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Simultaneous Estimation of Aliskiren and Amlodipine in Tablet Dosage form by UV Spectroscopy

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Abstract

Two simple, sensitive, rapid and accurate analytical methods have been developed for the simultaneous of ALISKIREN and AMLODIPINE in marketed formulation of pharmaceutical dosage forms. The Q-analysis based on measurement of absorptivity at 279nm and 289nm (as an isoabsorptive point). The second method developed and validated of simultaneous equation using 279/361nm. ALISKIREN and AMLODIPINE at their respective λmax 279nm and 361nm and at iso absorptive point 289nm show linearity in a concentration range of 20-100µg/ml and 5-25µg/ml.Recovery studies range from 99.51% for Aliskiren and 99.51% for Amlodipine in case of simultaneous equation method Aliskiren was 100.10% and Amlodipine was 100.47%.

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Aliskiren, Amlodipine, Q-analysis, Simultaneous equation.

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INTRODUCTION

Analytical chemistry[1] may be derived as the science and art of determining the composition of material in terms of the elements of compounds contained. In instrumental analysis, a physical property of the substance is measured to determine its chemical composition. Analysis of minute amounts of complex biological materials to the quality control of the final dosage form, the use of analytical technology covers an immense range of techniques and disciplines. The qualitative and quantitative analysis[2] can be done by various analytical methods. Modern analytical techniques employ a range of techniques that vary from simple qualitative chemical test to the use of most sophisticated and expensive computer controlled instruments. Analytical instrumentation

plays an important role in the production and evaluation of products. Analytical method is a specific application of a technique to solve an analytical problem.

Aliskiren (2(*S*), 4(*S*), 5(*S*), 7(*S*)- *N*-(2-carbamoyl-2-methylpropyl)- 5-amino-4-hydroxy-2,7-diisopropyl -8-[4-methoxy-3-(3-methoxypropoxy)phenyl]-octanamide hemifumarate) is an orally active renin inhibitor licensed for the treatment of essential hypertension. It is more expensive than most other antihypertensive agents and no long term clinical outcome data are available. Aliskiren metabolized slowly in the body resulting in stronger half lives which restrict it once a day dosing. The cytochrome P450 susceptibility is also less and a major proportion of the drug is eliminated unchanged via feces.

Amlodipine ((*RS*)-3-ethyl 5-methyl 2-[(2-aminoethoxy) methyl]-4-(2-chlorophenyl)-6- methyl-1, 4-dihydropyridine-3,5-dicarboxylate) is long acting calcium channel blockers used as an antihypertensive and in the treatment of angina. It acts by relaxing the smooth muscle in the atrial wall, decreasing total peripheral resistance and hence reducing blood pressure, in angina it increases blood flow to the heart muscle. Various analytical methods have been reported for the assay of Amlodipine[3] in pure form as well as in pharmaceutical formulation. They include HPLC[4, 5], HPTLC[6], RP-HPLC[7, 8], gas chromatography[9], mass-spectrometry[10], and flourimetry[11].

MATERIALS AND METHODS

A) Chemicals and reagents:

Spectral runs were made on a Jasco V-530 UV-Visible spectrophotometer. Aliskiren and Amlodipine reference standard was kindly provided by Novartis Pharmaceuticals Ltd, India. All the reagent was purchased from Merck Pvt. Ltd.The solution were protected from light and were analyzed on the day of preparation.

B) Preparation of Standard Drug solution for Method I and II:

Standard stock solution for Aliskiren and Amlodipine were prepared separately by dissolving 100mg of both drugs with methanol in 100ml volumetric flask i.e. 1000µg/ml. A 10ml solution was pipette out and the volume was made up to the mark with methanol i.e. 100 µg/ml each of Aliskiren and Amlodipine in two different 100ml volumetric flask.

C) Determination of Absorption Maxima for Method I and II:

Standard stock solutions of Aliskiren and Amlodipine were scanned in the range of 200 – 400 nm against Methanol as a blank. Aliskiren and Amlodipine showed absorbance maxima at 279 nm and 361 nm respectively. The overlain spectra showed λmax of both drugs was recorded (isoabsorptive point) at 289 nm.

