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Simultaneous estimation of atorvastatin calcium and aspirin in pure and capsule dosage form by using U.V. spectrophotometric method

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ABSTRACT

To develop simple spectrophotometric method development for simultaneous estimation of Atorvastatin calcium (ATR) and Aspirin (ASP) in pure and combined capsule dosage form. The method employed simultaneous equation method (method-1) and Q-absorbance ratio method (method-2) using 242 nm and 222 nm as absorbance maxima (λ_{max}) for ATR and ASP respectively and 232 nm as isoabsorbtive point. Methanol was used as a solvent. Linearity was observed in concentration range of 5-40 µg/ml for ATR and 5-30 µg/ml for ASP respectively. The method was validated statistically and recovery study was performed to confirm the accuracy of the method.

Keywords: Atorvastatin calcium, Aspirin, UV Spectrophotometric, Simultaneous equation.

INTRODUCTION

Atorvastatin calcium (ATOR) is chemically [R-(R*,R*)]-2-(4-flurophenyl)-β,δ-dihydroxy-5-(1-methylethyl)-3-phenyl-4-[(phenylamino)carbonyl]-1H-pyrrole-1-heptanoic acid, calcium salt trihydrate. Atorvastatin calcium is an inhibitor of 3-hydroxy-3-methylglutaryl Coenzyme A(HMG-CoA) reductase. This enzyme catalyses the conversion of HMG-CoA to mevalonate, an early and rate limiting step in cholesterol biosynthesis.

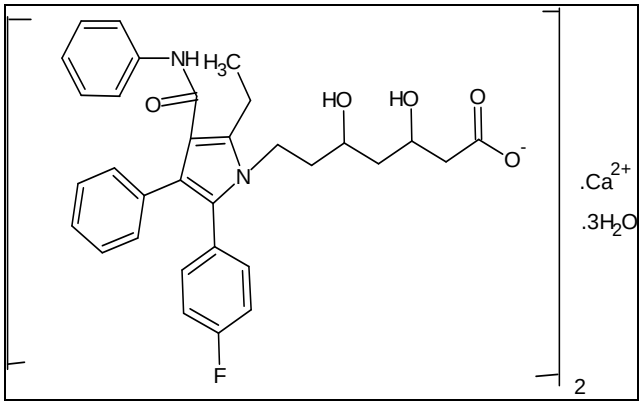
Aspirin is also known as acetylsalicylic acid is a salicylate drug, often used as an analgesic, antipyretic, anti-inflammatory and also has an antiplatelet effect by inhibiting the production of thromboxane, which under normal circumstances binds platelet molecule together to create a patch over damage of the walls within blood vessels. Chemically it is 2-acetoxybenzoic acid and is a nonsteroidal anti-inflammatory drug (NSAIDs) and shows inhibition of the enzyme cyclooxygenase. Atorvastatin and Aspirin both drug are official in Indian Pharmacopeia.

A survey of literature revealed that analytical methods like HPLC, HPTLC are reported for determination of Atorvastatin calcium and Aspirin individually and with other drug combination. The present work describe simple, precise, accurate and economical spectrophotometric method have been developed for simultaneous estimation of Atorvastatin calcium and Aspirin from combined dosage form.

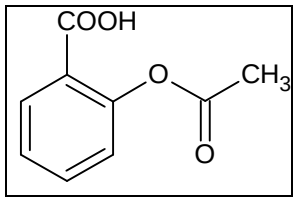
MATERIALS AND METHODS

Instrument:
A Jasco V-630 UV- Visible double beam spectrophotometer with spectral band width of 1.8 nm,wavelength accuracy of ±2 nm and matched quartz cells of 10 mm optical path length was used for all spectral and absorbance measurements. Schimadzu AX 200 Analytical balance was used for weighing purposes.

Reagents and chemicals:
The Reference Standard of Atorvastatin calcium and Aspirin was taken and the drug sample (capsules) Aztor ASP 75 manufactured by Sun pharmaceutical ind. Ltd. were procured from market and utilized for the study. All chemicals and reagent used were of analytical grade.



Atorvastatin calcium



Aspirin

A) Preparation of Standard Stock Solution and Calibration curve:

1. Pure Drug:

Accurately weighed 10mg pure drug of ATR and ASP were dissolved in the methanol in a two different 10ml volumetric flask and sonicated for 10min.It gives 1000 µg/ml concentration, consider it as stock solution A. Then from this solution pipette out 1ml from each in separate 10ml volumetric flask and named as stock solution B. The resultant stock solution contains 100 µg/ml ATR and 100 µg/ml ASP. Five working standard solution with concentration 5, 10, 15, 20, 25, 30, 35, 40 µg/ml of Atorvastatin calcium and 5, 10, 15, 20, 25, 30 µg/ml of Aspirin was taken. The absorbance of resulting solution were measured at their respective λmax and plotted a calibration curve to get linearity and regression equation.

