Acta Scientific Pharmaceutical Sciences

Volume 2 Issue 2 February 2018

Research Article

Dual Wavelength Method for Simultaneous Estimation of Aliskiren and Amlodipine in Combined Tablet Formulation

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Received: December 23, 2017; **Published:** January 30, 2018

Abstract

The renin inhibitor aliskiren was determined spectrophotometrically with amlodipine in its combined tablet formulation. The UV-spectrophotometric method utilized dual wavelength method for simultaneous estimation of aliskiren and amlodipine. From the overlain spectra of two drugs, the set of two wavelengths λ_1 (235.6 nm) and λ_2 (242.2 nm) were selected for estimation of aliskiren. Amlodipine was estimated directly at 365 nm as a single component without any interference, as aliskiren has zero absorbance at this wavelength. Developed method obeys Beer's law in the concentration range used for estimation of aliskiren and amlodipine. The mean percentage label claim of aliskiren and amlodipine using dual wavelength method was found to be 99.90 and 99.85, respectively. Accuracy of the method was found between 100.20 - 100.65%.

Keywords: Aliskiren; Amlodipine; UV-Spectrophotometric Method; Dual Wavelength Method

Introduction

Chemically aliskiren (ALS) is (2S, 4S, 5S, 7S)-5-Amino-N-(3-amino-2, 2-dimethyl-3-oxopropyl)-4-hydroxy-7-[[4-methoxy-3-(3-methoxypropoxy)phenyl] methyl]-8-methyl-2-propan-2-ylnonanamide [1]. It is a white to slightly yellowish crystalline powder. Aliskiren is the first in a class of drugs called direct renin inhibitors. It is used for essential (primary) hypertension [2]. It is highly soluble in water, ethanol and DMSO [3,4].

Amlodipine (AML) is chemically 3-Ethyl-5-methyl (±)-2-[(2-aminoethoxy) methyl]-4-(2- chlorophenyl)-1, 4-dihydro-6-methyl-3,5-pyridinedicarboxylate. Amlodipine besylate is white to off white powder, crystalline and has long-acting 1, 4-dihydropyridine calcium channel blocker [5,6]. It acts primarily on vascular smooth muscle cells by stabilizing voltage-gated L-type calcium channels in their inactive conformation. By inhibiting the influx of calcium in smooth muscle cells, amlodipine prevents calcium-dependent myocyte contraction and vasoconstriction. Amlodipine is used to treat hypertension and chronic stable angina [7,8]. Several analytical methods have been reported for estimation of ALS [9-11] and its combination with other drugs [12,13] which includes spectrophotometry and HPLC. Similarly, various spectrophotometric and HPLC methods have been reported for estimation of AML [14] and its combination with other drugs [15-18]. In the present work, a successful attempt has been made to estimate both these drugs simultaneously using dual wavelength UV spectrophotometric method. Structures of both the drugs ALS and AML are given in figure 1 and 2.

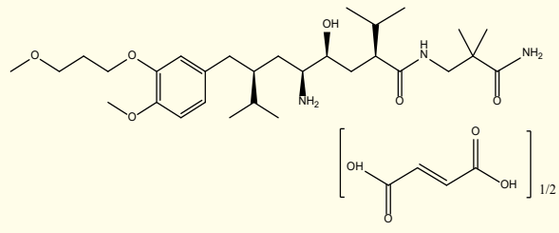

Figure 1: Structure of Aliskiren hemifumarate.

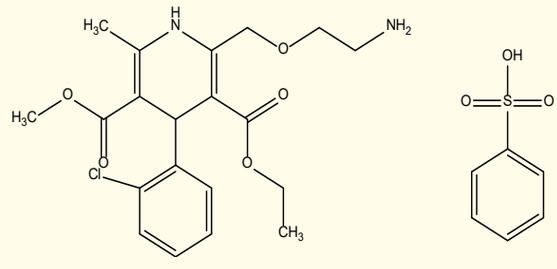

Figure 2: Structure of Amlodipine besylate.

Materials and Methods

Instrumentation

A double beam UV spectrophotometer (UV-1800, Shimadzu, Japan) with UV probe software version (2.31) and 10 mm quartz cells was used. All weights were taken on an electronic balance (Schimadzu - 220h).

Reagents and Chemicals

Pure drug, Aliskiren hemifumarate and amlodipine besylate was procured from Swapnroop Drugs and Pharmaceuticals, Aurangabad, Maharashtra, India. Marketed formulation was procured from local Pharmacy. All the chemicals and reagents used were of A.R. grade.

