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SIMULTANEOUS ESTIMATION OF AMLODIPINE AND ATORVASTATIN IN TABLETS USING ORTHOGONAL FUNCTION RATIO SPECTROMETRY

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ABSTRACT

Orthogonal polynomial function method has been developed for the simultaneous estimation of binary mixtures of Amlodipine and Atorvastatin in tablet formulations. All the parameters for orthogonal polynomial function method have been optimized by using computer programme in "C" language. The described 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 2.49 mg and Atorvastatin is 9.96 mg of the label claim 2.5 mg of amlodipine and 10 mg of Atorvastatin respectively. The linearity was validated by least square method. The recovery is within the limit of 98% to 102%. The proposed methods are simple, economical, accurate, reproducible and rapid.

Key words: Amloplipine, Atorvastatin, Orthogonal function ratio spectrometry.

INTRODUCTION

Orthogonal polynomial function method is a mathematical model for the elimination of irrelevant absorption proposed by Glenn[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 were as a linear curve will contribute to coefficients of zero degree polynomial and first degree polynomial not to that of second degree polynomial and hence, from the coefficient of second degree polynomial value of sample spectrum, calculated from the wavelength range in which the spectra of one component is linear and other is quadratic or cubic, it is

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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, analytical method has been developed for the simultaneous estimation of amlodipine besilate (AMLO) and atorvastatin calcium (ATOR) in table formulation. Amlodipine is 3-ethyl 5- methyl (4RS) - 2- [(aminoethoxy) methyl] – 4 – (2- chlocrophenyl) - 6- methyl -1,4-dihydropyindine-3 ,5 dicarboxylate benzene sulphonate is a calcium channel antagonist, used as an anti-hypertensive drug. Atorvastatin calcium is [R-(R*, R*)]-2-(4-fluorophenyl)-β, δ-dihydroxy-5-(1-methylethyl)-3-phenyl-4-[(phenylamino)carbonyl]-1H-pyrrole-1-heptanoic acid, calcium salt (2 : 1) trihydrate is used for treatment of hypercholesterolemia. This combination of amlodipine and atorvastatin can be safely used in the treatment of patients with concomitant hypertension and dyslipidemia. Two RP-HPLC methods[4,5], a spectrophotometric method[6] and HPTLC[7] methods have been reported for simultaneous determination of atorvastatin and amlodipine from their combination drug products.

EXPERIMENTAL

Materials

Amlodipine and Atorvastatin calcium was obtained by the courtesy of Madras Pharmaceuticals, Chennai as gift samples. The spectra were recorded in UV spectrophotometer (SHIMADZU, UV 1601 PC, Japan).

Method

Optimization of parameters

UV spectra of 10 μg/mL solution of amlodipine in methanol and 10 μg/mL of atorvastatin in methanol were recorded between 200 nm and 400 nm (Fig. 1). These recorded spectra are stored in ASCII format. From these spectral data, 112 convoluted graphs each for AMLO and ATOR were obtained. Convoluted graph of AMLO were compared with that of corresponding ATOR and the optimum conditions for orthogonal polynomial function method were selected taking following points into consideration. (Table 1)

