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APPLICATION OF THERMAL ANALYSIS IN THE CHARACTERIZATION OF ANTI-HYPERTENSIVE DRUGS

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Abstract

The present work reports studies of the thermal behaviour of some anti-hypertensive drugs. Their purities were determined by DSC and specialized pharmacopeial methods. The thermogravimetric data allowed determination of the kinetic parameters: activation energy, frequency factor and reaction order. The activation energy values suggest the following sequence of stability: nifedipine>propanolol hydrochloride>captopril. Analysis of the DSC data indicated that the degrees of purity of nifedipine, captopril and propanolol hydrochloride were similar to those found by pharmacopeial methods BP 93 and USP 23. The simplicity, speed and low operational costs of thermal analysis justify its application in the quality control of pharmaceutical drugs.

Keywords: anti-hypertensive drugs, quality control, thermal analysis

Introduction

Thermogravimetry is an analytical, quantitative and comparative method, capable of producing fast and reproducible results. It can be used in the quality control of drugs, with a view to improvement of the final product and for the determination of drug quality via the technological parameters [1].

Differential scanning calorimetry (DSC) can be used in the pharmaceutical industry as an analytical tool of great importance for the identification and purity testing of active drugs, yielding results rapidly and efficiently. DSC has been applied for the quality control of raw materials used in pharmaceutical products [2].

The present work reports studies of the thermal behaviour of some anti-hypertensive drugs, in comparison with the methods employed for identification and purity testing in the pharmaceutical industry [3–5] in relation to the application of thermal techniques in the quality control of medications.

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Methodology

Captopril, nifedipine and propanolol hydrochloride were donated by Pharmaceutical Technology Laboratory of the Federal University of Paraíba (LTF/UFPB); they satisfied the specifications USP 23 and BP 93. The dynamic thermogravimetric curves of the raw materials were obtained with a Shimadzu thermobalance, model TGA-50, under an air atmosphere with a constant flow of 20 ml min^{-1}, at a heating rate of 10°C min^{-1}, up to a temperature of 900°C. Samples with a mass of around 10 mg were packed in an alumina cell. The calorimetric curves of these substances were obtained with a Shimadzu differential scanning calorimeter, model DSC-50, under an atmosphere of nitrogen, with a constant flow of 50 ml min^{-1} and a heating rate of 5°C min^{-1}, up to a temperature of 500°C. Samples with a mass of 2 mg were packed in an aluminum cell.

The kinetic parameters of decomposition, the activation energy (E_a), reaction order (n) and factor frequency (Z), were obtained from the TG curves for the first step, using α values of 0.2–0.9 for captopril and propanolol hydrochloride and of 0.1–0.9 for nifedipine. The mathematical models of Coats and Redfern (CR) [6] and Madhusudanan *et al.* (MD) [7] were used for determination of the kinetic parameters.

UV/VIS spectrophotometry and volumetry were used for the identification and purity tests on the samples. The spectrophotometric data were obtained with a Milton Roy Spectronic 1201 spectrophotometer. The maximum absorbances for propanolol hydrochloride and nifedipine dissolved in methanol were measured at wavelengths of 390 and 340 nm, respectively, and their concentrations were obtained as averages of five determinations on the basis of standard curves. Captopril was determined by the oxi-reduction volumetry, with 0.1 N potassium iodate as titrant. Each sample was analysed five times [3–5].

Results and discussion

The TG curves were analysed by the tangent method, calculated from the curve of mass loss *vs*. temperature. Calculations on the range of temperatures and the respective mass losses were performed with the aid of Shimadzu Tasys software.

The TG curves of captopril (Fig. 1) revealed four thermal decomposition stages. The decomposition of captopril proceeds with turbulence formation, involving processes of product vaporization, as evidenced in the DSC curve (Fig. 1). Propanolol hydrochloride presented four stages of thermal decomposition (Fig. 2). The thermal decomposition of propanolol hydrochloride occurs with energy intermediate between those of captopril and nifedipine, possibly with volatilization of the product, as evidenced by the DSC curve (Fig. 2). The TG curve of nifedipine (Fig. 3) exhibited four thermal decomposition stages. Unlike captopril and propanolol hydrochloride, the DSC curve for the formation of the products of thermal decomposition of nifedipine involves a low consumption of energy (Fig. 3).

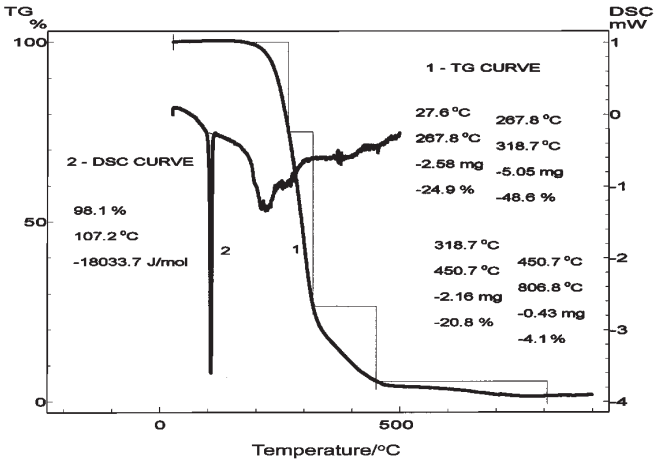

Fig. 1 TG and DSC curves of captopril

The kinetic parameters were obtained from the TG curves via the CR and MD methods through the use of Eqs (1–4), and corresponding to the first step of drug decomposition (Table 1).

