Simultaneous Spectrophotometric Determination of Amlodipine Besylate and Atorvastatin Calcium in Binary Mixture

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A rapid, simple, accurate and precise UV Spectrophotometric method using simultaneous equation was developed for the simultaneous determination of amlodipine besylate and atorvastatin calcium in a binary mixture. In the proposed method, the signals were measured at 238.2 and 246.6 nm corresponding to the absorbance maxima of amlodipine besylate and atorvastatin calcium in methanol, respectively. Linearity was observed in the concentration range of 5-30 µg/ml for both the drugs. Concentration of each drug was obtained by using the absorptivity values calculated for both the drugs at two wavelengths, 238.2 and 246.6 nm and solving the simultaneous equations. The method was validated statistically and recovery study was performed to confirm the accuracy of the method. Laboratory prepared synthetic mixture was successfully analyzed using the developed method.

Amlodipine besylate[1] (AMLB), 2-[(2-aminoethoxy)-methyl]-4-(2-chlorophenyl)-1,4-dihydro-6-methyl-3,5-pyridine dicarboxylic acid 3-ethyl-5-methyl ester, benzenesulfonate, is a potent dihydro pyridine calcium channel blocker. Atorvastatin calcium[2] (ATVC), (ßR,δR)-2-(4-fluorophenyl)-ß,δ-dihydroxy-5-(1-methylethyl)-3-phenyl-4-[(phenylamino)carbonyl]-lH-pyrrole-1-heptanoic acid, calcium salt (2:1) trihydrate, is a synthetic cholesterol-lowering agent. Combination therapy of AMLB and ATVC is recently launched by Pfizer Ltd. for the treatment of hypertension, chronic stable angina and vasospastic angina. Many analytical methods like HPLC[3-5], HPTLC[6], electrochemical[7], radioimmunoasay[8] and micellar electro kinetic chromatography[9] were reported for determination of AMLB alone or in combination with other antihypertensive drugs. There are only few analytical methods available for determination of ATVC alone in bulk drug, tablets, and human plasma[10-11]. However, no method is reported till date for simultaneous determination of these two drugs from their binary mixture. In this communication we report a new UV spectrophotometric method using simultaneous equation for simultaneous determination of both the drugs.

Spectrophotometric analysis was carried out on a Shimadzu 1601 double beam spectrophotometer with a fixed slit width (2 nm) using a pair of 1 cm matched quartz cells. All weighing were performed on an electronic single pan balance (Precisa 205A SCS). Calibrated borosilicate glassware was used in the study. Pure drug sample of AMLB and ATVC was kindly gifted by M/s. Torrent Pharmaceuticals Ltd., Ahmedabad and M/s. Alembic Ltd., Vadodara, respectively. The drugs were used as standards without further purification. Methanol analytical reagent grade (Allied Chemical Corporation, Vadodara) was used as solvent in this work.

ATVC and AMLB, 50 mg each, were accurately weighed and dissolved separately in 50 ml of methanol. Five ml of the above solutions were diluted separately to 50 ml with methanol to produce 100 µg/ml each of ATVC and AMLB in methanol. Suitable aliquots of these stock solutions of AMLB and ATVC were diluted with methanol to obtain 5 to 30 µg/ml of AMLB and ATVC separately. From the overlain spectra two wavelengths, 238.2 and 246.6 nm, were selected for the formation of simultaneous equation. The absorptivity values, E (1%, 1 cm), of both the drugs at both the wavelengths were determined. Different binary mixture solutions containing AMLB:ATVC (5:10, 10:10 and 10:5) were prepared by diluting suitable aliquots of the stock solutions with methanol. Selection of this ratio was based on the dosage strength of AMLB and ATVC in their commercial dosage forms. The quantitative estimation of the drugs were

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TABLE 1: OPTICAL CHARACTERISTICS OF THE PROPOSED METHOD

Parameters	AMLB	ATVC	AMLB	ATVC
Wavelength for measurement (nm)	238.2	238.2	246.6	246.6
Beer's Law limit (µg/ml)	5-30	5-30	5-30	5-30
Molar Absorptivity (l/mol cm)	3.2096×10^2	4.0083×10^2	2.3046×10^2	4.3232×10^2
Regression equation*				
Slope (β)	0.0319	0.0392	0.0229	0.0427
Intercept (α)	0.0024	0.0114	0.0017	0.0066
Correlation coefficient (r^2)	0.9986	0.9983	0.9991	0.9986

Where *$y=\alpha+\beta x$, x is the concentration of the analyte and y is the absorbance value

carried out by solving the simultaneous equations, $Cx=(A_2ay_1-A_1ay_2)-/(ax_2ay_1-ax_1ay_2)$–.(1), $Cy=(A_1ax_2-A_2ax)/(ax_2ay_1-ax_1ay_2)$....(2), where A_1 and A_{-2} are absorbances of the mixture at 238.2 and 246.6 nm respectively, ax_1 and ax_2 are absorptivities of x at 238.2 and 246.6 nm, respectively, ay_1 and ay_2 are absorptivities of y at 238.2 and 246.6 nm, respectively, Cx is the concentration of AMLB and Cy is the concentration of ATVC.

In this simultaneous equation method, the overlain spectra of both the drugs showed the λ_{max} of 238.2 nm for AMLB and 246.6 nm for ATVC. Hence these wavelengths were selected for estimation of AMLB and ATVC. Absorbances were determined at both the wavelengths. Both the drugs obeyed linearity in the concentration range of 5-30 µg/ml and the correlation coefficient (r^2) was <1 in both the cases (Table 1). The absorptivity was then calculated and along with absorbance, these values were submitted in the equations 1 and 2 to obtain concentration of drugs. The experiment was repeated five times in a day for intra-day and on five different days for inter-day precision. The method was found to be precise as % RSD for intra-day and inter-day precision were 1.066%, 1.051% respectively for AMLB and 0.566%, 0.903% respectively for ATVC. The accuracy of the method was determined by performing recovery studies by standard addition method in which preanalyzed samples were taken and standard drug was added at five different levels. The % recovery±SD lies in the range of 98.68±0.74% to 100.39±1.08% for AMLB and 99.67±0.67% to 100.63±1.841% for ATVC. The synthetic binary mixtures were prepared in laboratory in different dilutions. The value of % recovery±SD for 5:10 AMLB:ATVC mixture was 99.61±0.776 for AMLB and 100.58±0.881 for ATVC. The values were 99.99±1.119 and 98.72±0.459, respectively for 10:10 mixture and 99.75±1.251 and 99.52±1.362, respectively for 10:5 mixtures.

By observing the validation parameters viz., accuracy, intra-day and inter-day precision expressed as %RSD, linearity (correlation coefficient, $r^2<1$) and range, the method was found to be accurate and precise. Hence the method can be employed for routine analysis of the combination of these two drugs.

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