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Kinetics and Thermal Decomposition Studies of Oxomemazine by Isoconversional Protocols

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ABSTRACT

Thermogravimetry was used to investigate the thermal decomposition of oxomemazine. Oxomemazine has three distinct degradation processes during non-isothermal decomposition. The Arrhenius equation, Coats-Redfern (CR), Horowitz-Metzger (HM), and Flynn-Wall-Ozawa (F-W-O) equations were used in this research to perform kinetic analysis of the first decomposition stage. Oxomemazine thermal stability is very important when it comes to how it can be stored, quality control, and how long it can be used. Using thermal analysis, scientists have been able to learn more about how drug compounds are stable at different temperatures, as well as how fast they break down. Kinetic studies have emerged as a critical component of thermal analysis, with the primary goal of determining the kinetic model of thermal breakdown and calculating the Arrhenius equation parameters. The activation energy of the Arrhenius and Berthelot–Hood temperature functions was determined. The effect of different heating rates (5-20^{o}C/min) on thermogravimetric analysis (TG), Differential Thermal Analysis (DTA) is demonstrated.

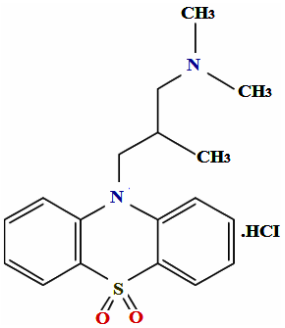
Keywords: Oxomemazine, Kinetic parameters, Thermal stability, Decomposition, Quality control.

INTRODUCTION

A phenothiazine derivative antihistamine, oxomemazine is used to relieve the symptoms of an allergic response. It is also used to treat coughs and the common cold as a component in a variety of cough syrups. It is considered one of the phenothiazine derivatives, Scheme 1.

Oxomemazine hydrochloride (OXO) chemically is defined as 3-(5,5-Dioxido-10H-phenothiazin-10-yl)-N,N,2-trimethylpropan-1-amine) hydrochloride. Oral oxomemazine dosages ranging from 10 to 40 mg per day are recommended[1-2]. In addition, suppositories of oxomemazine may be taken rectally. It has also been used by mouth, with the same results as Oxomemazine hydrochloride[1].

A review of the analytical literature for OXO determination indicates a variety of approaches, including spectroscopic[2-4], chromatographic[4-6], potentiometric[7], and electrochemical[8] methods.



Scheme 1. Chemical Structures of oxomemazinev

For pharmaceutical processes, such as oxomemazine, it is important to know the stability of drug samples such as oxomemazine's thermal behavior to estimate shelf life and ideal storage settings.

The thermal stability of the pharmaceutical drugs may be assessed from two perspectives: basic thermal analysis of the mass vs temperature profile and an assessment of the stability scope[9] or a more in-depth investigation utilizing kinetic analysis' techniques. Understanding the physicochemical characteristics and thermodynamic behaviour of substances under heat stress requires kinetic analysis[10]. Several kinetic approaches have been created over the years; however, the ICTAC 2000 recommendation suggests the advantages of isoconversional methods based on contemporary advancements in the thermal analysis[11].

To define any sort of mechanism in which thermal decomposition happens, kinetic data must be collected and analyzed; instead, kinetic analysis is directly associated with the process of thermal decomposition[12]. The use of thermoanalytical techniques may reveal new information regarding the temperature and energy involved with phenomena like melting, redox reactions, glass transition, boiling, sublimation, decomposition, crystallization, or the transition from gel to liquid crystal[13,14].

The current study is established since no published data on the thermal stability and decomposition kinetics of oxomemazine under thermal stress in non-isothermal circumstances in a nitrogen environment could be obtained.

EXPERIMENTAL

Materials

Oxomemazine hydrochloride was offered from AMOUN Pharmaceutical Co. Egypt, and the purity is 99.29%.