2. Assessment of absorption maxima

The two solutions were scanned separately in the range of 200-400 nm to determine respective wavelength of maximum absorption. ASP and ATR showed absorbance maxima at 222 nm (λ_1) and 242 nm (λ_2) respectively.

3. Marketed formulation

Twenty capsules were accurately weighed, and contents were removed. Average weight of the content per capsule was calculated. The contents of a capsule were reduced to fine powder. A quantity of capsule powder equivalent to 10mg of Atorvastatin calcium and 75mg of Aspirin accurately weighted and taken in a 10 ml of volumetric flask containing 10ml methanol .The solution was sonicated for 20min and was filtered through Whatman filter paper no.40 .From this solution appropriate aliquots of ASP and ATR within the Beer's law limit were taken. The absorbances of resulting solutions were measured at 222 nm and 242 nm. Values were substituted in the respective formula to obtain concentrations.

B) Method-1 (Simultaneous Equation Method)

The Simultaneous Equation Method of analysis based on the absorption of the drugs Aspirin and Atorvastatin calcium at their λmax. Two wavelengths selected for the development of Simultaneous Equation were 222 nm (λ1) and 242 nm (λ2). Absoptivities of both the drugs at both the wavelengths were determined. The equations obtained for the estimation of concentration were,

$$C_x = \frac{A_2\, ay_1 - A_1\, ay_2}{ax_1\, ay_1 . ax_1\, ay_2}$$

$$C_y = \frac{A_1\, ax_2 - A_2\, ax_1}{ax_2\, ay_1 . ax_1\, ay_2}$$

Where,

A_1 and A_2 are absorbance of Sample solution at 222 and 242 nm respectively.

ax1= Absorptivity of ASP at 222 nm

ax2 = Absorptivity of ASP at 242 nm

Ay1 = Absorptivity of ATR at 222 nm
Ay2= Absorptivity of ASP at 242 nm
C_X andC_Y are concentration of ASP and ATR in sample solution.

C) Method-2 (Q-Absorbance OR Absorbance Ratio Method)
The absorbance ratio method of analysis is based on the absorbance at two selected wavelengths; one is an isosbestic point and the other being the wavelength of maximum absorption of one of the two components. From overlain spectra (Fig. 5) wavelength 232 nm (isosbestic point) and 242 nm (λ max of ATR) are selected for Q-Absorbance equation.

$Cx = (Qm-Qy) \times A_1/(Qx-Qy) \times ax_1$
$Cy = (Qm-Qx) \times A_1/(Qy-Qx) \times ay_1$

Where
$Qm = A_2/ A_1$
$Qx = ax_2/ ax_1$
$Qy = ay_2/ ay_1$

Where,
A_1 and A_2 are absorbance of sample solution at 242 nm and 232 nm respectively,
ax_1 = Absorptivity of ASP at 242 nm, ax2= Absorptivity of ASP at 232 nm.
ay_1= Absorptivity of ATR at 242 nm, ay2= Absorptivity of ATR at 232 nm.
C_X and C_Y are concentration of ASP and ATR in sample solution.

Validation:
The method was validated according to ICH Q2B guidelines for validation of analytical procedures in order to determine the linearity, sensitivity, precision and accuracy for the analyte.

Accuracy:
To ascertain the accuracy of the proposed methods, recovery studies were carried at three different levels (80%, 100% and 120%). Percent recovery for ASP and ATR by this method was found as 98.04 and 99.14 respectively.

Linearity:
The linearity of measurement was evaluated by analyzing different concentration of the standard solution of ASP and ATR (Figure 1 & 2). For simultaneous equation method the Beer- Lambert's concentration range was found to be for 5-30 µg/ml for ASP and 5-40 µg/ml for ATR.

Limit of Detection (LOD) and Limit of Quantization (LOQ):
The LOD and LOQ of ASP and ATR by proposed methods were determined using calibration standards. LOD and LOQ were calculated as 3.3σ/S and 10σ/S respectively, where S is the slope of the calibration curve and σ is the standard deviation of response. The results of the same are shown in Table 3.

RESULTS AND DISCUSSION

Under experimental conditions described, calibration curve, precision and recovery studies were performed. The drugs obey beer's law in the concentration range 5-30 µg/ml for ASP and 5-30 µg/ml for ATR for all the methods with good correlation coefficient 0.994 and 0.996 respectively. The results of commercial formulation analysis are presented in Table 1. Results of recovery studies are shown in Table 2. The accuracy and reproducibility is evident from the data as results are close to 100 % and low standard deviation. The proposed methods are simple, economical, rapid, precise and accurate. Hence these can be used for routine analysis of ASP and ATR in capsule formulation.

