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Research Article

Determination of Methimazole in Tablets Using Spectrophotometric Methods

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ABSTRACT

This study describes the spectrophotometric quantification of methimazole in tablets using zero-order absorption spectrophotometry and first derivative spectrophotometry methods. In preliminary experiments, linearity range was found between 2.0-24.0 µg/mL in zero-order spectrophotometry and first-order derivative spectrophotometry. Calibration curves were obtained by measurements of the zero-order absorbances and their first derivative values at 260.0 and 269.0 nm for the zero-order spectrophotometry and first derivative spectrophotometry, respectively. The recovery and relative standard deviations were calculated as 103.3 % and 2.18 % for UV absorption spectrophotometry and 98.0% and 0.64% for first derivative spectrophotometry, respectively. The proposed techniques were used for the analysis of tablets preparations. The methods proposed in this study were verified by analyzing validation test samples containing methimazole. Determination results showed that the applied methods were found to suitable for the quantitation of the related drug.

Keywords: *Methimazole, UV-VIS Spectrophotometry, Tablet*

Spektrofotometrik Yöntemlerle Tabletlerde Metimazol Tayini

ÖZET

Bu çalışma doğrudan absorbans ölçüm ve türev spektrofotometrik yöntemlerini kullanarak tabletlerdeki methimazolün spektrofotometrik miktar tayinini açıklamaktadır. Yapılan ön çalışmalarda sıfırıncı derece ve birinci türev spektrofotometri yöntemlerinde doğrusal çalışma aralığı 2,0-24,0 µg/mL olarak bulunmuştur. Sıfırıncı derece spektrofometri yönteminde 260,0 nm, birinci derece türev spektrofotometri yönteminde ise 269,0 nm dalga boylarında ölçümler yapılarak kalibrasyon eğrileri elde edilmiştir. Geri kazanım ve bağıl standart sapma değerleri; doğrudan absorbans ölçüm yöntemi için % 103,3 ve % 2,18 ve birinci derece türev spektrofotometri için % 98,0 ve % 0,64 olarak bulunmuştur. Daha sonra önerilen teknikler tablet preparatlarının analizi için uygulanmıştır. Bu çalışmada metodların uygulanabilirliği, methimazol içeren test örneklerinin validasyon çalışmalarıyla doğrulanmıştır. Analiz sonuçları, ilacın miktar tayini için ilgili metodların uygulanabilir olduğunu göstermektedir.

Anahtar Kelimeler: *Methimazol, UV-GB Spektrofotometri, Tablet*

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I. INTRODUCTION

Methimazole, also called as thiamazole, is an antithyroid agent, has gained a distinct value in the medical world because it is very effective in hyperthyroidism [1-4]. The literature survey for methimazole reveals several analytical methods such as spectrophotometry [5-7], Pharmacopoeia method [8], voltammetry [9-11], HPLC [12-14], electrophoresis [15]. Spectrophotometric methods are commonly used in pharmaceutical analysis due to being simple, cheap and fast methods compared to other methods. The proposed spectrophotometric approaches in this study enables fast and accurate analysis of methimazole without the use of expensive equipment. These two spectrophotometric methods can be applied in routine analysis with a spectrophotometer and a personal computer. For pharmaceutical dosage forms containing single active pharmaceutical ingredient, the easiest analysis approach is the direct measurement of absorbance at the maximum absorbance wavelength in the spectrum. However, the main problem in the application of the direct absorbance measurement is usually the excipient effect on the analysis of the related active compound. In this case, derivative spectrophotometry is very suitable to eliminate the disadvantage of classical spectrophotometric measurement methods.

In this study, direct absorbance measurement and first derivative method were subject to quantitative analysis of methimazole in solid dosage form and laboratory-made solutions. Calibration equations were validated by analyzing laboratory-made samples. The analysis results of commercial tablets obtained by applying the proposed methods were in agreement with the label claim and with each other.

II. EXPERIMENTAL

A. INSTRUMENTATION

The measurements were performed with Shimadzu UV-1601 spectrophotometer with double beam. Absorbance spectra were recorded between the range of 200-320 nm and 1 cm quartz cells were used. The spectrophotometer was connected to a personal computer with Shimadzu UVPC software.

B. MATERIALS AND REAGENTS

Methimazole was purchased from Abdi İbrahim. Thyromazol® tablet containing 5mg methimazole was obtained from a local pharmacy. The reagents and solvents were analytical grade. Aqueous solutions were prepared with double distilled water.