The Coats-Redfern equations:

for $n=1$

$$\log\left[\frac{-\ln(1-\alpha)}{T^2}\right] = \log\frac{AR}{\phi E} - \frac{E}{2.303RT} \tag{1}$$

for $n\neq 1$

$$\log\left[\frac{1-(1-\alpha)^{1-n}}{T^2(1-n)}\right] = \log\frac{AR}{\phi E} - \frac{E}{2.303RT} \tag{2}$$

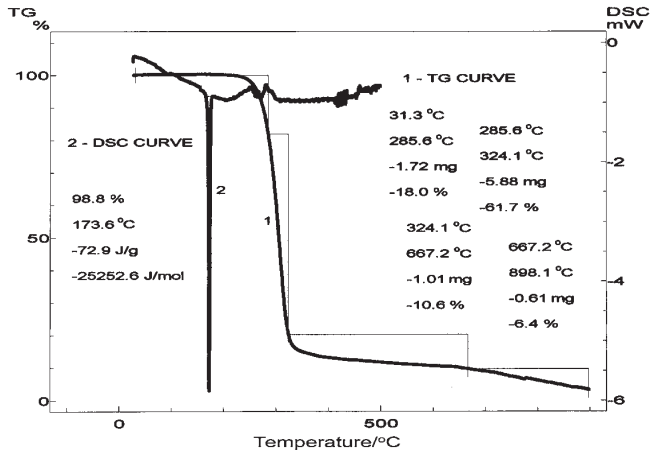

Fig. 2 TG and DSC curves of propanolol hydrochloride

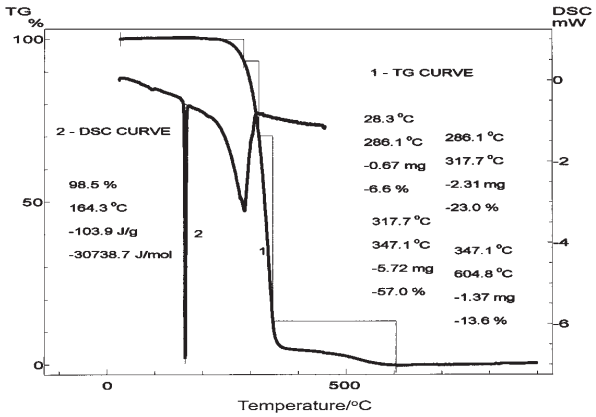

Fig. 3 TG and DSC curves of nifedipine

The Madhusudanan equations:

$$\text{for } n=1 \qquad \ln\left[\frac{-\ln(1-\alpha)}{T^{1.9206}}\right] = \ln\frac{AR}{\phi E} + 0.02 - 1.9206\ln\frac{E}{R} - 0.12040\frac{E}{RT} \tag{3}$$

$$\text{for } n\neq 1 \qquad \ln\left[\frac{1-(1-\alpha)^{1-n}}{T^{1.92062}(1-n)}\right] = \ln\frac{AR}{\phi E} + 3.7678 - 1.9206\ln\frac{E}{R} - 0.1204\frac{E}{RT} \tag{4}$$

The kinetic data were calculated for the two mathematicl models in the different α ranges in order to choose the best linear correlation coefficients (r). The results led to the following values: nifedipine (α=0.1–0.9): CR (r=1.000), MD (r=1.000); captopril (α=0.2–0.8): CR (r=1.000), MD (r=1.000); propanolol hydrochloride (α=0.2–0.8): CR (r=1.000), MD (r=1.000).

Table 1 Kinetic parameters obtained by the methods of Coats and Redfern (CR) and Madhusudanan *et al.* (MD)

Drug	Kinetic parameters					
	E_a/kJ mol^{-1}		N		Z/s^{-1}	
	CR	MD	CR	MD	CR	MD
Captopril	74.7	75.8	0.78	0.81	2.85E+4	4.11E+4
Propanolol:HCl	124.8	124.6	0.26	0.25	2.51E+8	2.57E+8
Nifedipine	146.1	149.1	0.07	0.13	2.52E+11	5.35E+11

The kinetic parameters (E_a) and (Z) demonstrated significant differences between the three molecules. The activation energy values suggested the following sequence of thermal stability: nifedipine > propanolol hydrochloride > captopril. The DSC curves allowed determination of the melting points and the degrees of purity of

the drugs, starting from the molecular masses of the substances, using the Shimadzu Tasys software (Table 2).

Table 2 Degrees of purity and melting points of captopril, propanolol hydrochloride and nifedipine, obtained by DSC and pharmacopeial methods

Drug	Degree of purity/%		Melting point/°C	
	DSC	pharmacopeial	DSC	pharmacopeial
Captopril	98.10	98.52*	107.3	106 [4]
Propanolol·HCl	98.54	98.81**	164.4	163–166 [4]
Nifedipine	98.80	98.61**	173.7	171–175 [5]

* – volumetry; ** – UV/VIS spectrophotometry

The results obtained by the volumetric and spectrophotometric methods afforded values similar to those found by DSC (Table 2). Comparison of the data on the anti-hypertensive drugs analyzed in this work reveals the importance of the DSC technique for the quality control of bioactive drugs. The melting points obtained by DSC reveal the precision of the technique in yielding this thermal parameter. This justifies the use of DSC as a routine technique for the identification of drugs destined for pharmaceutical use, through the melting point. The use of clean techniques, and the speed and the simplicity of the analytical methods applied to obtain the results are the reasons behind the even growing importance of thermal analysis in the quality control of active ingredients for medications.

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