Journal of Thermal Analysis and Calorimetry, Vol. 72 (2003) 545–548

THERMAL AND DISSOLUTION KINETICS OF AMPICILLIN DRUG AND CAPSULES

A. P. Barrêto Gomes, F. S. Souza and R. O. Macêdo[*]

Universidade Federal da Paraíba – UFPB Unidade de Desenvolvimento e Ensaios de Medicamentos, UDEM Cidade Universitária, Campus I, LTF, João Pessoa, Paraíba, Brasil

Abstract

This work aims to compare the thermal decomposition and dissolution kinetics of ampicillin drug and products *A*, *B* and *C*. The thermal decomposition reaction rate constants (*kT)* were determined by isothermal thermogravimetric method using the classical Arrhenius equations. The dissolution profiles were obtained using USP 23 method and rate constants (*kD)* were determined by Kitazawa equation. The results showed correlation between *kT* and *kD* can be used in the study of pre-formulation of drugs and also as a parameter in the studies of pharmaceutical equivalence.

Keywords: ampicillin, kinetic, pharmaceutical equivalence

Introduction

The ampicillin is a semi-synthetic penicillin, of wide spectrum, resistant to the action of the gastric, even so sensitive the action of the beta-lactamases. The ampicillin is bactericide, because it inhibits the biosynthesis of the cellular wall of the sensitive bacterias [1].

Thermal analysis is one of the most widely used methods for studying the solid state of pharmaceutical substances [2]. Macêdo *et al.* [3–5] used the thermal analysis as tool in the drugs characterization and herbal medicines, besides the determination of the thermal kinetics of the same ones.

The comparison of dissolution profiles has extensive application throughout the product development process and can be used to: develop in vitro – in vivo correlations, establish final dissolution specifications for the pharmaceutical dosage form and establish the similarity of pharmaceutical dosage forms [6].

The propose of this work is to determine the thermal and dissolution kinetics of the ampicillin drug and products *A*, *B* and *C*, aiming to establish parameters for the pharmaceutical equivalence studies.

Experimental

The samples were ampicillin drug and capsules. The ampicillin drug was donated by the Laboratory of Pharmaceutical Technology in the Federal University of Paraiba.

* E-mail: anapg@ig.com.br, ruimacedo@ltf.ufpb.br

1388–6150/2003/ $ 20.00
© 2003 Akadémiai Kiadó, Budapest
Akadémiai Kiadó, Budapest
Kluwer Academic Publishers, Dordrecht

The products *A* and *B* were acquired in the local trade. The product *C* was prepared in our laboratory.

The isothermal thermogravimetric curves were obtained in a Shimadzu thermobalance, model TGA-50H, under an air and nitrogen flows of 20 and 50 mL min^{-1}, respectively. The mass used was 8.0±0.3 mg. They were obtained curves in the temperatures: 473, 468, 463, 458 and 453 K with five repetitions in each temperature. The kinetic parameters of thermal decomposition were calculated, using the equation of Arrhenius [7].

The dissolution profiles were obtained in an automatizated dissolutor Vankel, model VK7010, coupled to a Varian spectrophotometer UV/Vis, model Cary 50. The metodology utilized were USP XXIII [8]. It were collected eigtheen points in the times: 2, 4, 6, 8, 10, 15, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90 and 95 min, in the temperature of the 310 K. The kinetic parameters of the dissolution were calculated, using the equation of Kitazawa [9].

Results and discussion

Thermal studies

Isothermal TG curves of the drug and products *A*, *B* and *C* showed a growing increase in the mass loss with the increase of the temperature, presenting similar profiles of decomposition in two stages. Isothermal TG data showed that thermal decomposition reaction obeyed a kinetic process of order zero. They were used to calculate the rate constants (Table 1) using Arrhenius equation [3]. The thermal kinetic can be seen in the Fig. 1.

