Asian Journal of Chemistry Vol. 18, No. 4 (2006), 2890–2894

Simultaneous Spectrophotometric Estimation of Amlodipine and Enalapril in Tablets Using Orthogonal Polynomial Function Method

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Orthogonal polynomial function method has been developed for the simultaneous estimation of binary mixtures of amlodipine and enalapril in tablet formulations. All the parameters for orthogonal polynomial function method have been optimized by using computer programme in "C" language. The method was applied for the determination of these combinations in synthetic mixtures and tablet dosage forms. The contents of amlodipine in tablets were found to be 5.05 mg and of enalapril 5.03 mg of the label claim (5 mg of amlodipine and 5 mg of enalapril), respectively. The linearity was validated by least square method. The recovery is within the limits of 98–102%. The proposed methods are simple, economical, accurate, reproducible and rapid.

Key Words: Spectrophotometry, Amlodipine, Enalapril, Orthogonal polynomial.

INTRODUCTION

Orthogonal polynomial function method is a mathematical model for the elimination of irrelevant absorption[1, 2]. The method is based upon the difference in the shape of the spectra of the components in a mixture in the selected wavelength range.

The absorption spectrum can be represented in terms of orthogonal functions and contribution to the coefficient of the given degree of orthogonal polynomial depends upon the shape of the spectrum and concentration. Thus a quadratic curve will contribute to coefficients of zero degree, first degree and second degree polynomials, whereas a linear curve will contribute only to coefficients of zero degree and first degree polynomials, not to that of second degree polynomial. Hence from the coefficient of second degree polynomial value of sample spectrum, calculated from the wavelength range in which the spectrum of one component is linear and of the other is quadratic or cubic, it is possible to estimate the content of the second component.

Though it is a potential method for the analysis of multi-component samples, the method involves complex calculations to select the right combinations of degree of polynomial, number of points in the spectrum, interval between the point and optimization of these parameters.

In the present work an interactive computer programme in 'C' language has been developed[3] for the optimization of parameters. Using the software, an analytical method has been developed for the simultaneous estimation of amlodipine (AML) and enalapril (ENL) in tablet formulation. Chemically, amlodipine is 3-ethyl-5-methyl (4RS)-2-[(aminoethoxy)methyl]-4-(2-chlocrophenyl)-6-methyl-1,4-di-

hydropyindine-3,5-dicarboxylate benzenesulphonate, used as antihypertensive as calcium antagonist, while enalapril maleate is (2S)-1-[(2S)-2-[(1S)-1-(ethoxy-carbonyl)-3-phenyl propyl]pyrrolidine-2-carboxylic acid (x)-butenedioate, used as antihypertensive as angiotensin-converting enzyme. Derivative spectrophotometry[4] method is reported for simultaneous determination of amlodipine-enalapril maleate and amolodipine-lisinopril in combined tablet preparations.

EXPERIMENTAL

Amlodipine and enalapril were obtained by courtesy of Cassel Research Lab., Chennai, as gift samples. The spectra were recorded in UV spectrophotometer (Shimadzu, UV 1601 PC, Japan).

Optimization of parameters

UV spectra of 10 μg/mL solution of amlodipine in distilled water and 10 μg/mL solution of enalapril in distilled water were recorded between 200 and 400 nm (Fig. 1). These recorded spectra were stored in ASCII format. From these spectral data, 112 convoluted graphs each for AML and ENL were obtained. Convoluted graphs of AML were compared with those of corresponding ENL and the optimum conditions for orthogonal polynomial function method were selected, taking the following points into consideration (Table-1).

1. The co-efficient value is negligible for one drug and as high as possible for the other.
2. As far as possible, the wavelength range where there was steep rise in co-efficient value of either drug, was avoided.

TABLE-1
OPTIMIZED PARAMETERS FOR ORTHOGONAL POLYNOMIAL FUNCTION METHOD OF ANALYSIS

Drug	Degree of polynomial	Number of points	Wavelengths (nm)
AML	Quadratic	6	345.5, 352.5, 359.5, 366.5, 373.5, 380.5
ENL	Quadratic	6	217.8, 224.8, 231.8, 238.8, 245.8, 252.8

Determination of $P^{1\%}_{1\,cm}$

Coefficient of polynomial is directly proportional to the concentration of analyte and it can be calculated by using equation (1) for AML and equation (2) for ENL where the factors are those of six point quadratic polynomials obtained from the text of numerical analysis[5].