D) Method I (Q-Analysis):

The method involves the overlain spectrum of two drugs, two wavelengths were selected one is the isoabsorptive point for both the drugs and the other is λ1 or λ2 max of either of the two drugs. The stock solutions are prepared and the absorptivity values for both drugs at the selected wavelengths are calculated. The method employs Qo - values and the concentrations of drugs in sample solution were determined by using the following formulas,

For Aliskiren

$$C_1 = \frac{Q_0 - Q_2}{Q_1 - Q_2} X \frac{a_1}{A}$$

For Amlodipine

$$C_2 = \frac{Q_0 - Q_1}{Q_2 - Q_1} X \frac{a_2}{A}$$

Where,

$$Q_o = \frac{\text{Absorbance of sample at } \lambda_1 \text{ or } \lambda_2}{\text{Absorbance of sample at isobestic point}}$$

$$Q_1 = \frac{\text{Absorptivity of drug A at } \lambda_1 \text{ or } \lambda_2}{\text{Absorptivity of drug A at iso absorptive point}}$$

$$Q_2 = \frac{\text{Absorptivity of drug B at } \lambda_1 \text{or } \lambda_2}{\text{Absorptivity of drug B at iso absorptive point}}$$

E) Method II (Simultaneous estimation):

The method involves selecting two wavelengths λ1 or λ2 for the simultaneous estimation of two drugs (A & B) are that are absorption maxima of the drugs. The stock solutions of both the drugs were measured at the selected wavelengths and absorptivity (A 1%, 1cm) for both the drugs at both the wavelengths were determined as mean of three independent determinations. Concentration in the sample were obtained by using following equations,

CX = A2 ay1- A1ay2 / ax2 ay1- ax1ay2 .....Eq (i)

CY = A1 ax2- A2ax1 / ax2 ay1- ax1 ay2..... Eq (ii)

Where,

A1 and A2 are the absorbances of mixture at λ1 and λ2 respectively.

ax1 and ax2 are absorptivites of drug A at λ1 and λ2 respectively and ay1 and ay2 are absorptivites of drug B at λ1 and λ2 respectively.

CX and CY are concentrations of drug A and drug B respectively.

RESULTS AND DISCUSSION

VALIDATION

Linearity: Linearity was checked by preparing standard solution at different concentration of Aliskiren and Amlodipine. For Q-analysis and simultaneous equation range was found to be 20-100 µg/ml and 5-25 µg/ml.

Table 1: Optical Characters And Precision Data With Their Respective Values For Q-Analysis And Simultaneous Method

Parameter	Q-analysis Method							
	Aliskiren		Amlodipine		Aliskiren		Amlodipine	
	279 nm	289 nm	279 nm	289 nm	279 nm	361 nm	279 nm	361 nm
Beer's law limits (µg/ ml)	20-100	20-100	5-25	5-25	20-100	20-100	5-25	5-25
Molar absorptivity (1/mol/cm)	2.08x 10 ^{3}	11.39x 10^3	0.213x 10^3	5.60x 10^3	1.40.x 10 ^{3}	0.11x 10 ^{3}	14.92x 10 ^{3}	0.18x 10 ^{3}
Correlation coefficient (R)	1.000	0.999	0.9987	0.9992	0.9998	0.9993	0.9994	0.9992
Sandell's sensitivity (mg/cm^2)	0.175	0.040	0.2673	0.1020	0.193	2.481	0.011	1.239
Regression equation (y)	Y=0.0052x +0.002	Y=0.001x - 0.0007	Y=0.0038x -0.007	Y=0.01x - 0.0012	Y=0.0051x +0.002	Y=0.0004x +0.004	Y=0.0357x +0.0058	Y=0.0038x +0.0007
Slope, b	0.0052	0.001	0.0038	0.01	0.0051	0.0007	0.0357	0.0038
Intercept, c	0.0002	0.0007	0.0007	0.0012	0.0002	0.0004	0.003	0.0007
Standard deviation	0.003	0.006	0.001	0.002	0.003	0.001	0.001	0.003
Relative standard deviation	0.870	3.12	1.103	1.612	1.217	3.21	1.103	0.687
Limit of detection (µg/ ml)	0.82	0.86	0.003	0.27	0.82	0.96	0.11	0.003
Limit of quantification (µg/ml)	2.50	2.60	0.01	0.83	2.60	2.91	0.33	0.01