Table 1: Analysis of Capsule formulation

Drug	Label claim (Mg/ tab.)	Amount found (mg)		%Drug found ±SD		Standard Error	
		Method A	Method B	Method A	Method B	Method A	Method B
ASP	75	74.96	74.29	99.94 ± 0.12	99.05 ± 0.19	0.14	0.16
ATR	10	9.89	9.73	98.90 ± 0.20	97.30± 0.18	0.25	0.29

SD.: Standard deviation., Values expressed mean± SD (n=6)

Table 2: Recovery study of ASP and ATR

Drug	Level of addition (%)	Amount added (µg/ml)	Amount recovered (µg/ml)		%Recovery ± SD	
			Method A	Method B	Method A	Method B
ASP	80	4	3.89	3.86	97.25± 0.055	96.5 ± 0.045
	100	5	4.96	4.95	99.20 ± 0.045	99.00 ± 0.043
	120	6	5.88	5.85	98.83 ± 0.062	97.50 ± 0.059
ATR	80	4	3.97	3.98	99.25 ± 0.081	99.50 ± 0.078
	100	5	4.95	4.92	99.20 ± 0.045	98.40 ± 0.041
	120	6	5.97	5.94	99.50 ± 0.041	99.00 ± 0.039

Values expressed mean±SD (n=3)

