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Simultaneous Estimation of Olmesartan Medoxomil and Amlodipine Besylate in Solid Dosage Form by UV Spectrophotometry

*** Tripti Sharma[1], Neelam Mishra[1], Sudam C.Si[1], D. G.Shankar[2]**

[1]*School of Pharmaceutical Sciences, Kalinga Nagar, Ghatikia, Bharatpur, Bhubaneswar, Orissa*
[2] *Pharmaceutical Analysis and Quality Assurance Division, College of Pharmaceutical Sciences, Andhra University, Visakhapatnam, India.*

ABSTRACT

Olmesartan medoxomil is an ACE inhibitor and Amlodipine besylate is calcium – channel blocker. Simple, precise, rapid and selective simultaneous equation and Q- analysis UV spectrophotometric methods have been developed for simultaneous determination of Olmesartan medoxomil and Amlodipine besylate from tablet dosage forms. The methods involve solving of simultaneous equations and Q-value analysis based on measurement of absorptivity at 256.8nm, 239nm, 235.6nm respectively. Linearity lies between 5-30µg/ml for both the drugs Olmesartan medoxomil and Amlodipine besylate.

Keywords: Olmesartan medoxomil, Amlodipine besylate, Simultaneous Equation method, Absorbance Ratio method.

Introduction

Olmesartan (OMS) is a selective AT_1 subtype Angiotensin II receptor antagonist. Olmesartan medoxomil is 2,3-dihydroxy-2-butenyl-4-(1-hydroxy-1-methylethyl)-2-propyl-1-[p-(o-1H-tetrazol-5-yl-phenyl)benzyl]imidazole-5-carboxylate, cyclic 2,3-carbonate[1]. Olmesartan medoxomil, a prodrug, is hydrolyzed to Olmesartan during absorption from the gastrointestinal tract. Literature survey reveals that few HPLC and spectrophotometric methods are reported for estimation of Olmesartan medoxomil in the biological samples [3-5] .

Amlodipine (AMD) (a dihydropyridine) is a calcium-channel blocker. It is given as besylate and used in management of hypertension and angina pectoris. It is chemically 3-ethyl-5-methyl-2-(2-aminoethoxymethyl)-4-(2-chlorophenyl)-1,4-dihydro-6-methyl pyridine-3, 5-dicarboxylate monobenzene sulphonate. It is official in BP [2].Literature survey reveals that there is UV [6-8] , HPLC [9-12] and HPTLC [13] methods reported for estimation of Amlodipine besylate in pharmaceutical formulations.

The review of the literature revealed that no method is yet reported for the simultaneous estimation of both the drugs in combined dosage forms. This paper describes simple, rapid, accurate, reproducible and economical method for the simultaneous estimation of the Olmesartan medoxomil and Amlodipine besylate in tablet formulations using simultaneous equation and absorbance ratio methods.

MATERIALS AND METHODS

Instrument

Jasco UV-Visible spectrophotometer V-630 model was used for spectral measurements with matched pair quartz cells corresponding to 1cm path length.

Preparation of stock solution:

Accurately weighed quantity of OMS (10mg)and AMD (10mg) was transferred to two separate 100ml volumetric flask dissolved in 100ml methanol and diluted to the mark with distilled water(stock solution:100µg/ml)

Method-1: Employing simultaneous equations using Cramer's Rule [14]

From the stock solution of 100µg/ml working standard solution of drugs were prepared by appropriate dilution and were scanned in entire UV range to determine the λmax.OMS has λmax at 256.8nm while AMD has λmax at 239nm respectively (Fig1). Serial dilutions of standard in the concentration range of 5-30 µg/ml for both the drugs. The absorbances of the standard solutions were measured at 256.8nm and 239nm and calibration curves were plotted at these wavelengths. Two simultaneous equations (in two variables C1 and C2) were formed using the Absorptivity co-efficient values. The absorptivity for the two drugs is presented in Table1.

Table 1 Absorptivity values for Olmesartan medoxomil and Amlodipine besylate

Concentration (µg/ml)		Absorpitivity at 256.8 nm		Absorpitivity at 239 nm		Absorpitivity at 235.6 nm (Isoabsorptive point)	
OMS	AMD	OMS	AMD	OMS	AMD	OMS	AMD
5	5	41.12	20.42	39.46	34.68	40.72	38.30
10	10	41.00	18.21	35.06	34.79	36.18	35.26
15	15	41.06	15.65	33.08	33.21	34.18	31.82
20	20	41.31	15.56	32.14	32.71	33.19	32.03
25	25	40.39	15.39	31.96	32.65	33.00	31.97
30	30	41.07	15.74	32.93	33.27	34.11	32.81
mean	mean	40.82	16.83	34.10	33.55	35.23	33.70

OLM – Olmesartan medoxomil, AMD –Amlodipine besylate

The method employs solving of simultaneous equations using Cramer's rule and matrices. The simultaneous equations formed were

$A_1 = (40.825)\ C_1 + (16.83)\ C_2$ (1)
$A_2 = (34.10)\ C_1 + (33.55)\ C_2$ (2)

Where A_1 and A_2 are the absorbance of sample solution at 256.8 nm and 239 nm respectively. C_1 and C_2 are concentrations of Olmesartan medoxomil and Amlodipine besylate respectively in sample solution. By substituting the value of C_1 from equation (1) into equation (2), the value of C_1 can be obtained. Similarly C_2 can also be obtained.