Method Development

Preparation of standard stock solution

The standard stock solutions of Aliskiren (ALS) and Amlodipine (AML) were prepared by dissolving 110.5 mg of aliskiren hemifumarate (110.5 mg of aliskiren hemifumarate is equivalent to 100 mg of aliskiren) and by dissolving pure drug of amlodipine besylate equivalent to 100 mg of amlodipine in separate 100 mL volumetric flask containing sufficient quantity of distilled water, the solutions were sonicated for 5 minutes then volume was made up to the mark with distilled water to get a concentration of 1000 µg/mL of each solution. The standard stock solutions were further diluted to obtain desired concentrations.

Preparation of sample solution

Twenty tablets were weighed and powdered. The quantity of the powder equivalent to 150 mg of ALS was transferred to 100 ml volumetric flask. The content was mixed with sufficient quantity of distilled water and sonicated for 20 minutes to dissolve the drug. The solution was then filtered through a Whatman filter paper no. 41 and made up to the mark with distilled water. An aliquot of solution (1.0 ml) was transferred to a 10 ml volumetric flask and the volume was adjusted up to the mark with distilled water to obtain required concentration of ALS (150 µg/ml) and AML (10 µg/ml).

Dual wavelength Method

Application of dual wavelength method is to calculate the unknown concentration of a component of interest present in a mixture containing both the components of interest and an unwanted interfering component by the mechanism of the absorbance difference between two points on the mixture spectra. This is directly proportional to the concentration of the component of interest, independent of the interfering components. The pre-requisite for dual wavelength method is the selection of two such wavelengths where the interfering component shows same absorbance whereas the component of interest shows significant difference in absorbance with concentration.

Selection of wavelength

For simultaneous analysis of ALS and AML using dual wavelength method, by appropriate dilutions from the standard stock solutions of ALS and AML, the solutions of ALS (50 µg/ml) and AML (20 µg/ml) were prepared respectively and scanned over the range of 200 nm to 400 nm. An overlain spectrum was observed for development of suitable method for analysis. The overlain spectrum of ALS and AML is shown in figure 3. From the overlay spectra, the set of two wavelengths 235.6 nm and 242.2 nm were selected as λ_1 and λ_2 for the estimation of ALS as AML shows same absorbance at these wavelengths. Estimation of AML was done as a single component at 365 nm.

The absorbance of final sample solution was measured against distilled water as blank at 235.6 nm and 242.2 nm for estimation of ALS. The absorbance difference values were measured and the amount of ALS present in the sample solutions was determined from the respective calibration curve, while the estimation of AML was done directly at 365 nm. The analysis procedure was repeated five times for marketed formulation.

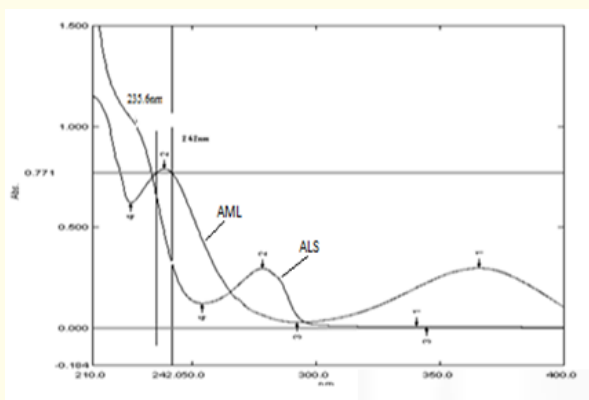

Figure 3: Overlain spectrum of Aliskiren and Amlodipine. Analysis of ALS and AML in tablet formulation by dual wavelength spectrophotometry

Method Validation

Linearity and Range

Aliquots of standard solution of ALS (0.25, 0.5, 0.75, 1.0, 1.25, 1.5, 2.0 and 3.0 ml) and AML (0.05, 0.1, 0.2, 0.3, 0.4, 0.5, 0.6 and 1.0 mL) were transferred in a series of 10 ml volumetric flasks. The volume was adjusted up to the mark with distilled water and mixed. Absorbance values were recorded at selected wavelengths against distilled water as blank. The absorbance difference of 235.6 nm and 242.2 nm was measured for ALS. The calibration curve was plotted between the concentration of component and absorbance difference value of ALS. The calibration curve for AML was plotted between the concentration of component and absorbance value of AML.

