AMERICAN JOURNAL OF PHARMTECH RESEARCH

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Quantitative Estimation of Carbimazole by UV Derivative Spectrophotometry in Bulk Drug and Tablet Formulation

Avinash V. Deosarkar*[1], Shruti D. Deshpande[1], Sanjay G. Walode[1]

1. Department of Pharmaceutical Chemistry, Sinhgad Institute of Pharmaceutical Sciences, Lonavala -410401, University of Pune, (Pune), Maharashtra, India

ABSTRACT

Development and validation of an analytical UV derivatives spectrophotometric method to quantify carbimazole as a single active principle in pharmaceutical formulation were done. Based on the spectrophotometric characteristics of carbimazole, a signal of first (314 nm), second (300 nm), third (289 nm), fourth (320 nm) order derivative spectrum was found to be adequate for quantification. The method obeyed Beer's law in the concentration range of (2-18 µg/ml) with square correlation coefficient (r^2 = 0.999). The mean percentage recovery was found to be 99.56 ± 0.7179. As per ICH guidelines the results of the analysis were validated in terms of linearity, precision, accuracy, limit of detection and limit of quantification, and were found to be satisfactory.

Key Words: Carbimazole, Derivative spectrophotometry, ICH, Validation.

*Corresponding Author Email: avinashvd10@gmail.com

Received 3 April 2012, Accepted 20 April 2012

Please cite this article in press as: Deosarkar AV. *et al.*, Quantitative Estimation of Carbimazole by UV Derivative Spectrophotometry in Bulk Drug and Tablet Formulation. American Journal of PharmTech Research 2012.

INTRODUCTION:

Derivative spectroscopy can effectively resolve many analytical problems, including resolution of multi-component system, removal of sample turbidity, matrix background and enhancement of spectral details. This technique can be successfully applied in qualitative and quantitative analysis in pharmaceutical and biomedical areas. Carbimazole, ethyl 3-methyl-2-sulfanylidene-imidazole-1-carboxylate, is a antihyperthyroidism drug. It is a pro-drug and after absorption it gets converted to active form, methimazole. Methimazole acts by preventing the thyroid peroxidase enzyme and reducing the production of the thyroid hormones T3 and T4 (thyroxine) [1]. Several analytical methods have been reported for the analysis of carbimazole such as an indirect bromometric[2], potentiometric[3], voltammetric[4], chromatographic[5-7], spectrophotometric [8-10], polarographic [11], and fluorometric titration [12]. Literature survey reveals that no derivative method is reported for determination of carbimazole in tablet dosage forms. The main objective of the proposed work was to develop a simple, accurate, precise and sensitive UV derivative spectroscopic method for the estimation of carbimazole in tablets. The method was further optimized and validated in accordance with guidelines suggested by International Conference on Harmonization (ICH).[13,14]

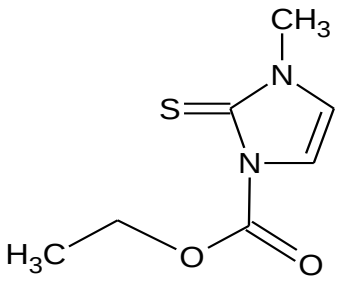

Figure.1 Chemical structure of carbimazole

MATERIALS AND METHODS:

Authenticate carbimazole sample was a kind gift from Gens Pharma International Pvt Ltd., Pune, India. Methanol AR grade (Merck Ltd, Mumbai, India) was used as solvent. Double beam UV/Vis spectrophotometer (JASCO V-530) with 1cm matched quartz cells was used to measure absorbance of resulting solution.

Preparation of standard stock solution:

Weighed accurately 10 mg of carbimazole and transferred to a 10 ml volumetric flask, add 5 ml of methanol and sonicate for 10 min. Finally the volume was made up to mark with methanol.

Study of spectra and selection of wavelengths:

Working standard solution of 10µg/ml was scanned between the range 230-400 nm in 1 cm cell against blank.

Analysis of tablet formulation:

Twenty tablets of carbimazole were triturated and mixed thoroughly. Accurately weighed quantity of tablet powder equivalent to 10 mg of carbimazole was transferred in 10 ml volumetric flask. Add 5 ml methanol and sonicate for 10 min. The resultant solution was filtered through 0.45µ membrane filter and finally diluted to volume with methanol. The absorbance of resultant solution was measured at 299 nm. The analysis data shown in Table 4.