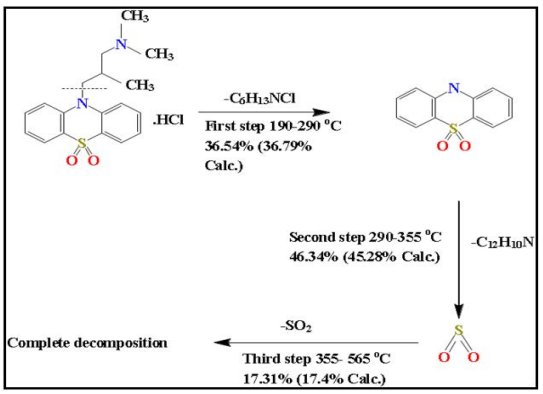
Instrumentation

Thermogravimetric analysis (TG), Differential Thermal Analysis (DTA), and differential thermogravimetry (DTG) were used to characterize oxomemazine hydrochloride. The TG curves (TGA60H Shimadzu thermobalance). Rates of heating of 5,10,15, and 20°C/min were applied from room temperature up to 600°C, with a dynamic N_2 atmosphere of 30 mL/min and a sample mass of 5.0 mg in a platinum pan.

RESULTS AND DISCUSSION

Oxomemazine Thermometric behavior

Figure 1 depicts the results of TG/DTG and DTA related to the decomposition of oxomemazine. As seen, the decomposition of oxomemazine in three disjointed stages. The first step relates to the liberation of 36.54% mass loss ($-C_6H_{13}NCl$) in the temperature range 190-290°C, Scheme 2. The second step represents the loss of 46.34% mass ($-C_{12}H_{13}NCl$) through 290 to 355°C, Scheme 2. While the third step is decomposition step is due to the loss of 17.31% ($-SO_2$) accompanied with complete decomposition, Scheme 2.



Scheme 2. The proposed thermal degradation of oxomemazine

Through the studied temperature range of 25-600°C, the DTA curve exhibits significant thermal events of interest. The endothermic thermal event at 248°C with no change in sample mass is correlating to oxomemazine melting[15]. While the exothermic events at 234, 330, and 480°C are attributed to the three decomposition steps.

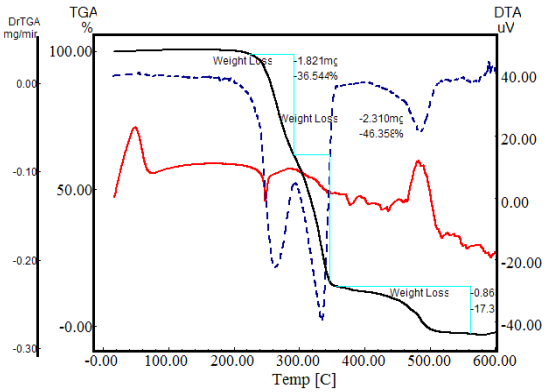


Fig. 1. Thermogravimetric analysis, TG/DTG and DTA curves of oxomemazine in dynamic N_2 atmosphere (30 mL min^{-1}) with heating rate at 5°C min^{-1}

The effect of varied heating rates on the TG and DTA curves

As can be seen from Fig. 2A and B, raising the rates of heating from 5 to 20°C/min caused the thermal events (TG stages and melting points) to be moved to the right, towards the higher temperature, resulting in the melting point being changed to the right as well. Table 1 summarizes the thermal event at 5 to 20°C/min heating rates.

Kinetic models

The kinetic factors acquired from the study conducted in non-isothermal circumstances were also used to assess the thermal stability of oxomemazine. The decomposition process was studied to complete the solid-state identification of oxomemazine, as there was no literature data to our knowledge. Arrhenius equation parameters and the mechanism of pyrolysis reaction are the fundamental goals of solid-state kinetic studies in thermal analysis, which are becoming more important. These data may be used to provide insight into how long and in what condition a storage unit has been in use[14].

