International Journal of Pharmaceutical Research and Development (IJPRD)
Platform for Pharmaceutical Researches & Ideas
www.ijprd.com

SIMULTANEOUS ESTIMATION OF ATENOLOL AND AMLODIPINE IN COMBINED DOSAGE FORM

Prianshu tangri[*1],
Mohit arya[1], Lakshmayya[1]

[1]GRD(PG)IMT, Dept. of Pharmacy, Dehrdaun, Uttarakhand, India

ABSTRACT
The quantitative estimation is the method to determine how much of each constituent is in the sample. Estimation of a given drug or medicine in the dosage forms needs the quantitative analysis of that drug or medicinal in it. The first quantitative analyses were gravimetric, made possible by the invention of a precise balance. If a sample contains two absorbing drugs (X and Y) each of which absorbs at the λ_{max} of the other, it may be possible to determine both drugs by the technique of simultaneous equations (Vierordt's method). The current objective of this research work is to establish a rapid, accurate and inexpensive method for the estimation of atenolol and amlodipine in combined dosage form.

Correspondence to Author

Prianshu tangri

GRD(PG)IMT, Dept. of Pharmacy, Dehrdaun, Uttarakhand, India

Email: prianshu_tangri@yahoo.co.in

Keywords atenolol, amlodipine, simultaneous, accuracy

INTRODUCTION

The quantitative estimation is the method to determine how much of each constituent is in the sample. Estimation of a given drug or medicine in the dosage forms needs the quantitative analysis of that drug or medicinal in it. The first quantitative analyses were gravimetric, made possible by the invention of a precise balance. It was soon found that carefully calibrated glassware made considerable saving of time through the volumetric measurement of gravimetrically standardized solutions. Although in recent years, spectrophotometric methods are extensively used, but it would be wrong to conclude that instrumental methods have totally replaced chemical methods. In fact, chemical steps are often an integral part of an instrumental method. The sampling, dissolution, change in oxidation state, removal of excess reagent, pH adjustment, addition of complexing agent, precipitation, concentration and the removal of interferences are the various chemical steps which are part of an instrumental method. In recent years HPLC (High Performance Liquid Chromatography) is extensively used, because HPLC is not limited by sample volatility or thermal stability. HPLC is able to separate macromolecules and ionic species, labile natural products, polymeric material and a wide variety of other high molecular weight poly-functional group because of the relatively high pressure necessary to perform this type of chromatography; a more elaborate experimental setup is required.[1,2]

Simultaneous equations method:- If a sample contains two absorbing drugs (X and Y) each of which absorbs at the max of the other , it may be possible to determine both drugs by the technique of simultaneous equations (Vierordt's method) provided that certain criteria apply.

The information required is:

(a) The absorptivities of X at 1 and 2, a_{x1} and a_{x2} respectively

(b) The absorptivities of Y at 1 and 2, a_{x1} and a_{x2} respectively

(c) The absorbance of the diluted sample at 1 and 2, A_1 and A_2 respectively.

Let C_x and C_y be the concentrations of X and Y respectively in the diluted sample.

Two equations are constructed based upon the fact that at 1 and 2 the absorbance of the mixture is the sum of the individual absorbance of X and Y.

At 1 $A1 = a_{x1}bc_x + a_{y1}bc_y$ (1)

At 2 $A2 = a_{x2}bc_x + a_{y2}bc_y$ (2)

For measurements in 1 cm cells, b = 1.

Rearranging eq. (2).

$C_y = A_2 – a_{x2}c_x / a_{y2}$

Substituting for Cy in eq. (1) and rearranging gives

$C_x = A_2\, ay_1 – A_1\, a_{y2} / \; a_{x2}ay_1 – ax_1\, a_{y2}$ (3)

$Cy = A_1\, ax_2 – A_2\, ax_1 \; / ax_2\, ay_1 – ax_1\, ay_2$ (4)

Modified equations containing a symbol (b) for path-length can be used for application in situations where A1 and A2 are measured in cells other than 1 cm path-length.