Linearity:

Standard stock solution was diluted with methanol so as to get different solutions i. e. 2, 4, 6, 8, 10, 12, 14, 16 and 18µg/ml. The absorbance were recorded at 314, 300, 289, 320 nm and were found to be linear in concentration range 2-18 µg/ml. The linearity was calculated by the least square regression method.

Recovery:

To check the accuracy of the proposed method, recovery studies were carried out by applying standard addition method. A Known amount of standard carbimazole, corresponding to 80, 100 and 120% of the label claim was added to pre-analysed sample of tablet. The recovery studies were carried out in triplicate at each level.

Precision:

Precision of analytical method is expressed in relative standard deviation (RSD) of a series of measurements. The intra-day and inter-day precisions of the proposed methods were determined by estimating the corresponding responses (i.e. three concentrations / three replicates each) of the sample solution on the same day and on three different days respectively (Table 2).

Limit of detection (LOD) and limit of quantification (LOQ):

The signal-to-noise ratio (*S/N*) method was adopted for the determination of limit of detection and limit of quantification. The limit of detection was estimated as three times the *S/N* ratio and the limit of quantification is estimated as ten times the *S/N* ratio. The results of validation data are given in Table 2.

RESULTS AND DISCUSSION:

The zero, first, second, third and fourth order derivative spectra were recorded. The peak amplitude of zero order at 299 nm (figure.2), first order at 314 nm (figure.3), second order at 300

nm (figure.4), third order at 289 nm (figure.5) and fourth order at 320 nm (figure.6) derivative spectra were measured.

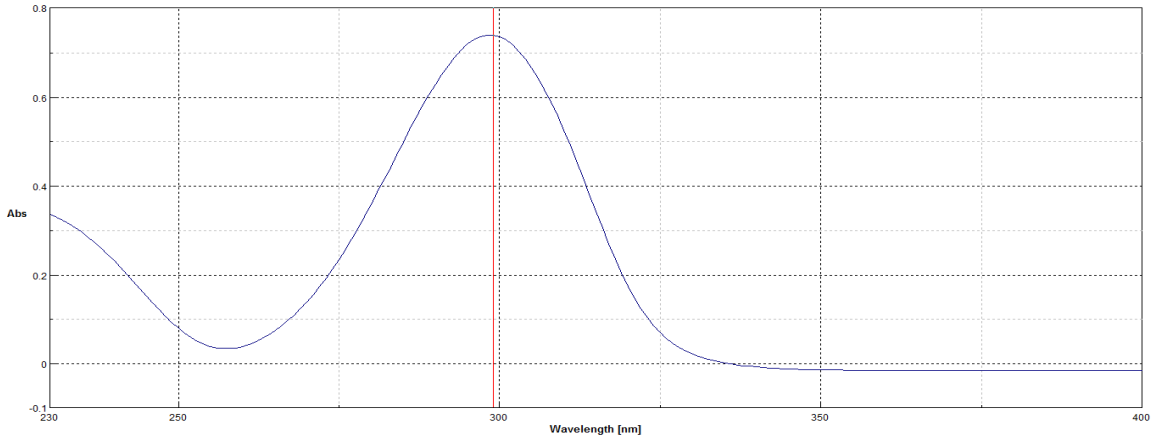

Figure. 2: Zero order derivative spectra (λ max 299 nm)