Table 1 Thermal kinetic and shelf-life of the amplicillin drug and products *A*, *B* and *C*

Kinetics parameters	Ampicillin drug	Product *A*	Product *B*	Product *C*
kT 473 K s^{-1}	$3.02\cdot10^{-4}$	$3.30\cdot10^{-4}$	$2.70\cdot10^{-4}$	$1.84\cdot10^{-4}$
kT 468 K s^{-1}	$1.84\cdot10^{-4}$	$1.49\cdot10^{-4}$	$1.60\cdot10^{-4}$	$1.12\cdot10^{-4}$
kT 463 K s^{-1}	$5.84\cdot10^{-5}$	$9.04\cdot10^{-5}$	$1.03\cdot10^{-4}$	$6.15\cdot10^{-5}$
kT 458 K s^{-1}	$3.38\cdot10^{-5}$	$3.84\cdot10^{-5}$	$4.78\cdot10^{-5}$	$3.03\cdot10^{-5}$
kT 453 K s^{-1}	$2.03\cdot10^{-5}$	$1.65\cdot10^{-5}$	$1.89\cdot10^{-5}$	$1.53\cdot10^{-5}$
kT 303 K s^{-1}	$1.01\cdot10^{-7}$	$1.20\cdot10^{-7}$	$1.00\cdot10^{-7}$	$1.05\cdot10^{-7}$
Shelflife (year)	2.39	2.01	2.41	2.39

It was used the inverse of the temperature and its respective rate constant for the construction of graphs, that were analyzed by the first order exponential decay function, being obtained the following the mathematical equation that defines the behaviour of thermal decomposition:

drug – $k=1.01\cdot10^{-7}+3.52\cdot10^{-4}\exp(-(1/T-0.00498)/2.13\cdot10^{-4}$,
product *A* – $k=1.2\cdot10^{-7}+3.5\cdot10^{-4}\exp(-(1/T-0.00498)/1.71\cdot10^{-4}$,
product *B* – $k=1.0\cdot10^{-7}+3.09\cdot10^{-4}\exp(-(1/T-0.00498)/3.01\cdot10^{-4}$ and
product *C* – $k=1.05\cdot10^{-7}+3.52\cdot10^{-4}\exp(-(1/T-0.00498)/2.67\cdot10^{-4}$.

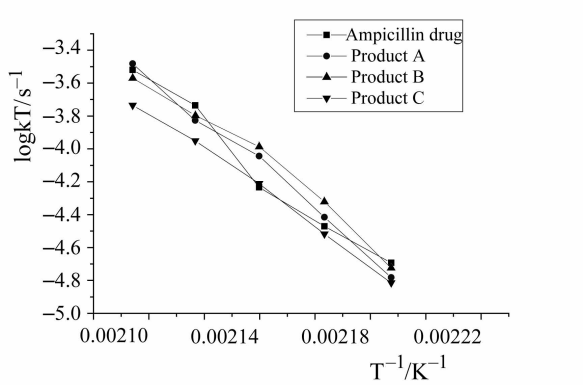

Fig. 1 log[kT (s^{-1})] of the ampicillin drug and products *A*, *B* and *C vs*. 1/*T*

The rate constants were extrapolated utilizing the mathematical equation previous to obtain the value of kT in 303 K to drug, products *A*, *B* and *C* were $1.0 \cdot 10^{-7}$, $1.2 \cdot 10^{-7}$, $1.0 \cdot 10^{-7}$ and $1.05 \cdot 10^{-7}$. This temperature is used in the storage of pharmaceuticals in the tropical whether. The thermal rate constants in 303 K allow to establish the following decreasing order of stability: product *B*>product*C*>product *A*. The rate constants in 303 K were used to estimate the time of shelflife of the drug, products *A*, *B* and *C*: 2.39, 2.01, 2.41 and 2.30 year, respectively.

Dissolution studies

The drug and products *A*, *B* and *C* presented maximum concentration of liberation with 15 min of 74.28, 75.13, 90.09 and 66.92%, respectively. The drug concentrations of the products *A*, *B* and *C* were used to calculate the dissolution rate using the Kitazawa equation:

$$\ln(w^{\infty}/w^{\infty} - w_t) = kDt$$

where w^{∞} is the amount of the drug in the infinite time, w_t is the amount of the drug in the time t, kD is the dissolution rate constant and t it is the time of dissolution.