C. PREPARATION OF SOLUTIONS

Stock solution of methimazole (50 µg/mL) were prepared in methanol. The standard solutions were prepared by diluting the stock solution of methimazol with methanol. All solutions were prepared freshly every day.

D. TABLET ANALYSIS PROCEDURE

Commercial Thyromazol® tablet preparation contains 5 mg methimazole. Ten tablets were weighed and finely powdered. A powder amount, equivalent to one tablet, was weighed and dissolved in the methanol in 100 mL volumetric flask. After 20 minutes of ultrasonication, this solution was filtered from a 0.45 µm filter. Then, final sample solution was obtained by diluting with the methanol. Their original spectra were recorded and then derivative spectra were calculated.

III. RESULTS AND DISCUSSION

The UV absorption spectra of methimazole in methanol was indicated in Figure 1. The standard calibration samples of methimazole in the concentration 2.0-24.0 µg/mL were prepared in methanol. The absorption spectra of these solutions were recorded in the wavelength range of 200-320 nm. Direct absorbance measurement method, which is also called zero-order UV-Vis spectrophotometry was developed for the quantification of methimazole in samples. The aim of applying first derivative method was developing a comparative method to direct absorbance measurement method. According to the obtained results from the application of direct absorbance measurement and first derivative methods to the analysis of tablets, excipient interference was not observed in the tablets.

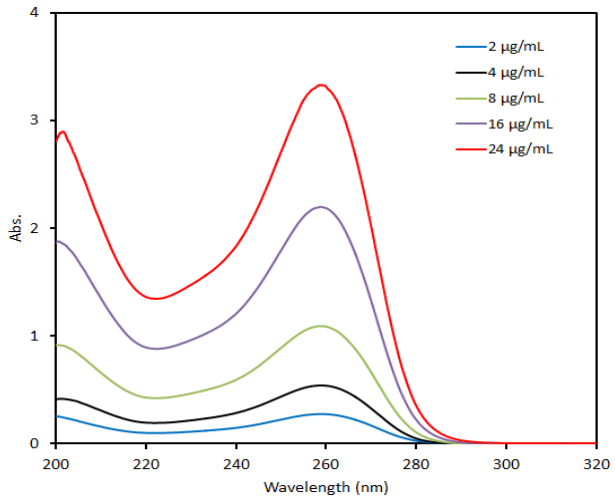

Figure 1. *Zero-order spectra of the calibration series of methimazole in the working range of 2.0-24.0 µg/mL*

A. DIRECT ABSORBANCE MEASUREMENT METHOD

The absorbance of calibration solutions of methimazole in the working range of 2.0-24.0 µg/mL were plotted as seen in Figure 1. The peak amplitudes at the maxima at 260.0 nm were measured. A straight-line was obtained by plotting the measured absorbance values against the concentration values. Calibration equations were linear in the concentration range from 2.0-24.0 µg/mL with a correlation coefficient 0.9990. The calculated calibration equation given by A=0.138C-0.012 was used to quantify methimazole in validation samples and tablets. The limit of detection and quantification were 0.17 and 0.55 µg/mL for methimazole. (See Table 1).

Table 1. *Statistical parameters of the calibration curves obtained by zero-order spectrophotometry and first derivative spectrophotometry*

Parameter	Zero-Order Spectrophotometry	First Derivative Spectrophotometry
Wavelength	260.0 nm	269.0 nm
Concentration Range	2.0-24.0 µg/mL	2.0-24.0 µg/mL
Regression Equation	A= 0.138xC - 0.012	A= 0.043xC + 0.00139
Regression Coefficient	0.9990	0.9950
Standard Error of the Slope	$5.65x10^{-4}$	$1.36\ x10^{-4}$
Standard Error of the Intercept	$7.65\ x10^{-3}$	$1.85x10^{-3}$
Limit of Detection (LOD, µg/mL)	0.17	0.13
Limit of Quantitation (LOQ, µg/mL)	0.55	0.43

The validity of the method was evaluated by analyzing test sample of methimazole at three different concentration levels (See Table 2). Then, the direct absorbance measurement method was applied to the analysis of solid dosage form containing methimazole.