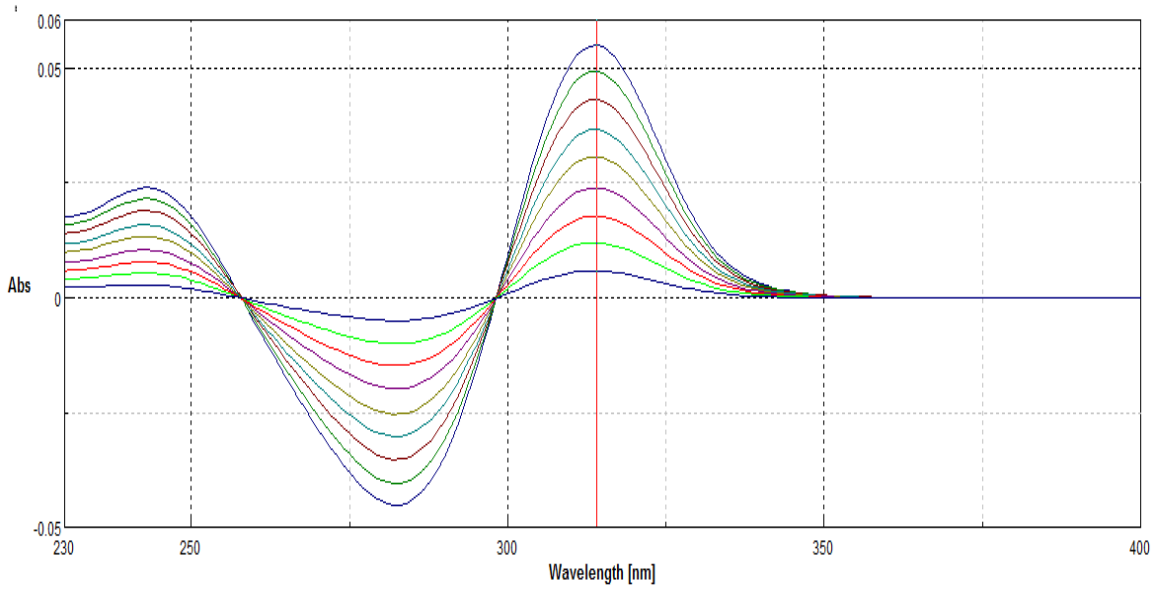

Figure.3: First order derivative spectra (λ max 314 nm)

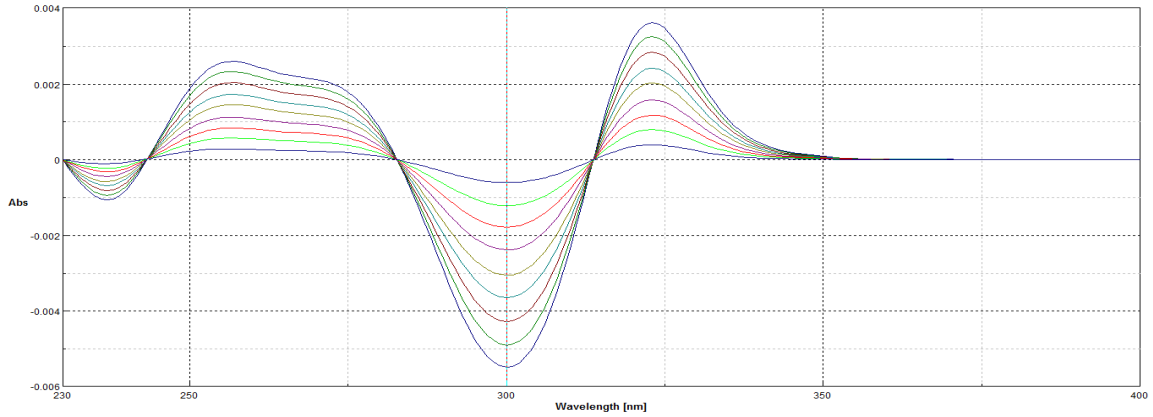

Figure.4: Second order derivative spectra (λ max 300 nm)

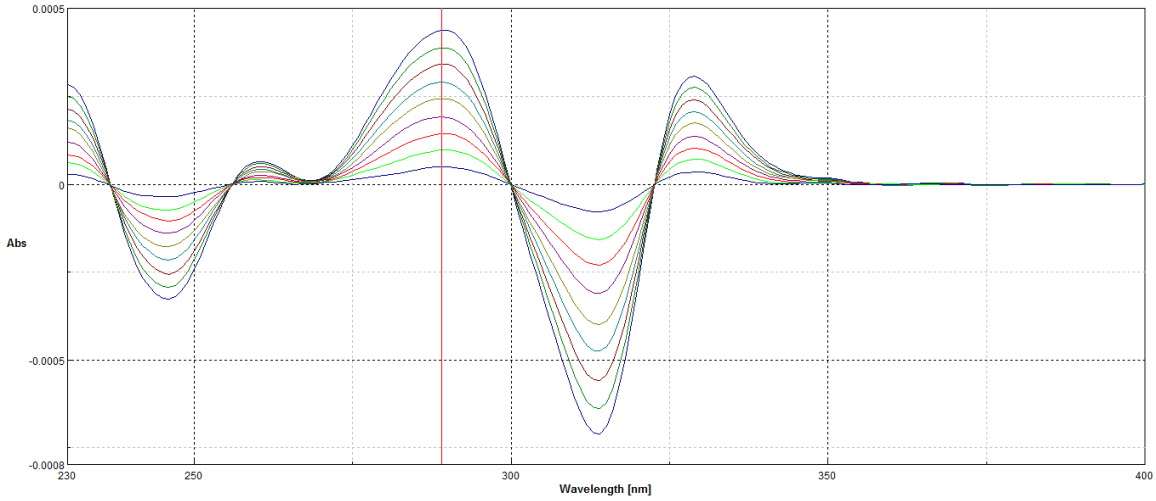

Figure 5: Third order derivative spectra (λ max 289 nm)