Criteria for obtaining maximum precision, based upon absorbance ratios, have been suggested [2,3] that place limits on the relative concentrations of the components of the mixture. The criteria are that the ratios

$\frac{A_2/A_1}{a_{x2}/a_{x1}}$ & $\frac{a_{y2}/a_{y1}}{A_2/A_1}$

Should lie outside the range 0.1-02 for the precise determination of Y and X respectively.

Amlodipine is in a group of drugs called calcium channel blockers. Amlodipine relaxes (widens) blood vessels and improves blood flow. Amlodipine is used to treat high blood pressure (hypertension) or chest pain (angina) and other conditions caused by coronary artery disease. Atenolol (Tenormin) is in a group of drugs called beta-blockers. Beta-blockers affect the heart and circulation (blood flow through arteries and veins). Atenolol is used to treat angina (chest pain) and hypertension (high blood pressure). It is also used to treat or prevent heart attack.

Amlodipine (AML):- chemically 3-Ethyl-5- methyl (4RS)-2-[(2-aminoethoxy) methyl]-4-(2-chlorophenyl)-6-methyl-1, 4-dihydropyridine-3, 5-dicarboxylate benzene sulphonate is a long-acting calcium channel blocker used for hypertension and angina pectoris [2-4]. Amlodipine Besylate block the inward movement of calcium by binding to L-Type calcium channels in the heart and in smooth muscle of the coronary and peripheral vasculature relaxing the smooth muscle and dilating arterioles thereby decreasing peripheral resistance. Hence improving blood pressure; in angina it improves blood flow to the myocardium.

Atenolol (ATE):- chemically 2-[4-{(2RS)-2-hydroxy-3-[(1-methylethyl) amino] propoxy} phenyl] acetamide is a β-adrenoreceptor blocking agent primarily used for hypertension, angina pectoris & myocardial infarction. It mainly acts by inhibition of renin release and angiotensin -II (AT-II) and aldosterone production.

MATERIALS AND METHODS

Materials: Shimadzu UV-1700 spectrophotometer with spectral band width of 1.8nm, wavelength accuracy of ± 2nm & matched quartz cell of 10mm optical path length was used for all spectral & absorbance measurement. All chemicals used were of analytical reagent grade and double distilled water was used to prepare the solvent medium. Pharmaceutical grade AML and ATE procured from Ranbaxy, Paonta Sahib, India were used as received

Method: Simultaneous equations method was used i.e. if a sample contains two absorbing drugs (X and Y) each of which absorbs at the max of the other , it may be possible to determine both drugs by the technique of simultaneous equations

(Vierordt's method) provided that certain criteria apply.[2-4]

Two equations are constructed based upon the fact that at 1 and 2 the absorbance of the mixture is the sum of the individual absorbance of X and Y.

At 1 $A1 = a_{x1}bc_x + a_{y1}bc_y$ (1)

At 2 $A2 = a_{x2}bc_x + a_{y2}bc_y$ (2)

For measurements in 1 cm cells, b = 1.

Solvent System: -Double distilled water was used as a solvent system

Preparation of stock Solution:-

Pure Drug: - Accurately weighted 100mg pure drug of AML & ATE were dissolved in the solvent system in a two different 100ml of volumetric flasks. The solution was kept on the sonicator for 15min and then volume was makeup to the 100ml.

Marketed formulation: - The average weight of 10 tablets was taken and it was found 0.999mg which contain claim of 5mg AML & 50mg ATE. Accurately weighted 1gm of drug was taken and in a 100 ml of volumetric flask and dissolved by adding a solvent system. The solution was sonicated for 15 min after that the volume was make up to the 100ml by adding the solvent system.

Determination of λmax: - From the stock solutions, a working standard was prepared. The absorption spectrum for AML was recorded using the concentration of 6µg/ml and it was found to show two absorption maxima at 239 nm. For ATE hydrochloride, the absorption spectrum was recorded using 8µg/ml solution and the maximum absorption was found to be 273nm.

