$	$1.08 \cdot 10^{-6}$
150	$5.80 \cdot 10^{-6}$	$1.64 \cdot 10^{-6}$	$9.37 \cdot 10^{-6}$	$1.97 \cdot 10^{-6}$
160	$1.26 \cdot 10^{-5}$	$2.85 \cdot 10^{-6}$	$1.32 \cdot 10^{-5}$	$3.79 \cdot 10^{-6}$
170	$2.23 \cdot 10^{-5}$	$5.70 \cdot 10^{-6}$	$3.03 \cdot 10^{-5}$	$5.81 \cdot 10^{-6}$
180	$3.88 \cdot 10^{-5}$	$8.33 \cdot 10^{-6}$	$5.24 \cdot 10^{-5}$	$9.73 \cdot 10^{-6}$

Conclusions

The kinetic and DSC-photovisual data allowed to evidence of differences between the formulations. The rate constants indicated the following sequence of thermal stability: Tablet A>Tablet C>Metronidazole drug>Tablet B.

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