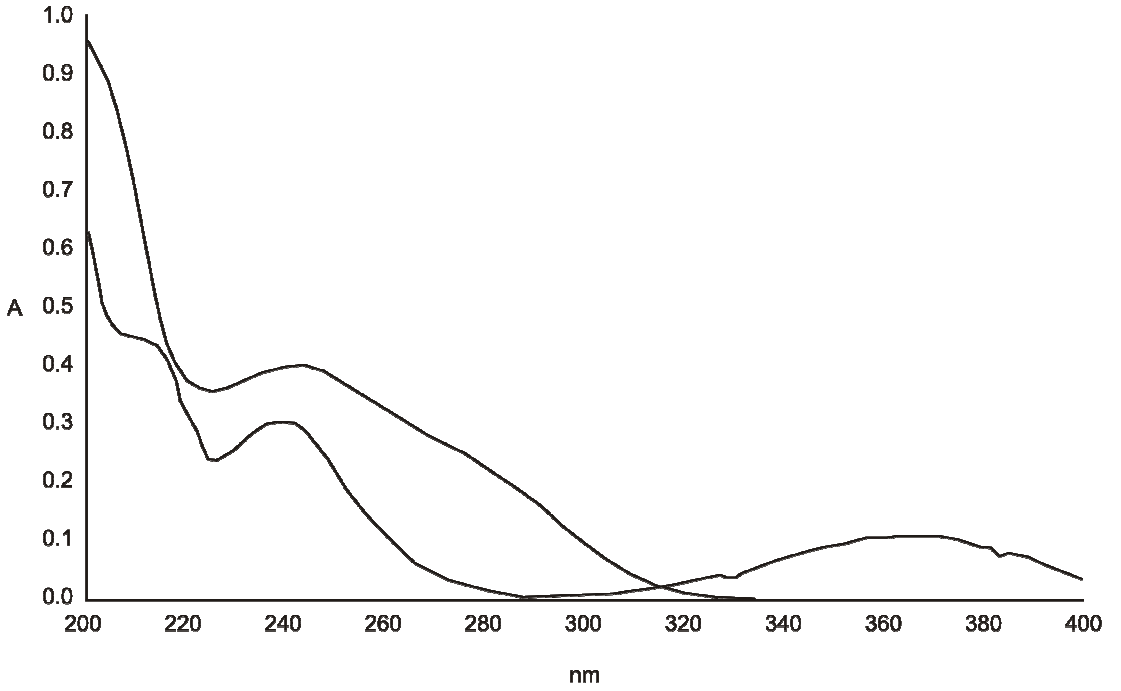

Fig. 1: UV Spectra of 10 μg/mL of amlodipine and 10 μg/mL atorvastatin in methanol

Table 1.Optimized parameters for orthogonal polynomial function method of analysis

Drug	Degree of polynomial	Number of points	Interval between the points	Wavelengths (nm)	Average nm
AMLO	Quadratic	9	2	251, 253, 255, 257, 259, 261, 263, 265 and 267	259.0
ATOR	Quadratic	10	5	292, 297, 302, 307, 312, 317, 322, 327, 332 and 337	314.5

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

Determination of $P_{1cm}^{1\%}$

Coefficient of polynomial is directly proportional to the concentration of analyte and it can be calculated by using equation (1) for AMLO and equation (2) for ATOR where the factors are those of six point quadratic polynomials obtained from the text of numerical analysis[8].

$$P_{AMLO} = 28\ (A_{251}) +7\ (A_{253}) - 8\ (A_{255}) - 17\ (A_{257}) - 20\ (A_{259}) - 17\ (A_{261}) - 8\ (A_{263}) +7\ (A_{265}) +28(A_{265}) \quad \ldots(1)$$

$$P_{ATOR} = 6\ (A_{292}) +2\ (A_{297}) - 1\ (A_{302}) - 3\ (A_{307}) - 4\ (A_{312}) - 4\ (A_{317}) - 3\ (A_{322}) - 1(A_{327}) +2\ (A_{332}) + 6\ (A_{337}) \quad \ldots(2)$$

Where, P_{AMLO} and P_{ATOR} are coefficients of polynomial of AMLO and ATOR, respectively and A is absorbance of respective wavelength. The $P_{1cm}^{1\%}$ 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 $\mu g.mL^{-1}$ solution of AMLO or ATOR in methanol were calculated as above and from this, the P (1%; 1 cm) values were calculated (Table 2).

Table 2. ($P_{1cm}^{1\%}$) for AMLO and ATOR

P Value for AMLO	P 1%, 1 cm for AMLO	P value for ATOR	P 1%, 1 cm for ATOR
0.8316	832	0.6661	666.12
0.0810	801	0.6487	648.75
0.7924	792	0.6469	646.93
0.7964	796	0.6425	642.53
0.7936	794	0.6521	652.1
Mean	803		651.18
% RSD	2.06		1.37

Analysis of physical mixtures

Solutions containing various proportions of the drugs were prepared (Table 3) in distilled water. For the estimation of AMLO, the absorbance of the solution was measured

Table 3: Analysis of physical mixture

Ratio of Amlo/Ator	Amlodipine			Atorvastatin		
	Theoretical Conc. (µg/mL)	Experimental Conc. (µg/mL)	% of theoretical value	Theor. Conc. (µg/mL)	Exp. Conc. (µg/mL)	% of theoretical value
1:01	10.12	10.05	99.3	10.21	10.5	102.8
1:02	5.06	4.96	98.02	10.21	9.91	98.1
1:03	2.53	2.47	97.62	7.65	7.72	100.9
1:04	2.53	2.48	98.02	10.21	10.47	102.5
1:05	2.024	2.07	101.7	10.21	10.23	100.19
2:01	10.12	10.2	100.7	5.105	6.2	121.5
3:01	7.59	7.49	98.68	2.55	3.4	133.33
4:01	10.12	9.94	98.22	2.55	3.2	125.49
5:01	10.12	10.05	99.3	2.042	2.7	132.22

at 251, 253, 255, 257, 259, 261, 263, 265 and 267 nm and the values were substituted in equation (1) to get "P" value. From the "P" value, the AMLO content was calculated by using P (1%,1 cm) value the AMLO. Similarly, ATOR content was determined by measuring the absorbance at 292, 297, 302, 307, 312, 317, 322, 327, 332 and 337 nm and the values were substituted in equation (2) to get "P" value and P (1%,1 cm) value of ATOR.