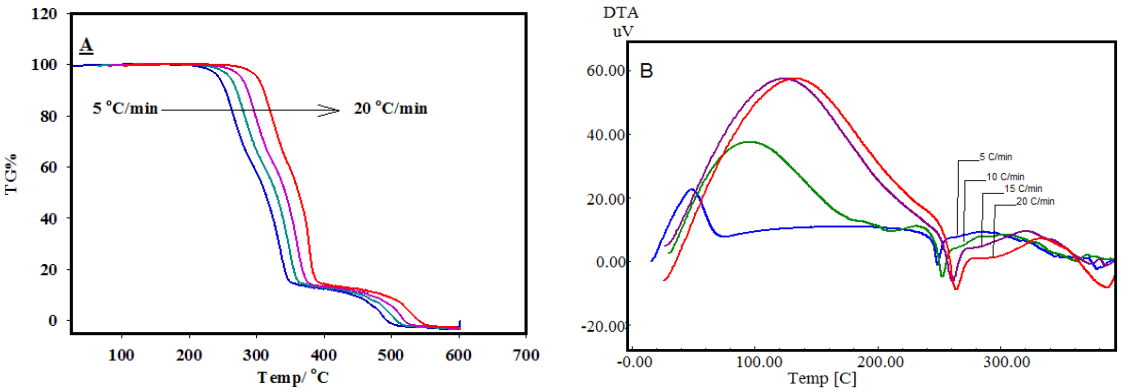


Fig. 2. A) TG of oxomemazine and B) DTA curves of oxomemazine in N_2 atmosphere at 5 to 20°C/minute

Table 1: Thermoanalytical measurements of oxomemazine at 5-20 oC/min rates of heating

Heat min^{-1}	TG and DTG flow/°C Decomposition temperature/°C			DTA	
	1st step	2nd step	3rd step	Endothermic peaks/°C	Exothermic peaks/°C
5	262	335	486	248	234, 330, 480
10	282	346	525	252	280, 341, 520
15	288	356	535	258	280, 350, 530
20	297	364	543	260	292, 358, 538

In this study, non-isothermal approaches such as the arrhenius equation[16-18], Horowitz-Metzger[19], Coats-Redfern[20], and Flynn-Wall-Ozawa[21] methods were used to extract kinetic parameters like activation energy and frequency factor of oxomemazine from TG/DTG data.

By applying the reaction rate at with a heating rate β:

$$d\alpha/dt = k(T).f(\alpha) = A.exp\left(-\frac{E}{R.T}\right).f(\alpha) \quad (1)$$

By using the rate of reaction formula in non-isothermal situations:

$$\beta = constant = d\alpha/dt \quad (2)$$

Equation (2) can be rewritten then into:

$$d\alpha/_{dt} = \beta.\frac{d\alpha}{dt} = A.exp(\frac{E}{R.T}).f(\alpha) \quad (3)$$

or

$$d\alpha/_{dt} = \frac{A}{\beta}exp(-\frac{E}{R.T}).f(\alpha) \quad (4)$$

Where α is referring to the conversion degree, t is denoting to the time, *f*(α) is denoting to reaction model, and *T* is denoting to temperature.

Arrhenius method

The Arrhenius equation was used to investigate the kinetics of oxomemazine first thermal degradation phase. The kinetic parameters were calculated using the Arrhenius equation[16-18], which was applied to solid-state processes. Using the value of conversion fraction (α), (dα/dt) is referred to the rate of the reaction, and *f*(α) = is defining the function of conversion, then the plot of ln [(dα/dt)/*f*(α)] vs 1/T is generated, Fig. 3A. Applying the slope and the intercept, the activation energy, and pre-exponential terms were calculated.