Preparation of Standard Curve:- The Calibration curves were prepared for AML and ATE in the concentration range of 2-16 µg/ml and 2-16 µg/ml at selected wave Lengths by diluting aliquot portions of stock solution of each drug. (fig no. 1,2)

Simultaneous Estimation:- First prepare the dilutions of 2 to 20µg/ml from stock solution of AML and ATE After that take its absorbance at both λmax of AML and ATE respectively . Absorptivity value of both drug was found by dividing its absorbance value with its concentration as shown in table. The marketed formulation of drug was also subjected at both wavelength of 239nm & 273nm to find out the absorbance.[5](FIG NO. 3)

Fig no. 1 Standard curve of Atenolol at λmax 273nm:-

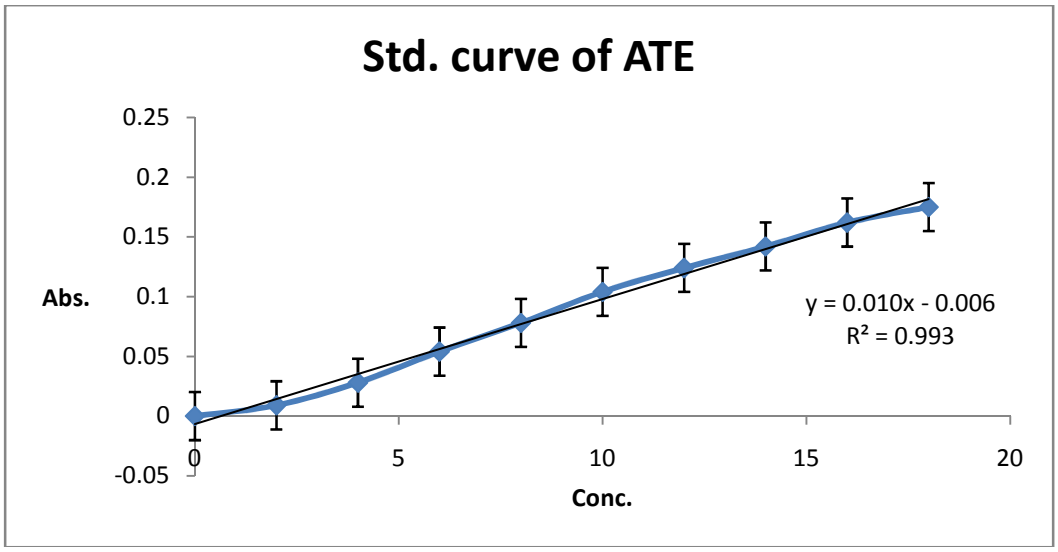


Fig. no. 2 Standard curve of Amlodipine at λmax 239nm:-

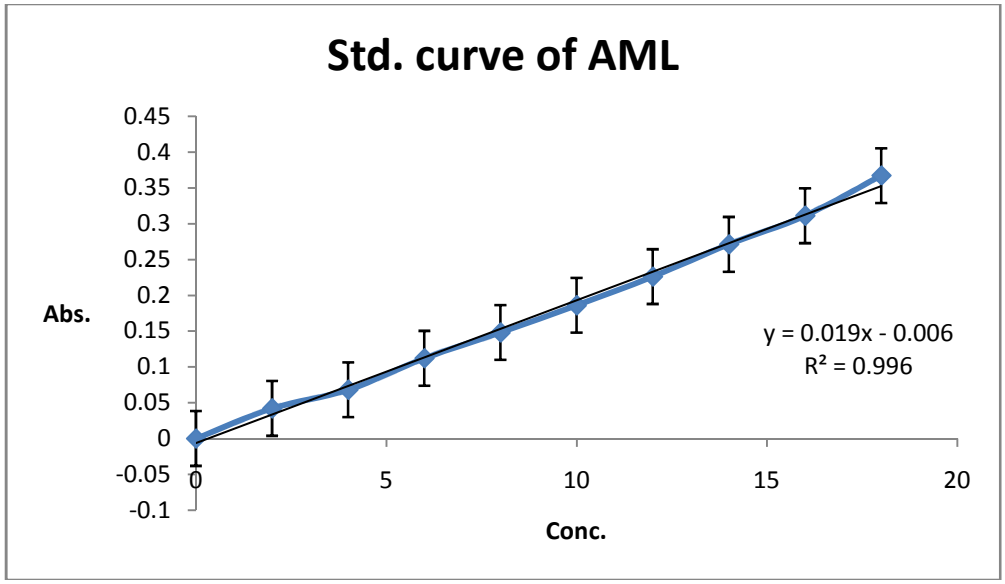
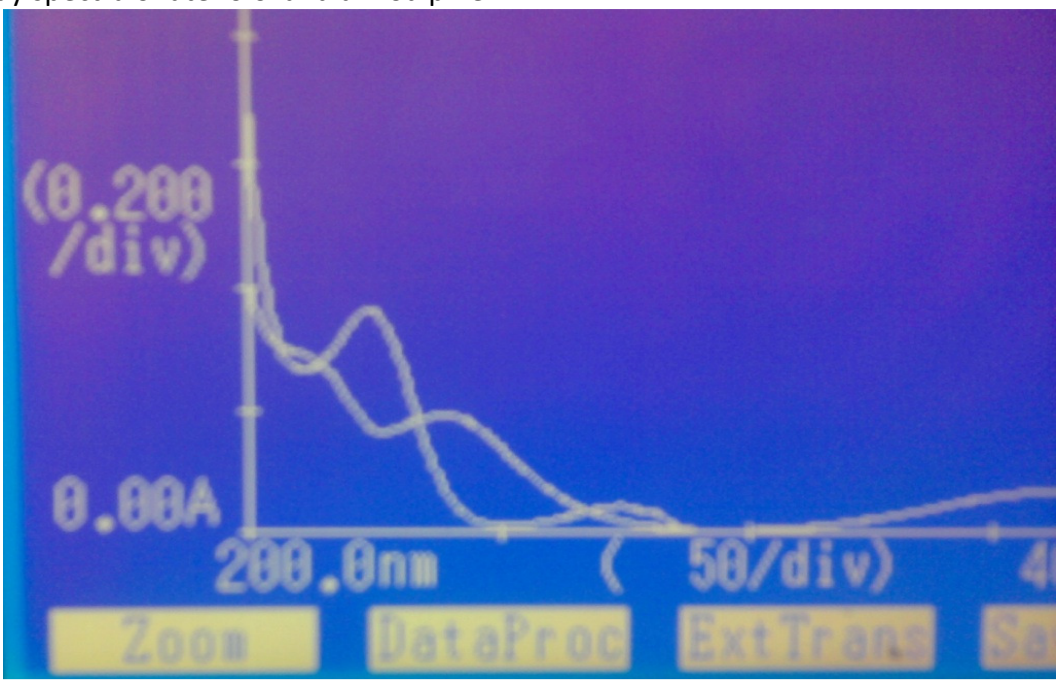


Fig no. 3 Overlay spectra of atenolol and amlodipine



Accuracy & precision:- The above mentioned procedure was repeated three times and all the standard were maintained .According the claim of marketed formulation i.e. AML-5mg & ATE -50mg the drug was précised.

RESULTS AND DISCUSSIONS:

Amounts of Amlodipine & Atenolol were determined by solving the simultaneous equations.

Two simultaneous equations were formed using absorptivity coefficient values.

A1 = 0.008 x C1 + 0.018 C2 ---------- (1)

A2 = 0.007 x C1 + 0.003C2 --------- (2)

The concentrations of Amlodipine & Atenolol were calculated using following two equations.

$C_1 = A_2\, ay_1 - A_1\, a_{y2} /\ a_{x2} ay_1 - ax_1\, a_{y2}$ --------- (3)

$C_2 = A_1\, ax_2 - A_2\, ax_1 / ax_2\, ay_1 - ax_1\, ay_2$ --------- (4)

Where C1 and C2 are concentration of Amlodipine & Atenolol respectively in gm/liter in the sample

solution, A1 and A2 are the absorbance of the mixture at 239 nm and 273 nm respectively. Amount of atenolol and amlodipine was calculated to be 49.78 mg and 4.97 mg respectively. (table no. 1-4)