Table 2. *Recovery results of methimazole in test samples by zero-order spectrophotometry and first derivative spectrophotometry*

		Zero-Order Spectrophotometry		First Derivative Spectrophotometry	
	Added (µg/mL)	Found (µg/mL)	Recovery (%)	Found (µg/mL)	Recovery (%)
1	6	6.34	105.7	5.89	98.2
2	12	12.35	102.9	11.81	98.4
3	18	18.22	101.2	17.5	97.2
		Mean :	103.3		98.00
		Standard Deviation :	2.25		0.63
		Relative Standard Deviation :	2.18		0.64

B. FIRST DERIVATIVE SPECTROPHOTOMETRIC METHOD

In the application of this method, the first derivative spectra were obtained by using a $\Delta\lambda$=2 nm interval to calculate the derivative data of the original spectra of samples (Figure 2). The calibration graph, which was obtained by measuring the $dA/d\lambda$ values at 269.0 nm, were used for the analysis of methimazole in the test samples and tablets. Regression equation, correlation coefficient and their statistical data were shown in Table 1. The calibration equation of the first derivative spectrophotometric method was validated by using the quantitative analysis of synthetic mixtures. Recovery results and with relative standard deviation were shown in Table 2. After validation study, first derivative spectrophotometric method was applied to the analysis of solid dosage form containing methimazole.

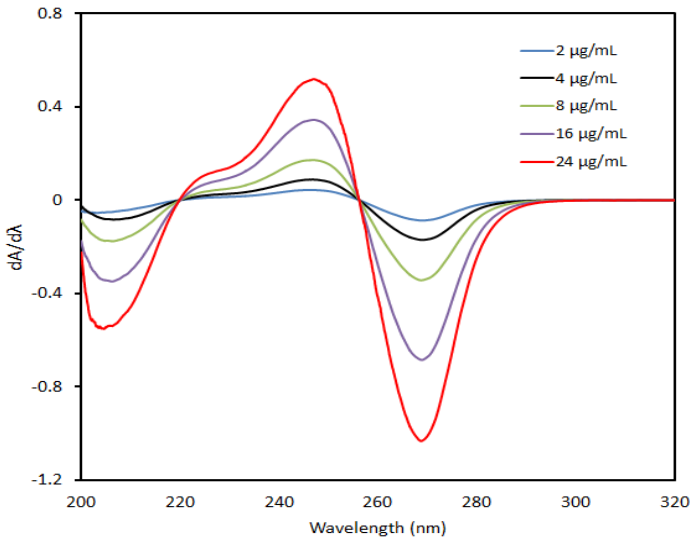

Figure 2. *First derivative spectra of the calibration series of methimazole in the working range of 2.0-24.0 µg/mL*

C. ANALYSIS OF TABLETS

Two fast spectrophotometric methods developed in this paper were then, applied for the quantitation of methimazole in tablets following the procedure mentioned above. The tablet assay results provided by these two methods were presented in Table 3. In practice, the direct absorbance measurements at 260.0 and first derivative amplitudes at 269.0 nm were found to be suitable to get calibration equations for the application of zero-order spectrophotometry and first derivative spectrophotometry to the analysis of commercial tablet samples. Analysis results were in agreement with the label claim. (Table 3).

Table 3. *Assay results of methimazole in tablets by zero-order spectrophotometry and first derivative spectrophotometry*

Number	Found (mg/tablet)	
	Zero-Order Spectrophotometry	First Derivative Spectrophotometry
1	5.13	4.93
2	5.12	4.92
3	5.18	4.99
4	5.12	4.97
5	5.16	4.96
6	5.12	4.93
7	5.11	4.93
8	5.15	4.97
9	5.32	5.10
10	5.30	5.10
Mean :	5.20	5.00
Standard Deviation :	0.08	0.07
Relative Standard Deviation :	1.45	1.36

IV. CONCLUSION

In this study, zero-order spectrophotometry and first derivative spectrophotometry were proposed for the determination of methimazole in commercial tablets. Analysis of solid dosage forms containing methimazole did not indicate interference from the excipiens. It was observed from the assay results in Table 1 that, the limit of detection and the limit of quantitation of the direct UV absorbance measurement method was bigger than those provided by derivative spectrophotometry. Particularly, derivative spectrophotometry is a useful method, enabling elimination of possible interferences from excipients in the dosage form. This can be considered as an advantage of derivative method over direct UV absorbance measurement technique. Therefore, these methods can be used instead of the methods in literature. This can be considered an advantageous of derivative method over direct UV absorbance measurement technique. These methods are easy with no requirement of any separation and extraction procedures. The methods can be applied to routine analysis performed in any laboratory having a UV spectrophotometer with a personal computer.

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