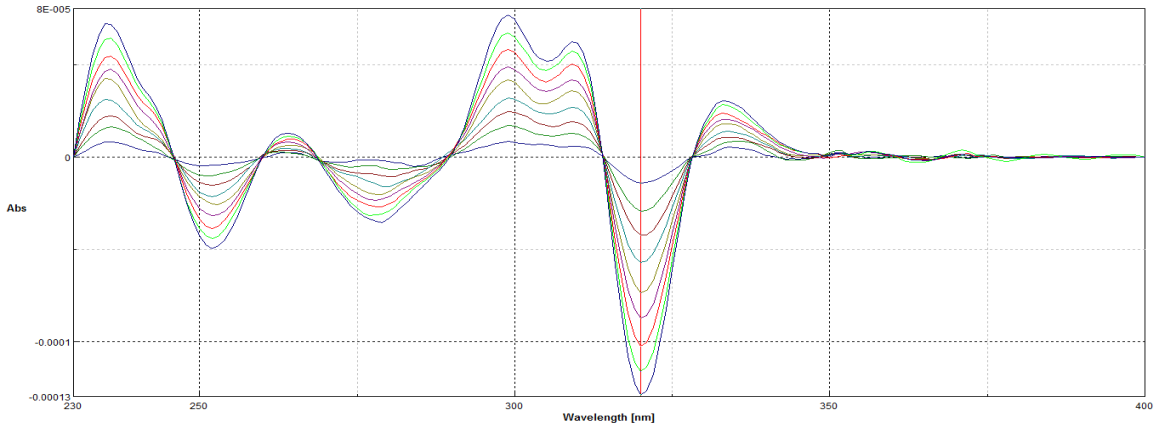

Figure 6: Fourth order derivative spectra (λ max 320 nm)

Table 1: statistical data of calibration curve.

Parameters	**Value**			
	1st order	**2nd order**	**3rd order**	**4th order**
Linearity and range (µg/ml)	2-18	2-18	2-18	2-18
Wavelength (nm)	314	300	289	320
Regression equation	y = 0.003x - 0.000	y = 0.000x – 0.00004	y =0.00002x + 0.00000003	y = 0.000007x -0.0000002
Correlation coefficient (r^2)	0.999	0.999	0.999	0.999

Y=mx+c; where x is the concentration of drug in µg/ml, y is the amplitude at specified wavelength, m is the slope and c is the intercept.

Validation of the proposed method was done according to ICH guidelines. Linearity was established by the least-square linear regression analysis of the calibration plots (Table 1). Carbimazole showed good linear response with first (Figure.7), second (Figure.8), third

(Figure.9) and fourth (Figure.10) derivative spectra. Reproducibility of the result was ascertained by replicate analysis, indicating that the method was precise(Table 2). Accuracy of the method was carried out by spiking the standard drug to tablet powder, which afforded recovery of almost 99.56% (Table 3), indicating non-interference of the sample matrix.