The maximum dissolution constant (kD_{max}) was obtained when the relation between concentration and time showed the maximum value. The dissolution profiles of ampicillin drug, products *A*, *B* and *C* can be seen in the Fig. 2. The kD_{max} values obtained for drug and products *A*, *B* and *C* are respectively: $8.5 \cdot 10^{-5}$, $1.0 \cdot 10^{-4}$, $1.28 \cdot 10^{-4}$ and $1.17 \cdot 10^{-4}$.

An evaluation was made to check if there was statistically significant correlation Fig. 3 between the two variables kT and kD. The results showed correlation between thermal constants (kT) and dissolution rate constants (kD_{max}), obeying a linear function, whose correlation coefficient was of 0.9753.

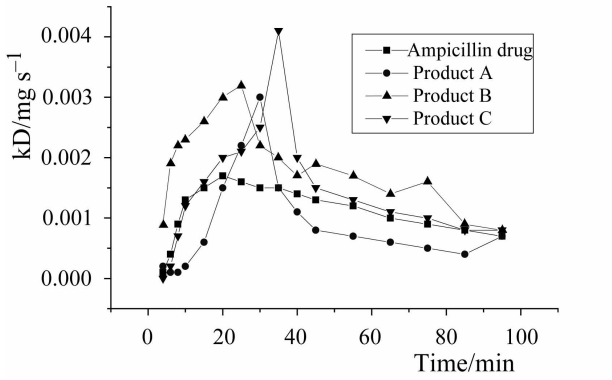

Fig. 2 Profiles maximum of dissolution of ampicillin drug, products *A*, *B* and *C*

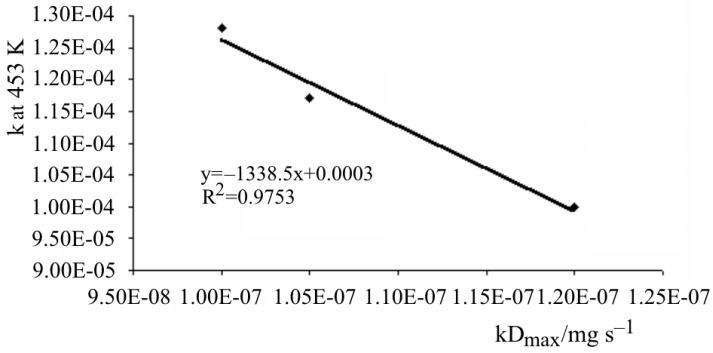

Fig. 3 Correlation between *kT* ext. at 453 K and kD_{max}

Conclusions

The thermal decomposition reaction and dissolution rate constants presented a good correlation among tablets *A*, *B* and *C*. The thermal and dissolution kinetics can be used to confirm pharmaceutical equivalence between reference and test products.

References

1 P. Silva, Farmacologia. 5ª Ed., Editora Guanabara Koogan, Rio de Janeiro 1998.
2 R. O. Macêdo and T. G. do Nascimento, Thermochim. Acta, 392–393 (2002) 85.
3 R. O. Macêdo and T. G. do Nascimento, J. Therm. Anal. Cal., 64 (2001) 751.
4 R. O. Macêdo, T. G. do Nascimento and J. W. E. Veras, J. Therm. Anal. Cal., 64 (2001) 757.
5 R. O. Macêdo, T. G. do Nascimento and J. W. E. Veras, J. Therm. Anal. Cal., 67 (2002) 483.
6 Th. O'Hara, A. Dunne, J. Butler and J. Devane, Res. Focus, 5 (1998) 214.
7 A. C. D. de Medeiros, N. A. B. de Cervantes, A. P. B. Gomes and R. O. Macêdo, J. Therm. Anal. Cal., 59 (2000) 657.
8 USP 23, NF18. The United States Pharmacopeia. The National Formulary, 1995.
9 V. Pillay and R. Fassihi, J. Pharm. Sci., 9 (1999) 843.