Research Article

Kinetic Study of the Degradation of Mesalamine by Dry Heat Using UV-VIS Spectrophotometric Method

Saroj H Gatkal *, Vitthal V Chopade, Priti R Mhatre and Pravin D Chaudhari

Department of Quality Assurance Techniques, Modern College of Pharmacy Nigdi, Pune-411044, Maharashtra, India.

ABSTRACT

The aim of the present work is to detect kinetic rate of reaction of Mesalamine in bulk. Determination of rate of degradation, half life of Mesalamine when subjected to the dry heat degradation condition. A kinetic investigation of the dry heat degradation of Mesalamine was carried out at 50ºC, 60ºC, 70ºC by monitoring the parent compound itself. The method development was carried out using distilled water. The linearity range was found to be 2-16µg/ml. The method showed high sensitivity with good linearity. The reaction order of followed pseudo-first order kinetics. Energy of activation was found to be 0.05169 joule mol^{-1}.

Keywords: Mesalamine, kinetic study of degradation, UV-Vis Spectrophotometric Method.

INTRODUCTION[1-3]

The quality of a drug substance or drug product varies with time under the influence of a variety of environmental factors such as temperature, humidity and light. The two main aspects of drug product that play an important role in shelf life determination are assay of active drug, and degradants generated, during the stability study.

Mesalamine is chemically (5-amino-2hydroxybenzoic acid) is an anti-inflammatory agent, structurally related to the salicylates, which is active in inflammatory bowel disease and active ulcerative colitis. It is a tan to pink crystalline powder, relatively insoluble in chloroform, ether, n-hexane and ethyl acetate and freely soluble in dil.HCl and alkali hydroxides, Mesalamine is available in tablet dosage forms and is an official drug of USP. (fig1).

The present work aimed is to carry out this study that the determination of the degradation rate or kinetics of Mesalamine. The no work is carried out in the determination of the degradation rate or kinetics of Mesalamine. During stability studies it was found that Mesalamine is sensitive towards the different temperature conditions. So we mainly focus on the study of the dry heat degradation rate or kinetics of Mesalamine.

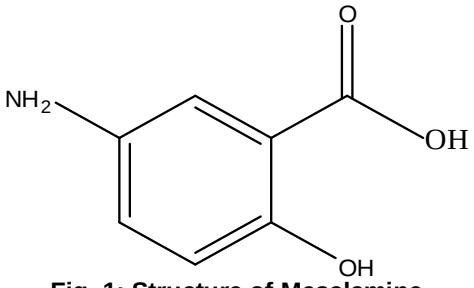

Fig. 1: Structure of Mesalamine

MATERIALS AND METHODS[4-6]

Materials

Mesalamine sample was obtained from Lupin Pharmaceuticals. The solvent used distilled water (AR grade), Methanol (AR grade). These chemicals were purchased from Merck Chemicals (Mumbai, India).

Equipment

The instrument used for the present study was Shimadzu Corporation, UV-Vis double beam (Model UV-1800 240V) high speed scanning spectrophotometer.

Kinetic studies[7-8]

Preparation of stock solution

Standard stock solution of Mesalamine was prepared by dissolving 10 mg of Mesalamine

in sufficient quantity of distilled water and make up the volume up to 100 ml, which gives 100 µg/ml solutions.

Preparation of working solution

From the above stock solution 0.8 ml was transferred into 10 ml volumetric flask and volume make up with distilled water to give 8µg/ml. Then sample was scanned with UV-Vis spectrophotometer in the range 200-400 nm and the wavelength corresponding to maximum absorbance was noted at 330 nm.

For studying the effect of concentrations of Temperature with respect to time

Bulk drug of Mesalamine was kept in oven at 50ºC, 60ºC, 70ºC. After the specific time interval i.e 3,6,9 hrs, 10mg sample was withdrawn and stock solution of 100 µg/ml was prepared using distilled water as solvent.. Calculate the % drug remaining by comparing the standard solution absorbance. Log of % drug remaining vs time in hrs. is plotted. (fig. 2)

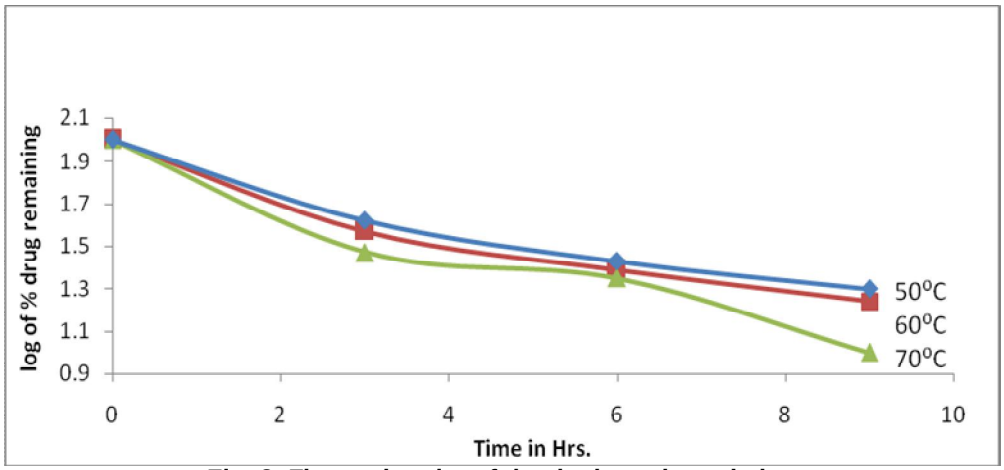

Fig. 2: First order plot of the dry heat degradation of Mesalamine with different temperature conditions

Method validation[9]

Linearity

Various aliquots were prepared from the stock solution (100µg/ml) ranging from 2-16 µg/ml. The samples were scanned in UV-Vis Spectrophotometer against distilled water as blank. It was found that the selected drug shows linearity between the ranges of 2-16 µg/ml(Fig. 3).

