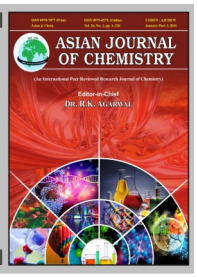
Asian Journal of Chemistry; Vol. 26, No. 2 (2014), 486-488

ASIAN JOURNAL OF CHEMISTRY

http://dx.doi.org/10.14233/ajchem.2014.15591



Study on Thermal Decomposition Kinetics of Sulfonamide Potentiator-Trimethoprim

LIN WANG[1,*], RULIN LI[2] and HONGWEI WANG[1]

[1]Chemistry and Pharmaceutical Engineering College, Nanyang Normal University, Nanyang 473061, Henan Province, P.R. China
[2]Chemical Engineering College, Nanyang Institute of Technology, Nanyang 473004, Henan Province, P.R. China

*Corresponding author: E-mail: yueyuewanglin@163.com

Received: 5 April 2013; *Accepted*: 14 August 2013; *Published online*: 15 January 2014; AJC-14572

Thermal stability of sulfonamide potentiator-trimethoprim is studied by thermogravimetry and differential thermogravimetry. One weight-loss phase is observed in the heating courses from room temperature to 700 °C in the inert atmosphere. Using Kissinger and Ozawa methods, the activation energy of thermal decomposition is obtained as 70.2276 KJ/mol. The kinetic equation of thermal decomposition can be expressed as $d\alpha/dt = 1.5238 \times 10^5 \exp(-\frac{78794}{RT})(1-\alpha)[-\ln(1-\alpha)^{0.5057}]$.

Keywords: Sulfonamide potentiator, Trimethoprim, Thermal analysis, Thermal decomposition kinetics, Thermogravimetry.

INTRODUCTION

Trimethoprim (TMP) is a kind of antibacterial drug and antiseptic with broad spectrum, high performance and low toxicity. It is often combined with sulphamethoxazole and sulphonamides (SMZ) to be an effective treatment of many kinds of bacterial infection[1-3]. World Health Organization was explicit to put forward TMP/SMZ should be the first choice therapy for mild pneumonia treatment in 2005[4-6]. Nowadays, TMP/SMZ is recommended to be used to prevent AIDS at primary stage[7]. Furthermore, trimethoprim can strengthen the antibacterial effect of Chinese Medicine when combined with Chinese Medicine and has broad prospects for development and utilization in the animal husbandry[8-10]. Therefore, the continuing study on trimethoprim is of great importance.

The processing technology, therapeutic effect and pharmacokinetics on trimethoprim are widely studied in literature[11,12]. However, to the best of our knowledge, this paper is among the first to address the thermal stability properties of trimethoprim. Thermal stability properties study could provide certain theoretical basis to the storage, stability value and period of validity prediction to the drug. With this in view, this work was undertaken to study the thermal decomposition kinetics of trimethoprim by means of thermoanalysis technology. Firstly, weight-loss process of trimethoprim is obtained by thermogravimetry (TG) and differential thermogravimetry (DTG). Secondly, pyrolysis kinetics parameters are calculated by thermal analysis theory. Lastly, the kinetic equation of thermal decomposition is derived.

EXPERIMENTAL

Reagent grade trimethoprim is provided by Shanghai Yantuo Biological Technology Co. LTD. The simultaneous TG/DTA and DSC curves are obtained with Netzsch STA 449S3 thermoanalyzer (German NETZSCH Co.) under nitrogen atmosphere.

Measurement of TG-DTG curves: Throughout this study, the TG thermoanalyzer works in a temperature range of 25-700 °C. Heating rate is controlled at 5, 10, 15, 20 and 25 °C min^{-1} in a dynamic nitrogen atmosphere with the flow of 30 mL min^{-1}. The sample of 8-10 mg is placed in an Al_2O_3 crucible sample cell of 100 μL volume[13].

RESULTS AND DISCUSSION

Fig. 1 presents the TG curves of trimethoprim at different heating rates and Fig. 2 indicats the TG, DTG, DSC curves of trimethoprim decomposition conducted at a heating rate of 15 °C min^{-1}. From the figures, one loss-weight process is found and all loss-weight yields are nearly 100 %, indicating the all decomposition products are gas state at the decomposition temperatures. The thermal decomposition temperature increases with the increased heating rate and the peak temperatures are 273.3, 296.8, 302.5, 318.7 and 323.8 °C at the heating rate of 5, 10, 15, 20 and 25 °C min^{-1}, respectively. DSC curve shows that there are two endothermic processes, in which the first endothermic process spans the temperature range between 196 and 215 °C with the maximum at 201.9 °C, while the second endothermic process appears at the peak temperature of 289.8 °C.