Standardization of the method by analysis of mixed standard solutions

To check the validity of the selected method, mixed standard solutions of ALS and AML were prepared and were subjected to determine absorbance values at 365 nm for AML and absorbance difference values between 235.6 nm and 242.2 nm for estimation of ALS.

Accuracy

The accuracy of the method was determined by calculating recoveries of ALS and AML by the standard addition method. Known amount of standard solution of ALS and AML were added at 80%, 100% and 120% levels to pre-quantified tablet sample solutions of ALS and AML. The results are reported in terms of % Recovery.

Results and Discussion

Method development and validation

The overlain spectra of the drugs suggested that a dual wavelength spectrophotometric method was a suitable method for simultaneous determination of ALS and AML. Distilled water was taken as solvent system, as both the drugs were soluble in this solvent. In dual wavelength method, wavelengths 235.6 nm and 242.2 nm were selected for determination of ALS, whereas AML was estimated directly at 365 nm as ALS has zero absorbance at this wavelength. Optimized method parameters for dual wavelength spectrophotometry are shown in table 1.

Linearity

The calibration curves of ALS and AML were linear in the range of 25 - 300 µg/ml and 5 - 100 µg/ml respectively. Regression equation and R^2 value are given in table 1.

Method parameters	Optimized parameters
Solvent	Distilled water
Scanning range	210 - 400 nm
Analytical wavelengths for determination of ALS	235.6 nm and 242.2 nm
Analytical wavelength for AML	365 nm
Regression equation and R^2 value for ALS	y = 0.007x + 0.004, R^2 = 0.999
Regression equation and R^2 value for AML	y = 0.012x + 0.004, R^2 = 0.999

Table 1: Optimized method parameters for Dual Wavelength spectrophotometry.

Standardization of the method by analysis of mixed standard solutions

The concentration of ALS and AML recovered from mixed standard solutions was within range and are given in table 2.

S. No.	Amount Present (µg/ml)		Amount Found (µg/ml)		%	
	ALS	AML	ALS	AML	ALS	AML
1	25	60	24.72	60.79	98.86	101.31
2	50	50	50.57	50.64	101.14	101.29
3	75	40	74.43	40.29	99.24	100.71
4	100	30	100.43	29.93	100.43	99.76
5	125	20	124.72	20.29	99.77	101.43
6	150	10	150.28	9.93	100.19	99.29

Table 2: Results of validation studies of Aliskiren and Amlodipine using mixed standards.

Accuracy

The percentage recoveries of drugs from sample were determined by standard addition of pure drugs at three known concentrations and recoveries were obtained at each level. The percent recoveries for ALS were found to be in the range of 100.19- 100.65% and the percent recoveries for AML were found to be in the range of 99. 62 - 100.13%. The results of accuracy studies are shown in table 3.

Application of the method in assay of tablets

The proposed UV method was applied for the determination of ALS and AML in their combined pharmaceutical formulation and the results are shown in table 4.

Accuracy Level (%)	Amount Added (µg/ml)		Amount Recovered (µg/ml)		% Recovery		Mean	
	ALS	AML	ALS	AML	ALS	AML	ALS	AML
80	80	5.33	80.57	5.29	100.71	99.17	100.65	99.62
	80	5.33	80.71	5.29	100.89	99.17		
	80	5.33	80.29	5.36	100.36	100.51		
100	100	6.66	100.57	6.64	100.57	99.74	100.52	100.10
	100	6.66	100.57	6.64	100.57	99.74		
	100	6.66	100.43	6.71	100.43	100.82		
120	120	7.99	120.57	8.0	100.48	100.13	100.20	100.13
	120	7.99	120.29	7.93	100.24	99.23		
	120	7.99	119.86	8.07	99.88	101.02		

Table 3: Results of Accuracy study for Aliskiren and Amlodipine.

Sample No.	Label Claim (mg/tab)		Amount Found (mg/tab)		% Label Claim	
	ALS	AML	ALS	AML	ALS	AML
1	150	10	149.86	10.07	99.90	100.71
2	150	10	150.14	9.85	100.09	98.57
3	150	10	150.28	9.92	100.19	99.28
4	150	10	149.43	10.14	99.62	101.42
5	150	10	149.57	9.92	99.71	99.28
Mean					99.90	99.85
S.D.					0.24	1.17
% RSD					0.24	1.17

Table 4: Analysis of Formulation of Aliskiren and Amlodipine.