$$P_{AML} = 5(A_{345.5}) - 1(A_{352.5}) - 4(A_{359.5}) - 4(A_{366.5}) - 1(A_{373.5}) + 5(A_{380.5}) \quad (1)$$

$$P_{ENL} = 5(A_{217.8}) - 1(A_{224.8}) - 4(A_{231.8}) - 4(A_{238.8}) - 1(A_{245.8}) + 5(A_{252.8}) \quad (2)$$

where P_{AML} and P_{ENL} are coefficients of polynomials of AML and ENL, respectively and A is absorbance of respective wavelength. $P^{1\%}_{1\,cm}$ is a constant, which represents the coefficient corresponding to absorbance of 1% solution kept in 1 cm cell which can be used for the calculation of concentration of sample similar to the use of A (1%; 1 cm) in conventional spectrophotometry. Coefficient values corresponding to the absorbance values of 10 mcg mL^{-1} solution of AML or ENL in distilled water were calculated as above and from this the P (1%; 1 cm) values were calculated (Table-2).

TABLE-2
($P^{1\%}_{1\,cm}$) FOR AML AND ENL

S. No.	Conc. of AML (mcg/mL)	P value for AML	$P^{1\%}_{1\,cm}$ for AML	Conc. of ENL (mcg/mL)	P value for ENL	$P^{1\%}_{1\,cm}$ for ENL
1	10.22	0.2219	217.12	10.07	1.5865	1575.00
2	10.41	0.2252	216.33	10.41	1.6452	1580.40
3	10.46	0.2116	202.33	10.18	1.6040	1575.63
4	10.01	0.2215	221.27	10.07	1.5438	1533.06
5	10.16	0.2186	215.15	10.15	1.5681	1544.92
	Mean		214.43			1561.80
	SD		±2.46			±4.77

Analysis of physical mixtures

Solutions containing various proportions of the drugs were prepared (Table-3). For the estimation of AML the absorbance of the solution was measured at 345.5, 352.5, 359.5, 366.5 and 380.5 nm and the values were substituted in eqn. (1) to get "P" value. From the "P" value the AML content was calculated by using P(1%, 1 cm) value the AML. Similarly, ENL content was determined by measuring the absorbance at 217.8, 224.8, 231.8, 238.8, 245.8 and 252.8 nm and the values were substituted in eqn. (2) to get "P" value and P(1%, 1 cm) value of ENL.

Analysis of AML and ENL in tablet formulations

The average weight of the tablets was determined and powdered. Tablet powder equivalent to 5 mg AML and 5 mg of ENL was weighed and transferred to a 100 mL volumetric flask. About 70 mL of distilled water was added and mixed in a wrist shaker for 15 min for complete dissolution of the drugs and made up to the volume with distilled water. Dilutions were made with distilled water to attain the concentration of AML (10 mcg/mL) and analysis was done as described above. Recovery study was carried out by adding known amounts of AML and ENL to the analyzed samples.

RESULTS AND DISCUSSION

UV spectra of AML in distilled water exhibited λ_{max} at about 364 nm, whereas ENL exhibited strong λ_{max} at about 257 nm (Fig. 1). These spectral properties make this an ideal combination for orthogonal polynomial function analysis. The optimum analytical conditions were arrived at by using the software custom developed for the purpose. When the software was executed the user entered the UV data file names, the degree of polynomial, number of wavelengths and interval between the wavelengths. When these informations were provided, the spectral file name was opened, the wavelengths were chosen starting from the first wavelength of the spectrum and the average was calculated. The corresponding absorbance values were substituted in the respective equations to calculate the coefficient of polynomial for the selected wavelength region.

The process was repeated successively to cover the entire spectra. The output can be used for construction of convoluted graph. Comparing the convoluted graph of AML with that of the corresponding convoluted graphs of ENL the optimum

conditions were arrived. The optimized conditions for the estimation of AML and ENL are given in Table-1. The convoluted graphs for the optimized conditions for the estimation of AML and ENL are given in Figs. 1 and 2. The linearity of the