As is indicated by the TG curve, during the first endothermic process no loss of weight is observed and the first endothermic peak temperature is highly consistent with the melting point of trimethoprim (201-203 °C). Therefore, the first endothermic process is dominated by the melting of trimethoprim. The second caloric absorbed is used for the thermal decomposition reaction which was indicated in TG and DTG curves.

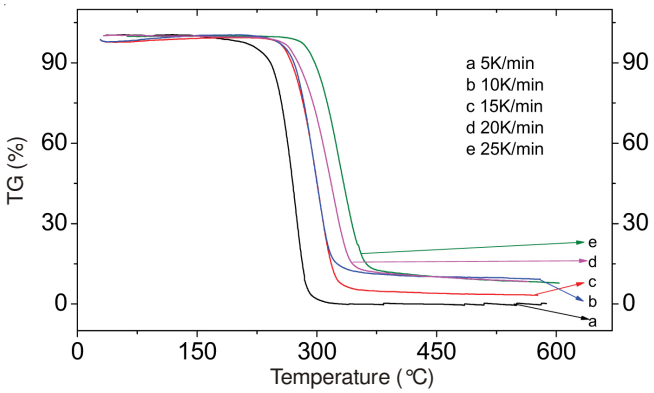


Fig.1. Plot of TG at different heating rates

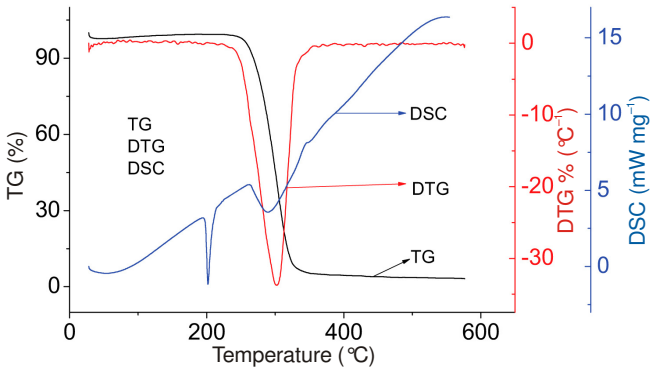


Fig.2. Plot of TG-DTG at 15 °C min^{-1} heating rate

Thermal decomposition kinetics study

Calculation of activation energy: The Kissinger method and the Ozawa's method based on TG curves at the multiple heating rates have been extensively applied in literatures to determine activation energy (E_a) of solid-state reactions without knowing the reaction kinetic function[14,15]. Therefore, in our study, Kissinger and Ozawa methods are utilized to calculate the values of thermal decomposition E_a for trimethoprim.

The Kissinger method[16] is expressed in the natural logarithm form (eqn. 1):

$$\ln\left(\frac{\beta}{T_p^2}\right) = \ln\left(\frac{AR}{E_a}\right) + \ln\left(-\frac{df(\alpha)}{d\alpha}\right)_{ap} - \frac{E_a}{RT_p} \quad (1)$$

where T_p is the peak temperature in the DTG curve, A is the preexponential factor, R is the gas constant, E is the apparent activation energy and β is the heating rate which is expressed as $\beta = dT/dt$. From this equation, E_a can easily be calculated based on the slope by plotting $\ln(\beta/T_p^2)$ *versus* $1/T_P$.

The Ozawa's method (eqn. 2)[17] which represents one of the integral methods can also determine E_a and the Kissinger equation (eqn. 2) is as follow:

$$\ln\beta + \frac{0.4567E_a}{RT} = C \quad (2)$$

From the equation (2), E_a can be obtained from the slope of $-0.4567E_a/R$ by a linear fitting of $\ln(\beta)$ *versus* $(1/T_p)$. The plots of $\ln(\beta/T_p^2)$ *versus* $(1/T_p)$ based on Kissinger's method and $\ln(\beta)$ *versus* $(1/T_p)$ from Ozawa's method are in Fig. 3. Results are presented in Table-1, where r is linear correlation coefficient and SD is standard square deviation.