Table no. 1 Absorbance of AML and ATE at both λmax 237 & 269 respectively:-

Conc.	AML λ max (nm)				ATE λ max (nm)			
	239 (nm)	ax1	273 (nm)	ax2	273 nm	ay2	239 nm	ay1
2	0.042	0.042	0.013	0.0065	0.009	0.0045	0.017	0.0085
4	0.068	0.068	0.017	0.0042	0.028	0.007	0.026	0.0065
6	0.112	0.112	0.022	0.0036	0.054	0.009	0.044	0.0073
8	0.148	0.148	0.025	0.0031	0.078	0.0097	0.062	0.0077
10	0.186	0.186	0.027	0.0027	0.104	0.0104	0.078	0.0078
12	0.226	0.226	0.029	0.0024	0.124	0.0103	0.095	0.0079
14	0.271	0.271	0.031	0.0022	0.142	0.0101	0.015	0.001
16	0.311	0.311	0.04	0.0025	0.162	0.0101	0.124	0.0077
18	0.367	0.367	0.042	0.0023	0.175	0.0097	0.14	0.0077

Table no. 2 Optical and regression parameters of AML and ATE in 0.1N HCl and DMF in the ratio of (9:1).

Parameters	**AML**		**ATE**	
λmax (nm)	239nm	273nm	273 nm	239 nm
Beer's law limit (mg/ml)	2-16	2-10	2-18	2-12
Correlation coefficient (r) (R^2)	0.996	0.979	0.993	0.987
Regression equation (y= mx + c)	y = 0.019x - 0.006	y = 0.009x - 0.003	y = 0.010x - 0.006	y = 0.06x - 0.004
slope (b)	0.019	0.009	0.010	0.06

Table no. 3 Summary of validation parameters for AML and ATE.

S. No.	Parameters	AML	ATE
1.	Accuracy %	99.46-99.78%	98.46-99.95%
2.	Limit of detection, mg mL^{-1}	0.288	1.51
3.	Limit of quantification, mg mL^{-1}	0.872	4.67

Table no. 4 Summary of estimation of AML and ATE in different brands.

S. No.	Brand	Labeled amount (mg)	Amount found [a] (mg)	% of Labeled amount [a]	RSD
1.	**Amlovas-AT**	5 (AML)	4.97 ± 0.026	99.4 ± 0.578	0.589
		50 (ATE)	49.78 ± 0.169	99.7 ± 0.339	0.340

CONCLUSION:

The proposed method was found to be simple, precise, accurate and rapid for simultaneous determination of Amlodipine and Atenolol from pure and in pharmaceutical dosage forms. The solvent system is simple to prepare and economical. The sample recoveries in all formulations were in good agreement with their respective label claims and they suggested non-interference of formulation excipients in the estimation. Hence, the method can be easily and conveniently adopted for routine analysis of atenolol & amlodipine in combined dosage forms and can also be used for dissolution or similar studies.

REFERENCES

1. B. M. Rao, M. K. Srinivasu, G. Sridhar, P. R. Kumar,K. B. Chandrasekhar and A. Islam, J. Pharm. Biomed. Anal., 2005, 39, 503.
2. P. K. Sahoo, R. Sharma,* and S. C. Chaturvedi, "Simultaneous Estimation of Metformin Hydrochloride and Pioglitazone Hydrochloride by RPHPLC Method from Combined Tablet Dosage Form", Indian J Pharm Sci. 2008, 70(3), 383–386.
3. Naidu K.R., Kale U.N. and Shingare M.S., Stability indicating RP-HPLC method for simultaneous determination of Amlodipine and Benazepril Hcl from their combination drug product, J. Pharm. Biomed. Anal., 2005, 39(1-2), 147-155.
4. Topale P.R., Simultaneous UV Spectrophotometric estimation of Amlodipine and Losartan Potassium in tablet dosage forms. Indian drugs, 2003, 40(2), 119-121.
5. Argekar A.P. and Powar S.G., Simultaneous determination of Atenolol and Amlodipine in tablets by HPTLC, J. Pharm. Biomed. Anal., 2000, 21(6), 1137-1142.

*****