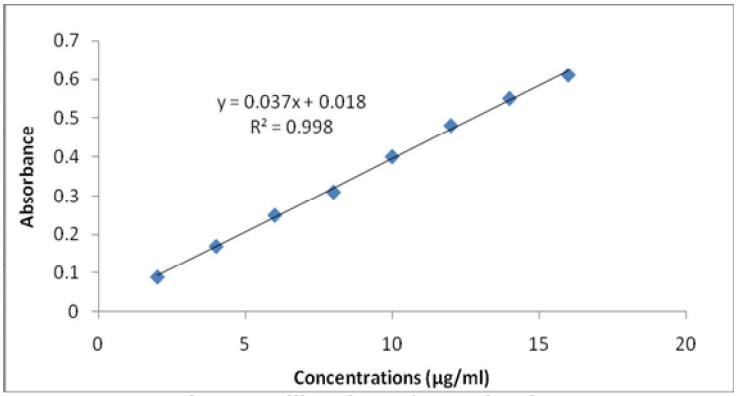

Fig. 3: Calibration of Mesalamine

Precision

Precision of the method was demonstrated by intraday and interday variation studies. In intraday variation study six different solutions of same concentration 8 µg/ml were analyzed three times in a day and the absorbance was noted. In the interday

variation studies, solution of same concentration 8 µg/ml were analyzed three

times for the three consecutive days and the absorbance result mean, standard deviation and % RSD was calculated and given in (Table 1 and 2)

Table 1: Inter-assay precision

Concentration (µg/ml)	%RSD			Average %RSD
	Day1	Day2	Day3	
8	1.176%	1.178%	1.176%	1.178%

Table 2: Intra-assay precision

Concentration (µg/ml)	Absorbance 1	Absorbance 2	Absorbance 3	Average %RSD
8	0.31	0.31	0.30	
8	0.32	0.31	0.31	
8	0.31	0.31	0.30	
8	0.31	0.32	0.31	
8	0.30	0.31	0.32	
8	0.31	0.30	0.31	1.374%
%RSD	1.178%	1.178%	1.766%	

Robustness, Ruggedness, LOD, LOQ was performed & summary of result shown in (Table 3).

Table 3: Summary of Validation parameters

Parameter	Result
Linearity indicated by correlation coefficient	0.998
Precision indicated by % RSD	1.275%
Accuracy indicated by % recovery	1.178%
Limit of Detection	0.83 µg/ml
Limit of Quantification	2.54 µg/ml
Range	2-16 µg/ml
Linear regression equation	0.037x + 0.018
Robustness indicated by % RSD	1.177%

RESULT

Kinetics of degradation

Different parameters that affect the rate of the reaction were studied. The effect of temperature was studied by conducting the reaction at different time interval. (fig.2) At each temperature the rate constant and $t_{1/2}$ were calculated and then the log of the rate constant was plotted against the reciprocal of the temperature in Kelvin units. (Arrhenius plot (fig. 4) to demonstrate the effect of temperature on the rate constant.

It was conclude that as the temperature increased the rate of degradation increased with decrease in the $t_{1/2}$ (Table 4).

Table 4: Kinetic data of Mesalamine

Different temperature conditions	K in hrs	$t_{1/2}$ in hrs	Log K
50°C	0.1750	3.96	-0.7569
60°C	0.1888	3.67	-0.7239
70°C	0.2395	2.89	-0.6206

Also, the energy of activation was determined by calculating the rate constant from the following equation. $\log \frac{k2}{k1} = \frac{Ea}{2.303R}\left(\frac{T2-T1}{T1T2}\right)$

Where,

Ea- Activation energy

T_1, T_2 – Temperatures degree in Kelvin

R- Gas constant

K_1,K_2- Rate constant at two temperature.

The calculated Ea was found to be 0.05169 joule mol^{-1}.

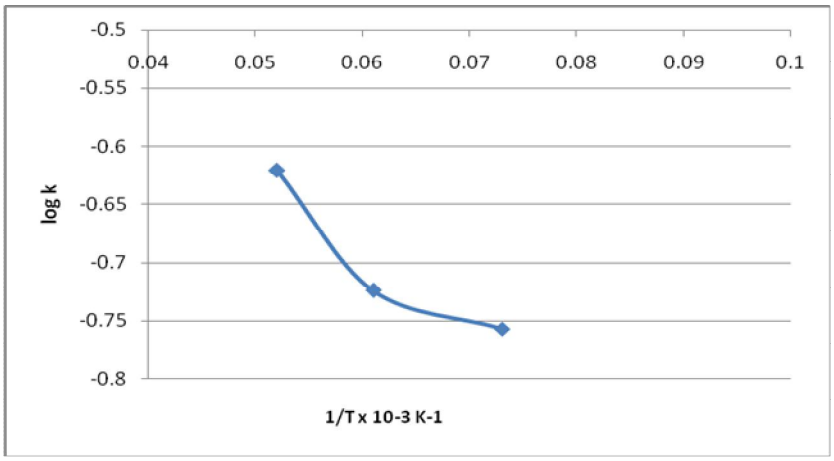

Fig.4: Arrhenius plot for the dry heat degradation of Mesalamine with 50ºC, 60ºC, 70ºC

CONCLUSION

In conclusion, the dry heat degradation of Mesalamine was found to follow a pseudo first order reaction rate. It was found that as the temperature increased the rate of degradation increased with decrease in the $t_{1/2}$ .The proposed method provides a simple, sensitive method sutaible for the quality control analysis of Mesalamine in the bulk .

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