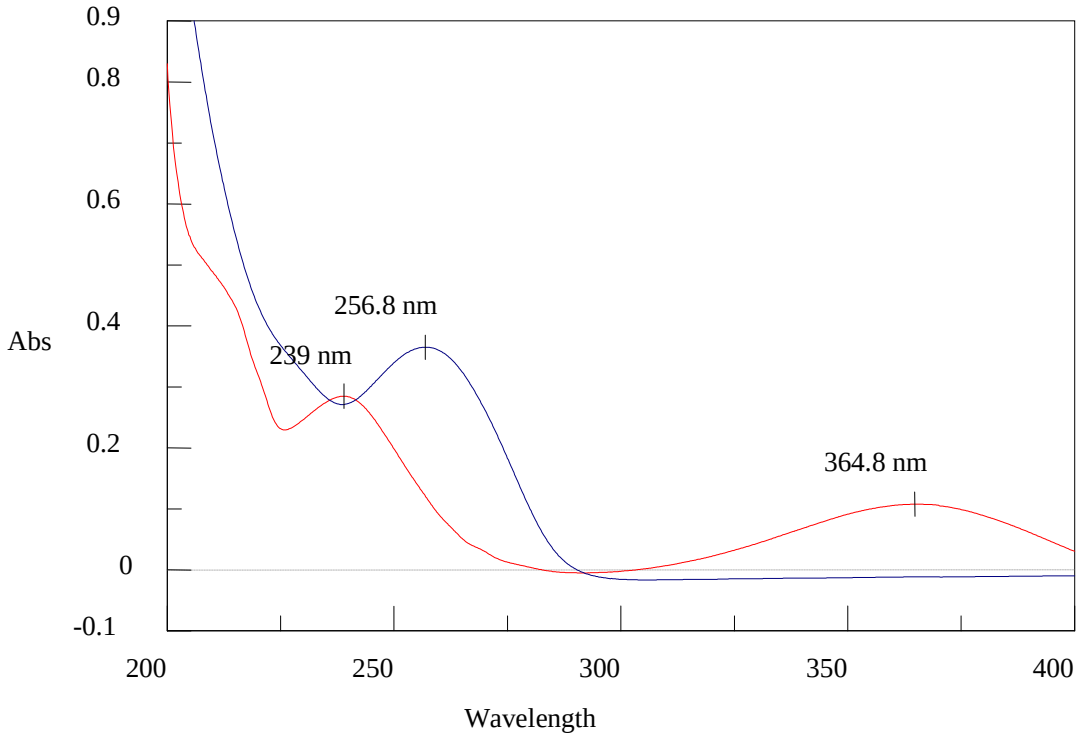

Figure 1 Overlain spectra of Olmesartan medoxomil and Amlodipine besylate

Method 2: Absorbance Ratio or Q-Analysis method [14]

Absorbance method uses the ratio of absorbance at two selected wavelengths, one at isoabsorptive point and other being the λmax of one of the two compounds. From the stock solutions, working standard solutions of OMS and AMD were prepared by appropriate dilution and were scanned in the entire UV range to determine the λmax and isoabsorptive point. OMS and AMD have λmax at 256.8nm and 239nm, respectively. Both the drugs were found to have same absorbance at 235.6nm, which was taken into consideration as isoabsorptive point (Fig 1). A series of standard solutions ranging from 5-30µg/ml for OMS and AMD both were prepared and absorbance of solutions were recorded at 256.8nm and 235.6nm to plot a calibration curve of absorbance versus concentration. The calibration curves were found to be linear in concentration

range under study. Absorptivity values of OMS and AMD were determined at selected wavelengths are presented in Table- I. The concentration of two drugs in mixture was calculated by using following equations

For Olmesartan medoxomil, the equation (3) is given below

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

For Amlodipine besylate, the equation (4) is given below

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

$$Q_0 = \frac{\text{Absorbance of sample at 256.8nm}}{\text{Absorbance of sample at 235.6nm}}$$

$$Q_1 = \frac{\text{Absorptivity of Olmesartan midoxomil at256.8nm}}{\text{Absorptivity of Olmesartan midoxomil at 235.6nm}}$$

$$Q_2 = \frac{\text{Absorptivity of amlodipine besylateat 256.8nm}}{\text{Absorptivity of amlodipine besylate at 235.6nm}}$$