Coats–Redfern and Horowitz–Metzger protocols

The Coats–Redfern approach[20], particularly, f(α) functions, may be used to find kinetic parameters. It can be written as follows:

$$\ln\frac{f(\alpha)}{T^2} = \ln\left[\frac{AR}{\beta E}\left(1-\frac{2RT}{Ea}\right)\right] - \frac{Ea}{RT} \quad (5)$$

(A) denotes the pre-exponential component. The energies of activation and pre-exponential parameters for each f(α) function may be computed using a least-squares linear regression approach based on Eq. (1) using the slopes and intercepts of the graphs of ln(f(α)/T2) vs 1/T, Figure 3B.

The Horowitz–Metzger equation is written as follows:

$$\log[\log\frac{W_f}{W_f - W}] = \frac{\theta.Ea}{2.303RT_s^2} - \log 2.303 \quad (6)$$

Where W_f denotes the mass loss at the end of the first decomposition process, W denotes the mass loss up to temperature (T), R denotes the universal gas constant, T_s denotes the DTG peak temperature, and θ=T-T_s denotes the total mass loss. A straight line could be drawn by plotting log [log $W_f/(W_f$-$W)$] against θ. E_a could be then derived from the slope, Figure 3C.

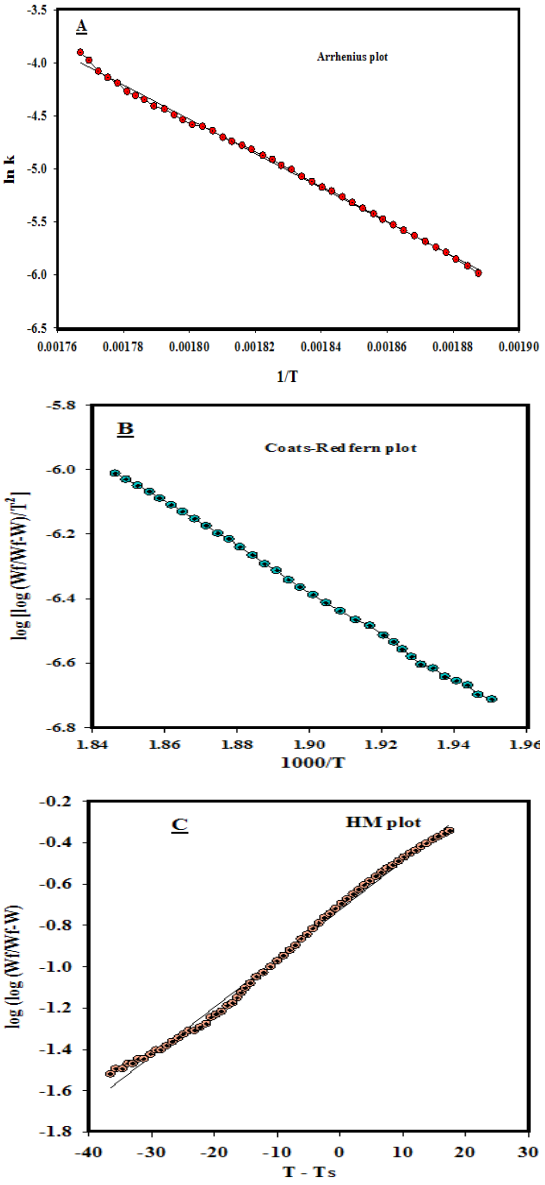


Fig. 3. Arrhenius, Coats-Redfern, and Horowitz-Metzger plots of oxomemazine first step thermal decomposition at 5°C/minute

Flynn–Wall–Ozawa protocol

Doyle's temperature integral calculation provides a base for the Flynn–Wall–Ozawa (FWO) approach, p(x)=exp(-1.052.x-5.331). The activation energies were determined using the FWO technique using the slope of the linear fitted function of lnβ vs 1/T, Fig. 4. In Table 2, the activation energy (E) values are listed. Ozawa's plots revealed that the reaction was the first order, with the slope of ln heating rate (β) vs 1/T being first order.