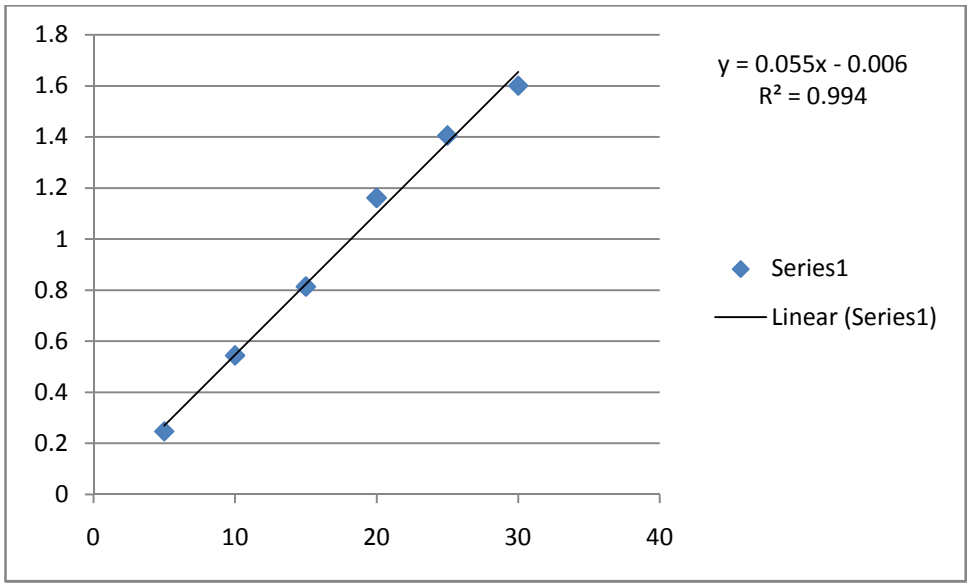


Figure: 1 Linearity curve of Aspirin

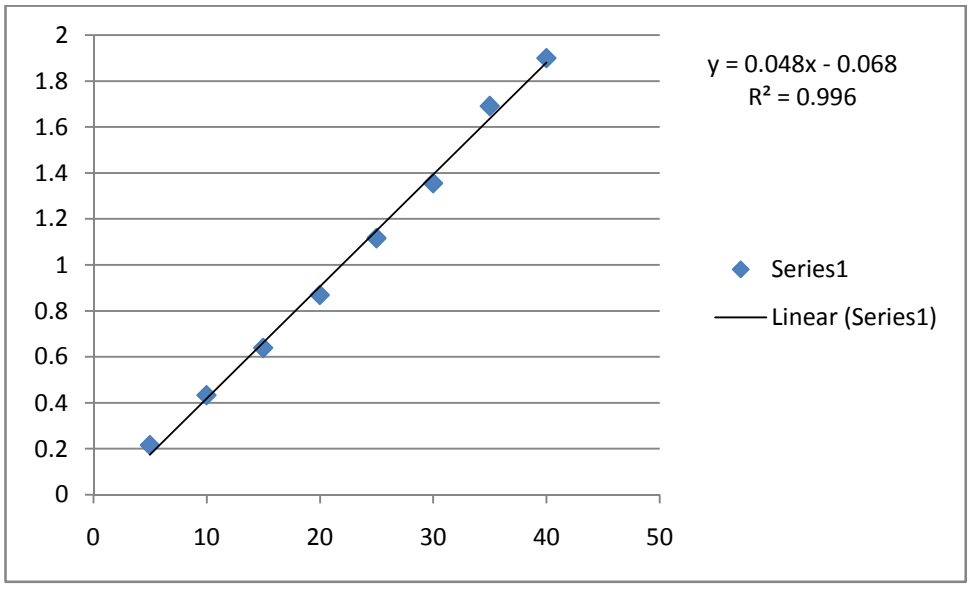


Figure: 2 Linearity curve of Atorvastatin calcium

Table 3: Optical characteristics data and validation parameters

Parameters	Values for ASP	Values for ATR
Absorption maxima (λ max)	222 nm	242 nm
Beer's law limit (µg/ml)	5-30	5-40
Regression equation	y = 0.055x-0.006	y = 0.048x-0.068
Correlation coefficient (R^2)	0.994	0.996
Accuracy (%Recovery ± SD)	98.04±0.051	99.14±0.054
Precision		
Intraday*(Analyst 1)	99.31±0.35	99.75±0.2
Interday*(Analyst 2)	100.86±0.86	98.66±0.81
LOD (µg/ml)	0.2582	0.3669
LOQ (µg/ml)	0.4823	0.5337

**Average of six determinations ±SD*

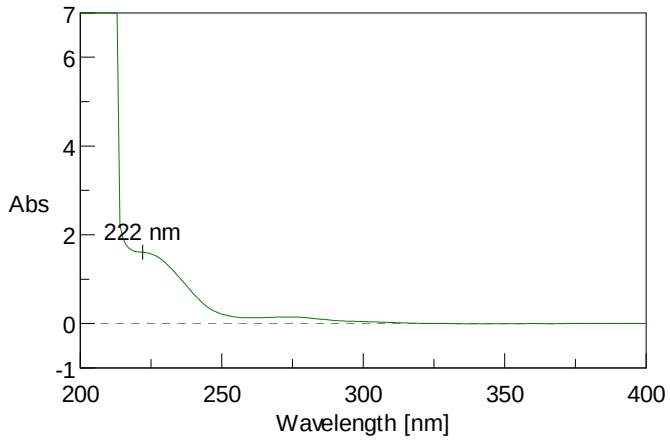


Fig: 3 Graph of Aspirin API

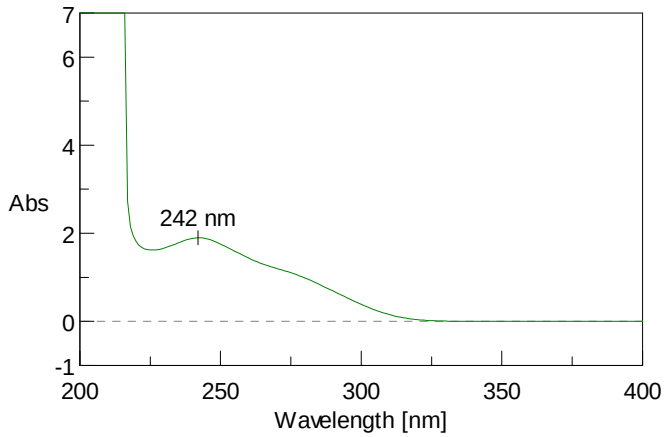


Fig: 4 Graph of Atorvastatin Calcium

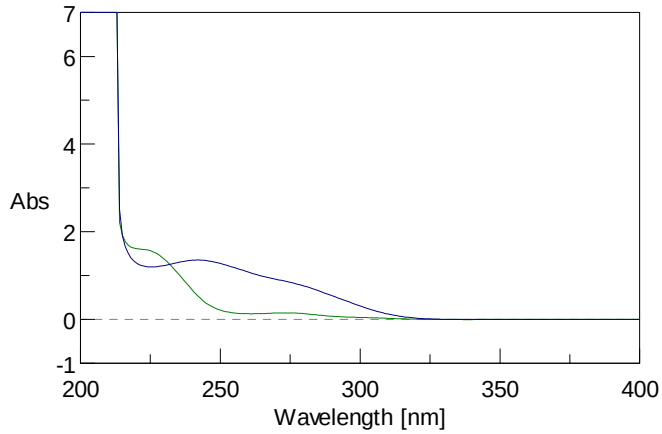


Figure: 5 Graph of Overlain spectra of Atorvastatin calcium (30µg/ml) and Aspirin (30µg/ml)

CONCLUSION

The most striking feature of this method is its simplicity, economy and rapidity, non- requiring consuming sample preparations such as extraction of solvents, heating, degassing which are needed for HPLC procedure. These are new and novel methods and can be employed for routine analysis in quality control analysis. The described methods give accurate and precise results for determination of Aspirin and Atorvastain calcium mixture in marketed formulation.

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