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DUAL WAVELENGTH AND SIMULTANEOUS EQUATION SPECTROPHOTOMETRIC METHODS FOR ESTIMATION OF ATENOLOL AND INDAPAMIDE IN THEIR COMBINED DOSAGE FORM

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ABSTRACT

Two simple, accurate and precise UV spectroscopic methods were developed for the simultaneous estimation of atenolol and indapamide in their combined dosage form. First method employs formation and solving of simultaneous equation using 246.4 nm and 266 nm as two wavelengths for formation of simultaneous equations. Second method being dual wavelength method, in which two wavelengths were selected for each drug in a way so that the difference in absorbance is zero for another drug. Atenolol has equal absorbance at 246.4 nm and 254.2 nm, where the differences in absorbance were measured for the determination of indapamide; similarly differences in absorbance at 266 nm and 270.2 nm were measured for the determination of atenolol. The results of analysis were validated statistically and by recovery studies and found to be free from interferences. These methods obey Beer's law in the concentration range 100 to 350 and 5 to 17.5 µg/mL for atenolol and indapamide, respectively.

Key words: Atenolol, Indapamide, Ultraviolet spectrophotometry, Simultaneous equation, Dual wavelength.

INTRODUCTION

Chemically, Atenolol is 4-[2-hydroxy-3-[(1-methylethyl)amino]propoxy] benzeneacetamide[1] and Indapamide is 3-(aminosulfonyl)-4-chloro-N- (2,3-dihydro-2-methyl-1H-indol-1-yl)benzamide[1]. Atenolol belongs to beta blocker group, a class of

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drugs used primarily in cardiovascular diseases such as hypertension. It is one of most commonly used beta blocker for hypertension and angina. Indapamide is a thiazide diuretic generally used in the treatment of hypertension and edema caused by congestive heart failure[2].

The combination of atenolol and indapamide is used in the therapy of arterial hypertension[3,4]. HPLC method has been reported for the estimation of atenolol and indapamide in combination[3], but no method has been reported for spectrophotometric determination of atenolol and indapamide in their combined pharmaceutical dosage forms. This paper illustrates two simple, economical, accurate, precise and sensitive spectrophotometric methods for simultaneous determination of atenolol and indapamide in their combined dosage forms by using simultaneous equation method[5] and dual wavelength method[6].

Dual wavelength spectroscopy offers an efficient method for analyzing a component in presence of an interfering component. For elimination of interferences, dual analytical wavelengths were selected in a way to make the absorbance difference zero for one drug in order to analyse the other drug. The difference in absorbance at 246.4 nm (λ_1) and 254.2 nm (λ_2) was zero for atenolol, so $\lambda_1 - \lambda_2$ were used to analyze indapamide whereas the difference in absorbance at 266 nm (λ_3) and 270.2 nm (λ_4) was zero for indapamide and hence, $\lambda_3 - \lambda_4$ were used to analyze atenolol.

EXPERIMENTAL

Materials and methods

Methanol used was of analytical grade (S.D.fine chemicals, Mumbai). A Perkin Elmer UV-Vis spectrophotometer – Lambda EZ 201, with 10 mm matched quartz cells, was used for the measurement of absorbance. Atenolol and indapamide pure drugs were obtained from Torrent Pharmaceuticals Ltd., Ahmedabad and Perfect Consultant, Pune, respectively as gift samples. Combined drug tablets containing atenolol and indapamide 50 mg and 2.5 mg, respectively were procured form the local market.

Stock solutions (1 mg/mL) of both drugs were prepared in methanol. For verification of Beer's law, a series of diluted solutions of atenolol and indapamide ranging from 100 -350 μg/mL (Series A) and 5 -17.5 μg/mL (Series B), respectively were prepared and mixture of both the drugs (Series C) were prepared in methanol. It was observed that atenolol and indapamide individually as well as in their mixtures, gave a good linear response at the selected wavelengths.

Method I: Simultaneous equation method

For estimation of pure drugs by the simultaneous equation method, solutions of 250 µg/mL atenolol and 12.5 µg/mL indapamide and a mixture containing 250 µg/mL and 12.5 µg/mL of both drugs were selected for determination of the absorbances values. The contents were calculated using the following equations $A_1 = 12.05C_x + 569Cy$ at 246.4 nm and $A_2 = 34.6\ C_x + 93\ C_y$ at 266 nm. Where, C_x and C_y are the concentrations of atenolol and indapamide, respectively; 12.05 and 34.6 are the absorbtivity values of atenolol at 246.4 nm and 266 nm, respectively; 569 and 93 are the absorbtivity values of indapamide at 246.4 and 266 nm respectively and A_1 and A_2 are the absorbances of the diluted sample at 246.4 nm and 266 nm respectively.