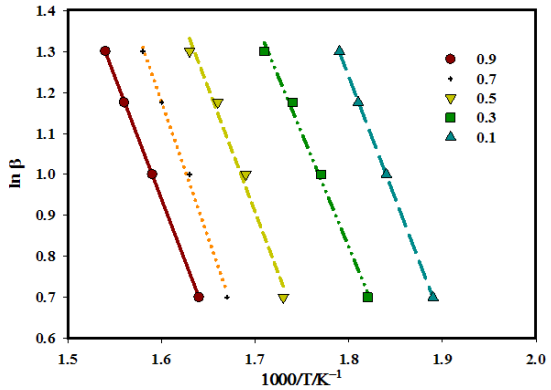


Fig. 4. The Flynn–Wall–Ozawa plots for oxomemazine at different heating rates

The kinetic parameters including activation energy (E), the activation entropy (S*), the activation enthalpy (H*), and the Gibbs free energy (G*), were all determined from the TG thermograms, as shown in Table 2. Thermal analysis system TA 60-WS (Shimadzu) software can produce conversion versus time curves for selected constant temperatures based on kinetic characteristics gleaned from non-isothermal data samples. The α (t) plots representing the temperatures from the measurement area were determined at 230, 250, 260, 270, and 280°C (Fig.5) using Berthelot–Hood temperature function. The calculated activation energy is found to be 132 kJ/mol with a good agreement with the previous calculated methods.

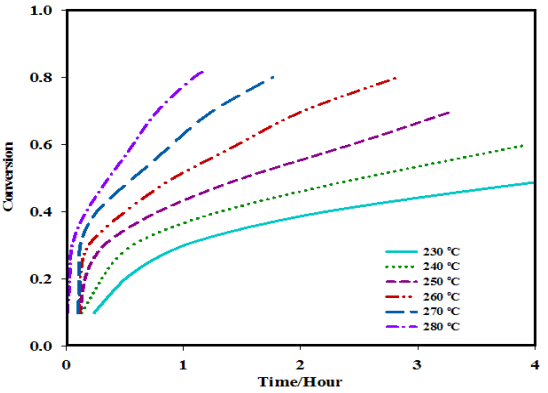


Fig. 5. Calculated conversion-time dependences (Berthelot–Hood model) in the selected temperature range at different heating rates

Table 2: Evaluation of kinetic values of the oxomemazine achieved by different methods

Parameters	Arrhenius	CR	HM	F-W-O
E_a/kJ mol^{-1}	133.85	132.59	128.78	133.12
A/min^{-1}	1.13x10^{12}	1.01 x10^{12}	1.02 x10^{12}	1.60 x10^{12}
ΔS*/kJ mol^{-1}	-20.96	-20.01	-19.91	-21.02
ΔH*/kJ mol^{-1}	129.39	128.14	124.34	128.66
ΔG*/kJ mol^{-1}	140.62	138.84	134.99	139.91

Herein, the outcomes depend on the OZAWA and Berthelot–Hood temperature functions providing almost like graphs as the temperature functions are practically in the same part of the measurement.

Table 2 also contains oxomemazine's computed kinetic parameters. Comparing the results of several kinetic techniques shows that the predicted activation energies of oxomemazine are comparable. To estimate activation thermodynamic parameters, kinetic parameters were acquired. The oxomemazine decomposition entropy (S) is negative. A negative value of S suggests a very well-ordered activated complex (transition theory)[22,23]. The outcome is a "slow" stage. The disintegration has positive H and G values, indicating that it is a heat-induced process.

CONCLUSION

The thermal decomposition of oxomemazine occurs in three phases that are clearly distinguished from one another. The isoconversional kinetic analysis of the first step, which resulted in the release of 36.54%, was performed. The values of the thermodynamic functions derived by integral approaches agreed well. This demonstrates the techniques' precision. There is high agreement and a small range of activation energy (E) values (128.78–133.85 kJ/mol) between the groups of approaches, indicating that the methods used were valid. The computed activation energy and thermodynamic characteristics may be used in medication quality control and preformulation phases.

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Conflicts of interest

The authors declare no conflict of interest.

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