Conclusion

The proposed dual wavelength method gives accurate and precise results for determination of aliskiren and amlodipine in marketed formulation (tablet) without prior separation and is easily applied for routine analysis. The most striking feature of the dual wavelength method is its simplicity and rapidity. Method validation has been demonstrated by variety of tests for linearity, accuracy, precision. The proposed method was successfully applied to determination of these drugs in commercial tablet.

Acknowledgement

The authors express their sincere gratitude to Swapnroop Drugs and Pharmaceuticals, Aurangabad, Maharashtra, India for providing the pure drug samples of Aliskiren Hemifumarate and Amlodipine Besylate and are also thankful to colleagues and authorities of Department of Pharmacy, SRMSCET, Bareilly, U.P. who helped us in this work.

Bibliography

1. Lam S and Choy M. "Aliskiren: an oral renin inhibitor for the treatment of hypertension". *Cardiology Review* 15.6 (2007): 316-323.

2. Schmieder RE. "The effect of angiotensin-converting-enzyme inhibition on diabetic nephropathy". *Journal of Renin Angiotensin Aldosterone System* 7 (2006): S16.

3. Daugherty KK. "Aliskiren - A review". *American Journal of Health System Pharmacy* 65 (2008): 1323.

4. Pranay Wal., *et al*. "Aliskiren: An orally active rennin inhibitor". *Journal of Pharmacy and Bioallied Sciences* 3.2 (2011): 189-193.

5. Triggle DJ. "Calcium channel antagonists: clinical uses-past, present and future". *Biochemical Pharmacology* 74.1 (2007): 1-9.

6. Taylor SH. "Usefulness of amlodipine for angina pectoris". *American Journal of Cardiology* 73.3 (1994): 28A-33A.

7. Abernethy DR. "Pharmacokinetics and pharmacodynamics of amlodipine". *Cardiology* 80.1 (1992): 31-36.

8. Hermida RC., *et al*. "Chronotherapy with nifedipine GITS in hypertensive patients: improved efficacy and safety with bedtime dosing". *American Journal of Hypertension* 21.8 (2008): 948-954.

9. Babu KS., *et al*. "Simple and sensitive method for the determination of aliskiren hemifumarate using hplc-uv detection". *Journal of Chemistry* 4.2 (2011): 285-288.

10. Wrasse-Sangoi M., *et al*. "Determination of Aliskiren in Tablet Dosage Forms by a Validated Stability-indicating RP-LC Method". *Journal of Chromatography Science* 49.2 (2011): 170-175.

11. Sangoi WM., *et al*. "Development and validation of an UV spectrophotometric method for the determination of aliskiren in tablets". *Quimica Nova* 33.6 (2010): 1330-1334.

12. Ezzeldin MI., *et al*. "Application of chromatographic and spectrophotometric methods for the analysis of selected antihypertensive combinations". *International Journal of Analytical Pharmaceutical and Biomedical Sciences* 2.3 (2013): 6-15.

13. Sangoi MDS., *et al*. "Simultaneous determination of aliskiren and hydrochlorothiazide from their pharmaceutical formulations by monolithic silica HPLC column employing experimental designs". *Journal of Liquid Chromatography and Related Technology* 34.17 (2011): 1102-1112.

14. Zarghi A., *et al*. "Validated HPLC method for determination of amlodipine in human plasma and its application to pharmacokinetic studies". *Farmaco* 60.9 (2005): 789-792.

15. Runja CP., *et al*. "A Validated Stability Indicating RP-HPLC Method Development and Validation for Simultaneous Estimation of Aliskiren Hemifumarate and Amlodipine Besylate in Pharmaceutical Dosage Form". *Chromatography Research International* 3.6 (2014): 1-7.

16. Patel SR and Patel ChN. "Development and validation of absorbance correction method for simultaneous estimation of aliskiren and amlodipine in combined dosage form". *Asian Journal of Pharmaceutical Research and Health Care* 5.2 (2013): 43-51.

17. Chaitanya KK., *et al*. "RP-HPLC method development and validation of amlodipine and losartan in binary mixture". *Journal of Global Trends in Pharmaceutical Sciences* 4.3 (2013): 1144-1152.

18. Mehulkumar P., *et al*. "Simultaneous Spectroscopic Estimation of Amlodipine Besylate and Olmesartan Medoximil in Tablet Dosage Form". *Asian Journal of Research in Chemistry* 2.2 (2009): 127-130.

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