A=Absorbance of sample at isoabsorptive point, a_1 and a_2 = absorptivities of Olmesartan medoxomil and Amlodipine besylate respectively at isoabsorptive point

Procedure for Analysis of Tablet Formulation by Method I and II

Twenty tablets were weighed accurately. The average weight was determined and then ground to a fine powder. A quantity equivalent to 10mg of Olmesartan medoxomil and 2.5mg of Amlodipine besylate were transferred to a 100ml volumetric flask. The contents were ultrasonicated for 10 min with methanol, made to volume with distilled water and filtered through whatmann filter paper No.41. The solution was further diluted with distilled water to give concentrations of 10µg/ml and 2.5µg/ml of Olmesartan medoxomil and Amlodipine besylate respectively. Absorbances of these solutions were measured at 256.8nm and 239nm as A_1 and A_2 respectively and concentrations of these two drugs in the sample were calculated using equation (1) and equation (2).

The tablet sample solution was also subjected to analysis by Q-Analysis method. Absorbance of sample solutions were recorded at 235.6nm and 256.8nm and the concentration of two drugs in the sample were determined by using equation 3 and 4. The analysis procedure was repeated 6 times with tablet formulations. The result of analysis of tablet formulation is reported in Table-2

Table 2 Determination of Olmesartan medoxomil and Amlodipine besylate in combined tablet dosage form

Brands	Method	Tablet content	Label content (mg)	Amount found (mg)	% of amount*	± SD*	RSD (%)*
I	I	OLM	20	19.9	99.50	±0.013	0.066
		AMD	5	4.96	99.20	±0.028	0.570
	II	OLM	20	19.9	99.50	±0.031	0.155
		AMD	5	4.95	99.00	±0.035	0.707
II	I	OLM	20	20	100.00	±0.026	0.132
		AMD	5	5	100.00	±0.021	0.435
	II	OLM	20	20.01	100.07	±0.029	0.145
		AMD	5	5.01	100.2	±0.024	0.488

* Mean of six readings, OLM – Olmesartan medoxomil, AMD –Amlodipine besylate

Recovery Studies:

To study the accuracy of the proposed methods recovery studies were carried out by standard addition methods at three different levels. A known amount of drug was added to preanalyzed tablet solution and percentage recovery were calculated. The result of recovery studies were satisfactory and are presented in table 3.

Table 3 Results of Recovery Studies

Brands	Amount of drug added (mcg/ml)		Amount of drug recovered (mcg/ml)*		% Recovery ± SD*	
	OLM	AMD	OLM	AMD	OLM	AMD
I	3.8	0.8	3.78	0.804	99.47±0.130	100.5±0.021
	4	1	4.02	1.004	100.5±0.038	100.4±0.032
	4.2	1.2	4.22	1.206	100.47±0.041	100.5±0.034
II	3.8	0.8	3.802	0.802	100.0±0.037	100.25±0.019
	4	1	4.002	1.00	100.0±0.018	100.0±0.015
	4.2	1.2	4.204	1.19	100.0±0.021	99.16±0.016

* Mean of six readings, OLM – Olmesartan medoxomil, AMD –Amlodipine besylate

Table 4 Validation and sensitivity of the proposed methods

Parameters	OLM	AMD
Wavelength (nm)	256.8	239
Beer's law limit (mcg/ml)	5-30	5-30
Sandell's sensitivity (mcg/ml/cm^2/0.001 absorbance unit)	0.0232	0.0054
Absorptivity	40.82	33.55
Regression equation	Y = 0.0407x + 0.0011	Y = 0.0325x + 0.0128
Intercept	0.0407	0.0325
Slope	0.0011	0.0128
Coefficient of correlation	0.9996	0.9992

RESULT AND DISCUSSION

The proposed methods are economical, as they can be done with very less specifications. The absorptivity values of OLM and AMD at their respective λmax and isoabsorptive point are presented in table 1. The values of standard deviation and standard error were satisfactorily low and recovery lying between 99.47 to 100.5 (for OLM) and 99.16 to 100.5 (for AMD) indicates the accuracy of the method. The methods employing Simultaneous equation and Absorbance ratio method are very simple and can be easily applied to routine analysis. The results of analysis of tablet formulation, statistical evaluation and recovery studies are shown in table 2 and 3 respectively. The proposed methods were validated according to ICH guidelines [15]. The validation and sensitivity parameters of both the methods are presented in Table 4. The overlain spectrum of OLM and AMD used for analysis is given in Figure 1.

The proposed methods are accurate, precise, economical, rapid and selective for the simultaneous determination of Olmesartan medoxomil and Amlodipine besylate in tablet dosage form. Analysis of authentic samples containing Olmesartan medoxomil and Amlodipine besylate showed no interference from the common additives and excipients. Hence it can be conveniently adopted for the routine quality control analysis in its combined dosage forms.

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