For the estimation of drugs in the marketed preparations, 20 tablets containing 100mg of Atenolol and 5 mg of indapamide were weighed and finely powdered. A quantity of powder equivalent to 100 mg atenolol and 5 mg indapamide was accurately weighed and transferred to a 100 mL volumetric flask, dissolved in methanol and solution was filtered through Whatman filter paper no. 41. Aliquots of this tablet solution were diluted to get the concentrations of 250 µg/mL atenolol and 12.5 µg/mL indapamide and absorbance of these solutions were measured at 246.4 nm and 266 nm and from the absorbance values, the concentration of drugs in the sample solution was determined by using the simultaneous equations. The results of formulation analysis are shown in Table 1.

Table 1. Analysis of Combined Tablet Formulations

Dosage Form	Labeled Claim (mg)		Estimated % of drugs from formulations by using the proposed methods			
			Method I		Method II	
	ATN	IND	ATN	IND	ATN	IND
Tablet - I	50	2.5	100.68	100.10	98.78	98.62
Tablet - II	50	2.5	100.75	100.16	98.81	99.17

Method II : Dual wavelength method

The spectrum of atenolol showed that the absorbance of atenolol is identical at 246.4 nm (λ_1) and 254.2 nm (λ_2), so these two wavelengths were selected for the analysis of indapamide. All the solutions of series A were scanned to ensure that the difference between λ_1 and λ_2 is zero. Similarly, the indapamide solutions were scanned to determine the two wavelengths, where absorbance is same. These two wavelengths were found to be

266 nm (λ_3) and 270.2 nm (λ_4). All the solutions of series B were scanned to ensure that the difference between λ_3 and λ_4 is zero. Thereafter, the solutions of series C were scanned to ensure that the varying concentration of atenolol and indapamide are not affecting the absorbance at selected wavelength. Results of these studies are shown in Table 2. Optical characteristics of this method are given in Table 3. The method was used to analyse marketed preparations and the same procedure was followed for preparation of solutions as mentioned in method I and differences in absorbances at different wavelengths were measured as mentioned above.

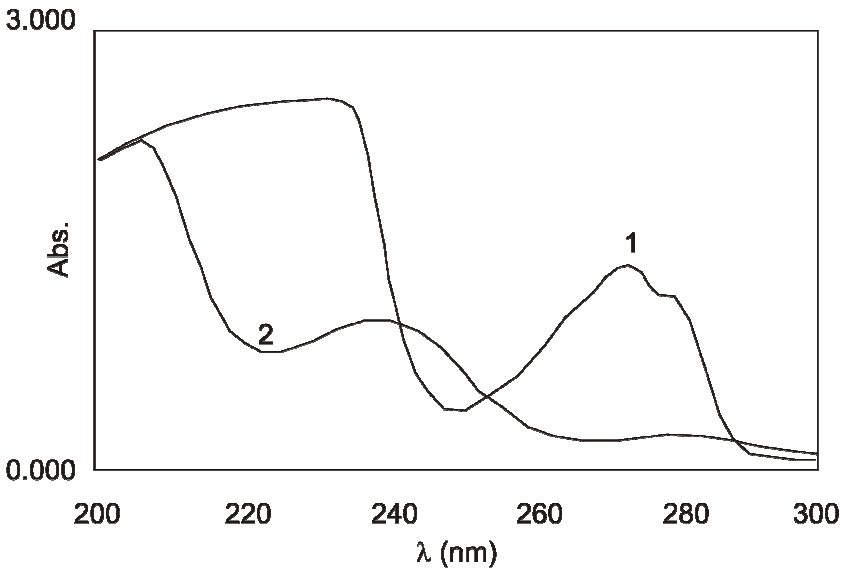

Fig. 1: UV absorbance spectrum of atenolol (1) and indapamide(2) at conc. 300 and 15 µg/mL, respectively in methanol