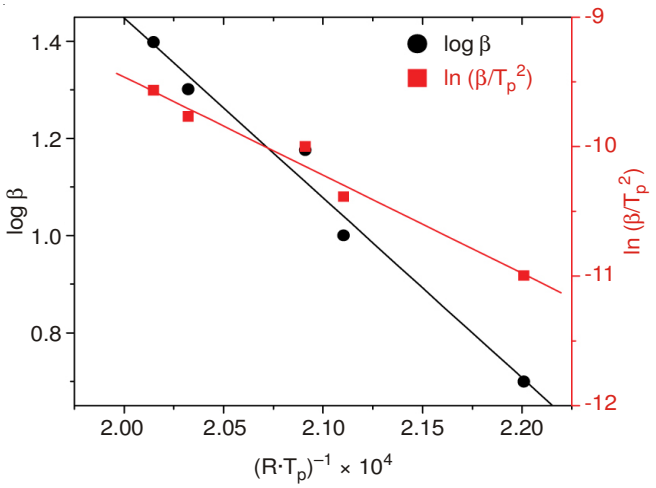


Fig.3. Relation curve of finding activation energy from Kissinger and ozawa method

Fig. 3 and Table-1 show that linear correlations of $\ln(\beta/T_p^2)$ *versus* $(1/T_p)$ and $\ln(\beta)$ *versus* $(1/T_p)$ by the two methods are apparent and the linear correlation coefficients of both are higher. These calculating results also illustrate that the two methods agree very well with each other in estimating the activation energy of the thermal decomposition of trimethoprim. The mean value of E_a is 78.4936 kJ mol^{-1}.

TABLE-1
DERIVATION OF ACTIVATION ENERGY BY KISSINGER'S AND OZAWA'S METHOD

Method	r	SD	SD Eα [kJ mol^{-1}]
Kissinger	-0.9862	0.1084	80.1462
Ozawa	-0.9891	0.0470	76.8381

Calculation of pre-exponential factor and reaction order: To establish the most probable kinetic functions for the decomposition of trimethoprim, the data of α(conversation ratio), dα/dT (the rate of conversation) and T (absolute temperature) are calculated from TG/DTG curve at the heating rate of 15 °C min^{-1}. The thermal decomposition kinetics equation under non-isothermal conditions could be expressed as follows[18]:

$$d\alpha/dt = A\exp(-E_a/RT)\, f(a) \quad (3)$$

$$G(\alpha) = A\exp(-E_a/RT).t \quad (4)$$

where $f(\alpha)$, $G(\alpha)$ are the differential and integral kinetics functions, respectively. Their relationship could be expressed as:

$$f(\alpha) = \frac{1}{d[G(\alpha)]/d\alpha} \quad (5)$$

In the study, the following differential and integral equations could be employed to determine the most probable kinetic equation and values of A and n(reaction order)[19]. Among integral equations, Satava-Sestak integral equation is in the following form[20].

$$\ln[G(\alpha)] = \lg(\frac{AE_a}{\beta R}) - 2.315 - 0.4567\frac{E_a}{RT} \quad (6)$$

Based on the decomposition differential and integral kinetics equations:

$f(\alpha) = n(1-\alpha)[-\ln(1-\alpha)]^{1-1/n}$ and $G(a) = [-\ln(1-\alpha)]^{1/n}$

the values of A and n are calculated by Satava-Sestak integral method. After fitting linear relationship between $\ln[-\ln(1-\alpha)]$ and 1/T, n and A are obtained from the slope and intercept of the plot, respectively. The thermal decomposition kinetics parameters are found using TG data at the heating rate of 15 °C min^{-1}.

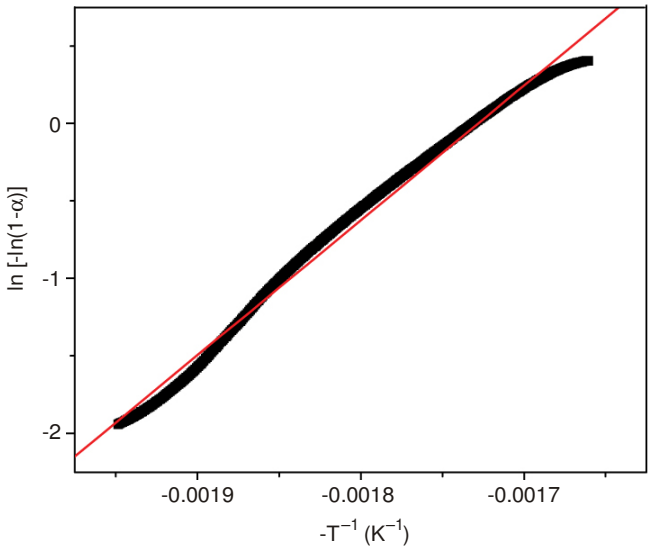


Fig. 4. Relation curve of $\ln[-\ln(1-\alpha)]$ *vs* $1/T_p$

The fitting curve is shown in Fig. 4. Based on 357 samples, the linear correlation coefficient r is 0.9961 and the calculating effects are as follows: n = 2.02298, $A = 1.5238 \times 10^5$, SD = 0.0642. The thermal decomposition kinetics equation of trimethoprim is obtained by substituting $f(\alpha)$, E_a and A into eqn. 3.