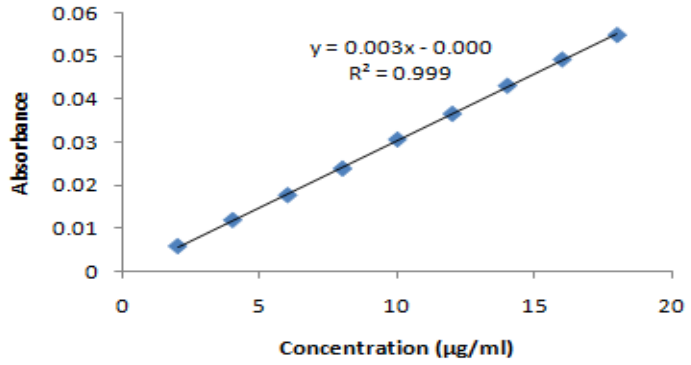

Figure.7: Linearity of carbimazole by first order derivative spectroscopy

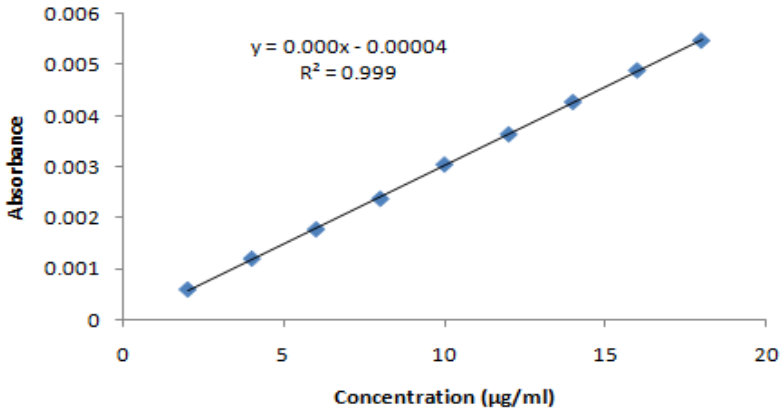

Figure. 8: Linearity of carbimazole by second order derivative spectroscopy

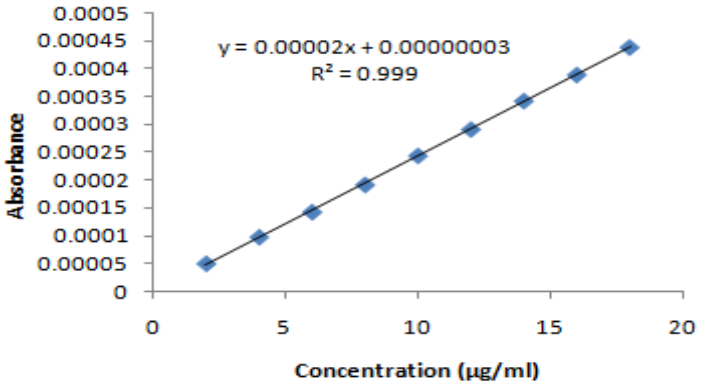

Figure 9: Linearity of carbimazole by third order derivative spectroscopy

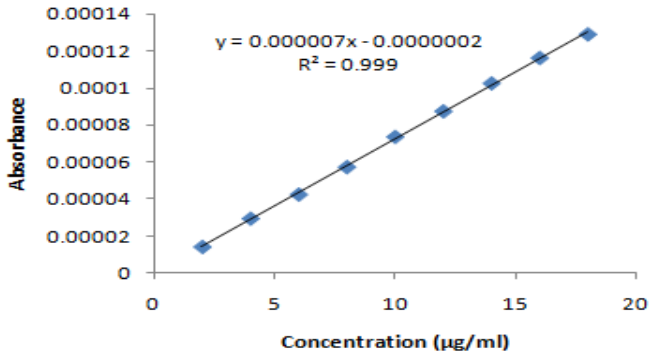

Figure. 10: Linearity of carbimazole by fourth order derivative spectroscopy

Table 2: Result of Validation Studies of Proposed Method

Parameters	Values
Limit of detection (µg/ml)	0.50
Limit of quantitation(µg/ml)	1.60
Precision (n = 3)	
Intra-day*	100.12 ± 1.8774
(% estimated ± S.D.)	101.22 ± 1.6082
	101.87 ± 0.9602
Inter-day*	98.85 ± 0.5443
(% estimated ± S.D.)	100.37 ± 0.1657
	100.53 ± 0.9602

SD is standard deviation, * indicates mean of three replicates

Table 3: Recovery Study Data

Level of standard addition (%)	Amount of tablet powder (mg)	Amount of pure drug added (mg)	Amount of pure drug recovered (mg)	%Recovery ± SD
80	10	8	7.89	98.67 ±0.9165
100	10	10	10.03	100.34 ± 0.3676
120	10	12	11.96	99.68 ± 0.8697

The analysis of tablet formulation absorbance of resultant solution was measured at 299 nm. The analysis data shown in Table 4

Table 4: Analysis Data for Tablet Formulation

Formulation	Taken amount	Amount estimated	% estimated	% RSD
Thyrocab	10 mg	10.007 mg	100.07	0.7385

RSD is relative standard deviation

CONCLUSION:

The proposed first, second, third, and fourth order derivative spectrophotometric method is simple, accurate, precise and selective for the estimation of carbimazole. The method is economical, rapid and do not require any sophisticated instruments contrast to chromatographic method. Hence it can be effectively applied for the routine analysis of carbimazole in bulk drug & pharmaceuticals.

ACKNOWLEDGMENT:

Authors are grateful to Gens Pharma International Pvt Ltd., Pune, for providing gift sample of carbimazole and to Dr. S. B. Bhise, Principal of Singad Institute of Pharmaceutical Sciences for providing necessary facilities to carry out the research work.

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