Analysis of AMLO and ATOR in tablet formulations

The average weight of the tablets was determined and powdered. Tablet powder equivalent to 2.5 mg AMLO and 10 mg of ATOR was weighed and transferred to a 100 mL volumetric flask. About 70 mL of methanol was added and sonicated for 15 minutes for complete dissolution of the drugs and made up to the volume with metahnol. Dilutions were made with distilled water to attain the concentration of AMLO (5 μg/mL) and analysis was done as described above.

Recovery study

Recovery study was carried out by adding known amount of pure AMLO and pure ATOR to the preanalyzed market sample. Three different levels, 50%, 100% and 150% were used for spiking.

RESULTS AND DISCUSSIONS

The UV spectra of AMLO in methanol exhibited λ_{max} at about 364 nm and 238 nm, where as ATOR exhibited strong λ_{max} at about 243 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 will enter the UV data file names, the degree of polynomial, number of wavelengths and interval between the wavelength. When these information are provided, the spectral file name is opened, the wavelength are chosen starting from the first wavelength of the spectrum and the average is calculated. The corresponding absorbance values are substituted in the respective equations to calculate the coefficient of polynomial for the selected wavelength region.

The process is repeated successively to cover the entire spectra. The output can be used for construction of convoluted graph. Comparing the convoluted graph of AMLO with that of corresponding convoluted graphs of ATOR the optimum conditions were arrived at. The optimized conditions for the estimation of AMLO and ATOR are given in

Table 1. The convoluted graph for the optimized conditions for the estimation of AMLO and ATOR are given in (Fig. 2) and (Fig. 3).