Table 2. Determination of atenolol and indapamide using dual wavelength method

Series A Composition of the solution		**Absorbance**	**Series B Composition of the solution**		**Absorbance**	**Series C Composition of the solution**		**Absorbance**	
ATN	**IND**	**$A\lambda_{266}$ - $A\lambda_{270.2}$**	**ATN**	**IND**	**$A\lambda_{246.4}$- $A\lambda_{252.2}$**	**ATN**	**IND**	**$A\lambda_{266}$- $A\lambda_{270.2}$**	**$A\lambda_{246.4}$- $A\lambda_{252.2}$**
100	0	0.075	0	5	0.120	100	5	0.074	0.125

Cont…

Series A Composition of the solution		Absorbance	Series B Composition of the solution		Absorbance	Series C Composition of the solution		Absorbance	
ATN	**IND**	**$A\lambda_{266}$ - $A\lambda_{270.2}$**	**ATN**	**IND**	**$A\lambda_{246.4}$- $A\lambda_{252.2}$**	**ATN**	**IND**	**$A\lambda_{266}$- $A\lambda_{270.2}$**	**$A\lambda_{246.4}$- $A\lambda_{252.2}$**
200	0	0.156	0	10	0.238	200	10	0.154	0.232
250	0	0.184	0	12.5	0.293	250	12.5	0.187	0.290
300	0	0.228	0	15	0.360	300	15	0.224	0.363
350	0	0.269	0	17.5	0.424	350	17.5	0.266	0.420

ATN – Atenolol, IND - Indapamide

Table 3. Optical characteristics of dual wavelength method (Method II)

Parameter	Atenolol	Indapamide
Analytical wavelength (nm)	266 and 270. 2	246.4 and 252.2
Linearity range (µg/mL)	100 -350	5 – 17.5
Regression Equation[p]:		
Slope[b]	0.00076	0.024243
Intercept[a]	-0.001621	-0.00391
Correlation coefficient	0.9986	0.9994
LOD (µg /mL)	10.38	0.26
LOQ (µg /mL)	31.47	0.79
Precision (%RSD):		
Interday	0.637	0.720
Intraday	0.529	0.309

[P]means Y = a + bc, where c is concentration in µg/mL, a – intercept, b – slope and Y – absorbance units.

To study the accuracy and precision of the proposed methods, recovery studies were carried out by adding a known quantity of standard to the preanalyzed formulations.

The procedure was repeated six times and it was observed that the excipients present in the tablets did not interfere in the estimation of atenolol and indapamide. Result of analysis of combined tablet formulations are given in Table 1 and results of recovery studies are shown in Table 4.

Table 4. Recovery Studies

Name of drug	Initial conc. (µg/mL)	Added conc. (µg/mL)	% Recovery by using proposed methods	
			Method I	Method II
ATN	125	125	101.12	100.59
IND	6.25	6.25	101.14	99.20

Thus, the proposed methods are simple, accurate, precise and economical for routine analysis of two drugs without prior separation. The amount found was in good agreement with the labeled claim of the formulation. The value of standard deviation was satisfactorily low, indicating the reproducibility and accuracy of the methods developed.

RESULTS AND DISCUSSION

Simple, precise and accurate simultaneous equation and dual wavelength methods were developed for the simultaneous estimation of atenolol and indapamide in combined dosage forms. The wavelengths used for the simultaneous equation were 246.4 nm and 266 nm; and for dual wavelength method, it was 246.4, 254.2, 266, 270.2 nm. Beer's law obeyed in concentration range 100-350 µg/mL for atenolol and 5-17.5 µg/mL for indapamide for both the methods. The absorbtivity and absorbance were determined and the values were substituted in the equation to obtain the results. Two commercial formulations containing atenolol and indapamide were analyzed by the proposed method. The percentage relative standard deviation for precision and accuracy was found to be low, which indicates that the method has considerable accuracy and precision.

Standard calibration curves of atenolol and indapamide for method II were linear with correlation coefficient (r^2), slope and intercept 0.9986, 0.00076 and - 0.0016216; 0.9994, 0.024243 and - 0.003918, respectively. For intraday precision method was repeated 5 times in a day and the average % RSD was found to be 0.637 for atenolol and 0.720 for indapamide. Similarly, the method was repeated on five different days and average % RSD was found to be 0.529 for atenolol and 0.309 for indapamide. These values

confirm the intra and interday precision of the method. Accuracy of the method was confirmed by recovery studies on preanalyzed formulations. Recovery greater than 98% with the low standard deviation justifies the accuracy of the method. The results are in good agreement with the label claim. The proposed method is found to be simple, precise, accurate and sensitive and therefore, can be used as a quality control tool for the simultaneous estimation of both drug from their combined dosage form in quality control laboratory.

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