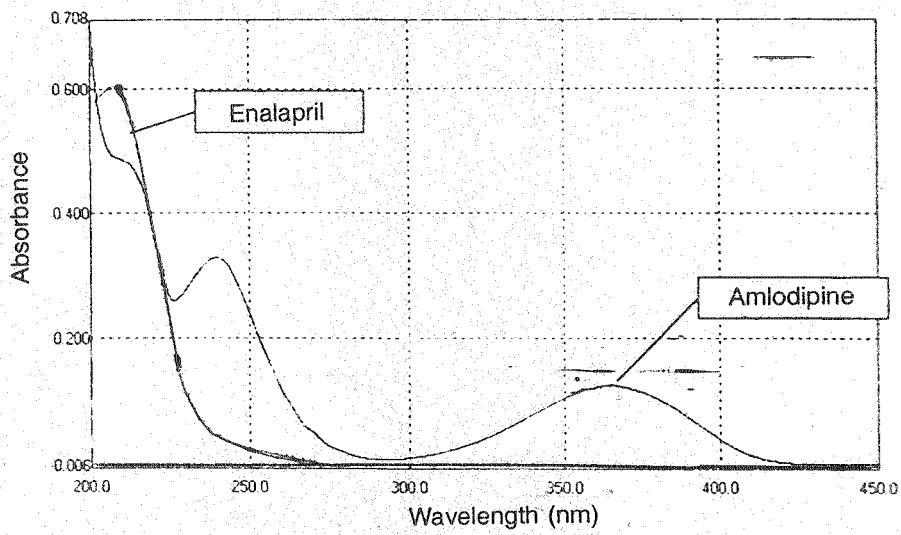

Fig. 1. UV Spectra of 10 mcg/mL of amlodipine and 10 mcg/mL enalapril in distilled water

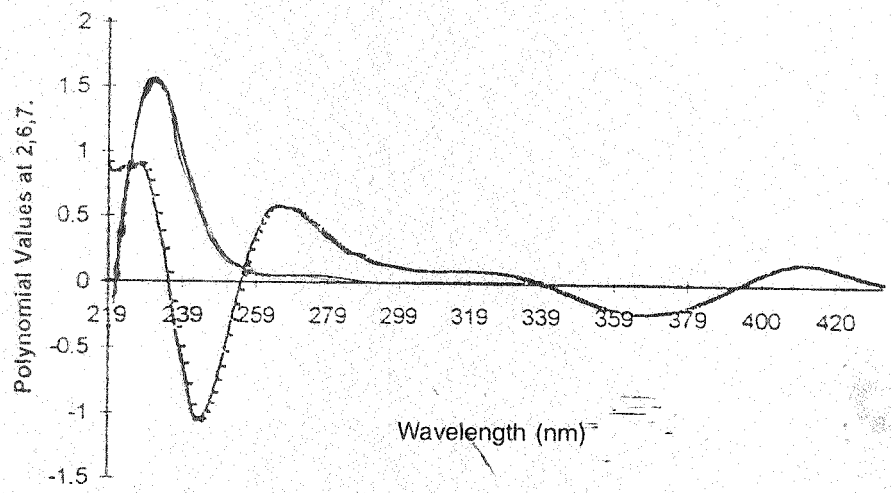

Fig. 2. Convoluted graph for the estimation of AML and ENL

method was determined by plotting the coefficient values against concentration and found to be 2–10 mcg/mL with regression coefficient of 0.9968 for AML and 2–10 mcg/mL^{-1} with regression coefficient of 1.000 for ENL. Both the solutions were stable for 3 h. Under the optimized conditions, the P(1%, 1 cm) values were established and are given in Table-2. The method was tested by analyzing the laboratory physical mixture containing AML and ENL in the ratio of 1 : 1 to 3 : 1. The results (Table-3) indicate that the method is suitable for the simultaneous estimation of these drugs when present within this ratio limit and can be used for the analysis of tablet formulation since AML and ENL are present in the ratio of 1 : 1. This analysis was followed by recovery study. The results (Table-4) are within the acceptable limits of precision and accuracy as indicated by recovery study 99.85–101.26 for AML and 99.69–101.66 for ENL.

TABLE-3
ANALYSIS OF PHYSICAL MIXTURE

Ratio of AML/ENL	Amlodipine			Enalapril		
	Theoretical conc. (mcg mL^{-1})	Experimental conc. (mcg mL^{-1})	% of theoretical value	Theoretical conc. (mcg mL^{-1})	Experimental conc. (mcg mL^{-1})	% of theoretical value
1 : 1	5.15	5.01	97.28	4.90	4.86	99.18
1 : 2	10.31	10.11	98.06	10.30	10.15	98.54
1 : 3	15.46	15.12	97.80	15.45	15.28	98.89
2 : 1	5.15	5.19	100.77	5.15	5.25	101.94
3 : 1	5.15	5.14	99.80	5.15	5.10	99.02

TABLE-4
ANALYSIS OF TABLET FORMULATION

S.No.	Enalapril content		Amlodipine content	
	mg/tab	Label claim (%)	mg/tab	Label claim (%)
1	5.17	103.40	5.21	104.20
2	5.06	101.20	4.86	97.20
3	5.06	101.20	5.13	102.60
4	4.92	98.20	4.95	99.00
	Mean	101.00		100.75
	RSD	11.16		11.29

Label claim: Each tablet contains 5 mg AML and 5 mg ENL.

TABLE-5
RECOVERY STUDIES

S.No.	Level added (%)	Recovery (%)	
		ENL	AML
1	20	99.81	102.50
2	40	101.66	99.85
3	69	99.69	101.26

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(*Received*: 29 September 2005; *Accepted*: 2 May 2006) AJC-4817