Accuracy: To check the accuracy of the developed methods recovery studies were carried out by using three different levels (50%, 100%, and 150%) for both the drugs.The total amount of drug found, the percentage was calculated. The results revealed no interference of excipients.

Table 2: Results of Reovery studies of Aliskiren and Amlodipine by Simultaneous equation method simultaneous method

Drug	Amount present in formulation (µg/ml)	% Amount added	Method I % Recovery±SD* (n=3)	Method II % Recovery±SD* (n=3)
Aliskiren	20	50	99.98 ± 0.5718	100.10 ± 0.5718
		100		
		150		
Amlodipine	5	50	99.51± 0.6148	100.47 ± 0.5519
		100		
		150		

Method Precision: The precision of the methods was checked by repeated measurement of the absorbance of standard solutions (n = 6) of 20 µg/ml without changing the parameters for the method. The repeatability was expressed in terms of Relative Standard Deviation (RSD).

Table 3: Results of method Precision (Repeatability)

Concentration in µg/ml	Method I		Method II	
	Absorbance at 279 nm	Absorbance at 361 nm	Absorbance at 279 nm	Absorbance at 361nm
20	0.123	0.06	0.123	0.185
20	0.121	0.061	0.121	0.184
20	0.118	0.061	0.118	0.186
20	0.120	0.059	0.120	0.182
20	0.124	0.061	0.124	0.181
20	0.121	0.059	0.121	0.183
MEAN	0.121	0.060167	0.121	0.1835
SD	0.002	0.000983	0.002	0.001871
% RSD	1.76	1.634114	1.76	1.019525

Intermediate Precision: Intraday precision carried out by taking 3 different concentrations at various days and performed as per method and calculated mean absorbance and % RSD.

Table 4: Results of intermediate precision or reproducibility at different conc of Aliskiren and Amlodipine (Method I)

Sr. No	Conc. Range (µg/ml) in 10ml	Day	Abs. at 279 nm	Mean	% RSD	Abs. at 289 nm	Mean	% RSD
1.	40 µg/ml	1	0.238	0.237	0.877	0.125	0.124	1.235
		4	0.235			0.124		
		7	0.239			0.122		
2.	60 µg/ml	1	0.359	0.358	0.979	0.181	0.184	1.37
		4	0.355			0.186		
		7	0.362			0.184		
3.	80 µg/ml	1	0.486	0.485	0.238	0.233	0.233	0.657
		4	0.484			0.231		
		7	0.486			0.234		

Table 5: Results of intermediate precision or reproducibility at different conc of Aliskiren and Amlodipine (Method II)

Sr. No	Concentration Range (µg/ml) in 10ml	Day	Abs. At 279 nm	Mean	% RSD	Abs. At 361 nm	Mean	% RSD
1.	40 µg/ml	1	0.238	0.237	0.877	0.364	0.365	0.418
		4	0.235			0.365		
		7	0.239			0.367		
2.	60 µg/ml	1	0.359	0.358	0.979	0.542	0.544	0.382
		4	0.355			0.545		
		7	0.362			0.546		
3.	80 µg/ml	1	0.486	0.485	0.238	0.768	0.768	0.199
		4	0.484			0.767		
		7	0.486			0.770		

CONCLUSION

The three proposed methods to be linear, precise, accurate, simple, and selective and sensitive have been developed. The order of sensitivity is as follows M I>M II.When compare to M I and MII, M I is considered for simultaneous estimation by Q-analysis method, MII is considered for simultaneous estimation by equation method. The described methods give accurate and precise results and can be used for simultaneous analysis of Aliskiren and Amlodipine.

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