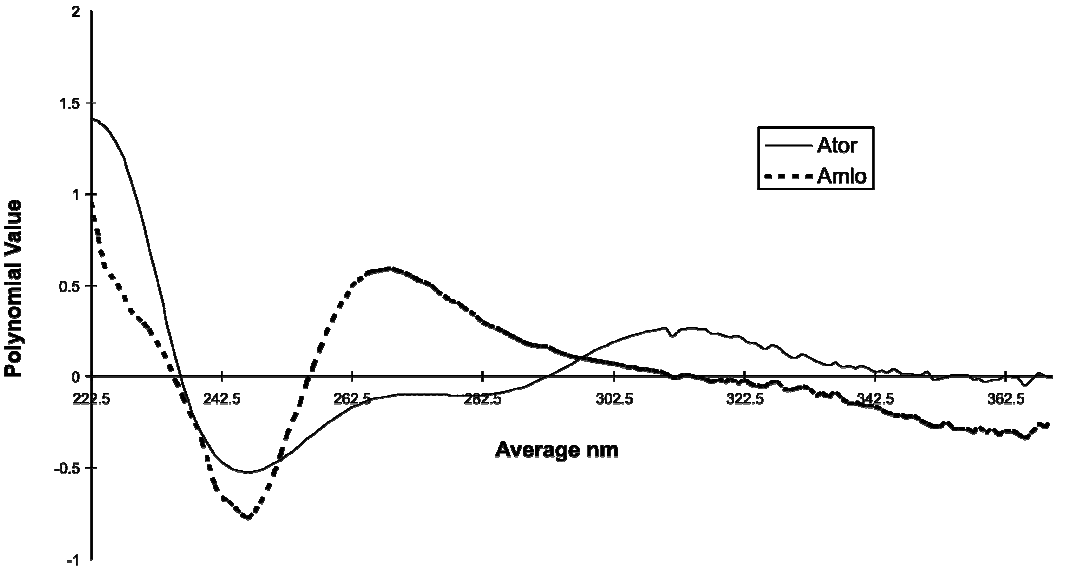

Fig. 2: Convoluted graph for estimation of atorvastatin

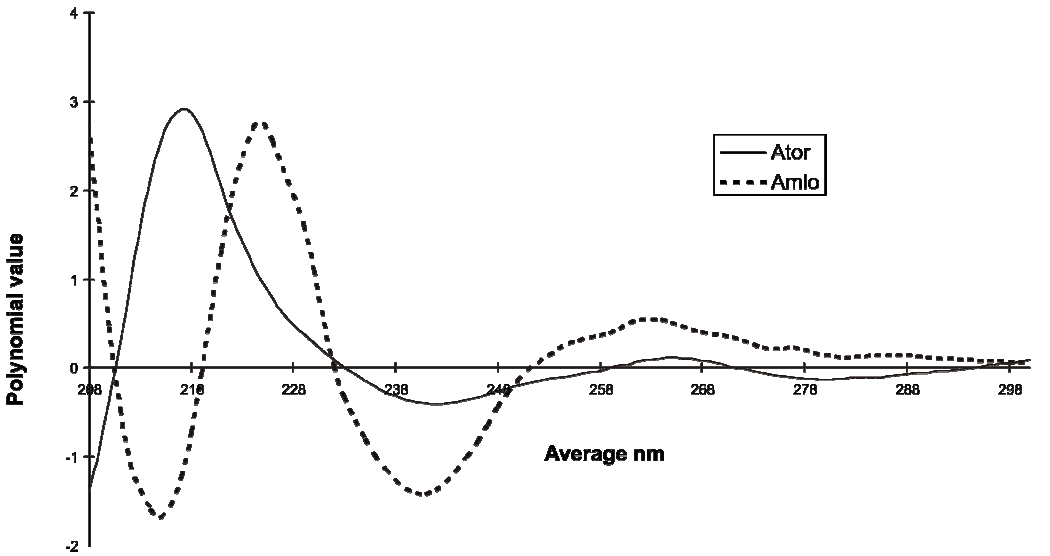

Fig. 3: Convoluted graph for estimation of amlodipine

Table 4: Analysis of tablet formulation

Amlodipine		Atorvastatin	
mg/tab	**% label claim**	**mg/tab**	**% label claim**
2.495	2.485	9.98	9.96
2.50	2.51	10.02	9.92
2.52	2.50	10.08	10.1
2.50	2.51	10.01	9.85
2.51	2.507	10.04	10.05
2.50	2.487	10.01	9.90
Mean	2.499	Mean	9.96
% RSD	0.4887	% RSD	0.952

Label claim: Each tablet contains 2.5 mg of amlodipine and 10 mg atorvastatin

Table 5: Recovery studies

Amlodipine		Atorvastatin	
Level added %	**Recovery (%)**	**Level added %**	**Recovery (%)**
50	100.83	50	100.40
100	102.00	100	101.35
150	100.57	150	102.92

The linearity of the method was determined by plotting the coefficient values against concentration and found to be 5 μg/mL to 25 μg/mL with regression coefficient of 1.0000 for AMLO and 10 μg/mL to 50 μg/mL with regression coefficient of 0.9999 for ATOR. Both the solutions were stable for three hours. Under the optimized conditions, the P (1%, 1 cm) values were established and given in Table 2. The method was tested by analyzing the laboratory physical mixture containing AMLO and ATOR in the ratio of 1 : 1 to 5 : 1. The results (Table 3) indicated that the method is suitable for the simultaneous estimation of these drugs, when present with in this ratio limit and can be used for the analysis of tablet formulation since the AMLO and ATOR are present in the ratio of 1 : 4. Analysis of tablet formulation was performed with the proposed method and it was observed that the proposed method is precise and the results are given in Table 4.

This analysis was followed by recovery study. The results (Table 5) are within the acceptable limits of precision and accuracy as indicated by recovery study 100.57 to 102.00 for AMLO and 100.40 to 102.92 for ATOR

REFERENCES

1. A.H. Beckett, and J. B. Stenlake, Practical Pharmaceutical Chemistry Part II, 4th Ed; CBS Publishers and Distributors, New Delhi, (1997) p. 290.
2. A. L. Glenn, J. Pharm. Pharmac**., 15**, 123T - 130T (1963).
3. N. Kannappan, K. Kannan and .R. Manavalan, Indian Drugs, **40**, 517, (2003).
4. K. R. Rajeswari, G. G. Sankar, A. L. Rao and J. Seshagirirao, Indian J. Pharm. Sci, **68**, 275 (2006).
5. B. G. Chaudhari B., N. M. Patel, P. B. Shah, Chemical and Pharmaceutical Bulletin, **55(2)**, 241, (2007).
6. M. R. Khan and Deepti Jain, Indian J. Pharm. Sci., **68(4)**, 546 (2006).
7. B. G. Chaudhari, N. M. Patel and P. B. Shah, Indian Drugs**, 43(8)**, 649 (2006).
8. R.A. Fisher and F. Yates, Statistical Tables for Biological, Agricultural and Medical Research, 4th Edn., Oliver and Boyd, Edinburg, (1953) p. 80.

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