$$d\alpha/dt = 1.5238 \times 10^5 \exp(-\frac{78494}{RT})(1-\alpha)[-\ln(1-\alpha)]^{0.5057} \quad (7)$$

Conclusion

The thermal decomposition process on trimethoprim is studied by thermoanalysis technique and thermodynamic treatment. Trimethoprim has one loss-weight phenomenon in the course of increasing temperature in inert atmosphere. Furthermore, its thermal decomposition kinetics equation is derived by TG and DTG data. The study is of great significance in terms of predicting property and thermal stability.

REFERENCES

1. T. Sakai, T. Matsuishi, S. Yamada, H. Komori and H. Iwashita, *J. Neural Transm.*, **102,** 159 (1995).
2. H. Boran, E. Terzi, I. Altinok, E. Capkin and N. Bascinar, *Aquaculture*, **396-399**, 396 (2013).
3. S.W. Wright, K.D. Wrenn and M.L. Haynes, *J. Gen. Intern. Med.*, **14**, 606 (1999).
4. Z.A. Rasmussen A. Bari and S. Quazi, *Bull World Health Organ.*, **83**, 10 (2005).
5. G.S. Leoung, J.F. Stanford, M.F. Giordano, A. Stein, R.A. Torres, C.A. Giffen, M. Wesley, T. Sarracco, E.C. Cooper, V. Dratter, J.J. Smith and K.R. Frost, *J. Infect. Dis.*, **184**, 992 (2001).
6. J.P. Ioannidis, J.C. Cappelleri and P.R. Skolnik, *Arch. Intern. Med*, **156**, 177 (1996).
7. R. Alonso Campero, R. Bernardo Escudero, D. Del Cisne Valle Alvarez, M. González de la Parra, S. Namur Montalvo, V. Burke Fraga, R. Silva Hernandez and A. De Lago Acosta, *Clin. Ther.*, **29**, 326 (2007).
8. T.S. Zheng, *Chin. J. Veter. Med.*, **48**, 68 (2012).
9. X. Wang, Y.Z. Cui, H. Shao and T.S. Han, *China An. Husb. Vet. Med.*, **37**, 169 (2012).
10. K.Y. Zhou, Y.C. Cao, C. Tan, X.C. Xiang and H.Y. Zhang, *J. Hunan Agric. Univ.*, **25**, 483 (1999).
11. L. Wang, D.F. Qui, W.R. Xing, H. Yang and W. T. Chen, *J. Henan Uni. (Nat. Sci.)*, **33**, 36 (2003).
12. L. Wang, H. Yang, W.T. Chen, W.R. Xing and X.Z.Yao, *Chin. J. Appl. Chem.*, **19**, 1072 (2002).
13. Z.H. Liu, L.Z. Guishan, Analytical Chemistry Handbook, Thermal Analysis, Chemical Industry Press, Peking, p. 46 (2000).
14. C. Ma, J. Huang, H.-X. Ma, K.-Z. Xu, X.-Q. Lv, J.-R. Song, N.-N. Zhao, J.-Y. He and Y.-S. Zhao, *J. Mol. Struc.*, **1036**, 521 (2013).
15. V.A. Blagojevic, M. Vasic, D.M. Minic and D.M. Minic, *Thermochimica Acta*, **549**, 35 (2012).
16. H.E. Kissinger, *Anal Chem*, **29**, 1702 (1957).
17. T. Ozawa, *Bull Chem. Soc. Jpn.*, **38,** 1881 (1965).
18. R.Z. Hu, S.L. Gao and F.Q. Zhao, Kinetics for Thermal Analysis, Science Press, Beijing, p. 268 (2008).
19. V. Satava and J. Sestak, *J. Therm. Anal*. **8**, 477 (1975).
20. T. Ozawa, *J. Therm. Anal*, **2**, 301 (1970).