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A NOVEL UV SPECTROPHOTOMETRIC METHOD FOR SIMULTANEOUS ESTIMATION OF METOPROLOL TARTRATE AND ATORVASTATIN CALCIUM BASED ON ABSORBANCE CORRECTION PRINCIPLE

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ABSTRACT

A novel, economical UV spectroscopic method for the simultaneous estimation of metoprolol and atorvastatin has been developed based on the absorbance correction principle. UV Spectrophotometric methods are rapid and economical and the absorbance correction principle is increasingly being employed for analysis as a convenient UV method of analysis. Methanol was used as solvent and water as diluent throughout the analysis. The wavelengths of 244.8 nm (λ_{max} of atorvastatin) and 221.4 nm (λ_{max} of metoprolol) were selected as λ_1 and λ_2 respectively. The method was validated as per ICH guidelines and was found to be accurate, precise, sensitive, and robust. The % assay value for the synthetic mixture was found to be 99.10% for metoprolol and 98.18% for atorvastatin which was within the acceptance value of 90 – 110%. The developed UV spectroscopic method is thus a valuable quality control tool in analysis.

Keywords: Metoprolol Tartrate, Atorvastatin Calcium, Absorbance Correction Principle, Method Validation, ICH Guidelines.

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INTRODUCTION

Two peril factors fundamental to cardiovascular diseases are hyperlipidemia and hypertension. These are the leading cause of death the world over.[1] Fixed dose combinations are in demand today due to convenience, better patient compliance, and fewer side effects.[2] Metoprolol tartrate (MET) (Fig.-1) and atorvastatin calcium (ATS) (Fig.-2) are used for the treatment of hypertension associated with hyperlipidemia. Literature survey reveals that some spectroscopic methods[3-15] and chromatographic methods like GC-MS[16], RP-HPLC[17-21], and RP-UPLC[22] have been reported for the analysis of metoprolol tartrate and atorvastatin calcium either individually or in combination. There has been a renewed interest in UV Spectrophotometric methods due to the methods being economical and rapid. The absorbance correction principle is increasingly being employed for analysis as a convenient UV method of analysis. Hence, the development of a cost-effective, UV method for the simultaneous estimation of the two drugs based on the Absorbance Correction Principle would be beneficial in the analysis of the drugs.

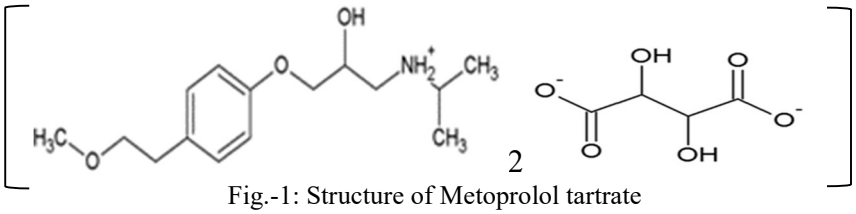

Fig.-1: Structure of Metoprolol tartrate

EXPERIMENTAL

Active pharmaceutical ingredients, metoprolol tartrate, and atorvastatin calcium were obtained as gifts from Shree Anand Life science, Ltd., Belagavi, Karnataka, India, and Zydus Cadila, Kundaim, Goa, India respectively. Methanol AR grade was used as a solvent and distilled water was employed as diluent throughout the analysis.

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Preparation of Working Standard Solution of Drugs
About 25mg of metoprolol tartrate and atorvastatin calcium were weighed accurately into two 25 ml volumetric flasks. The drugs were dissolved using methanol and the volume was adjusted with methanol to get a concentration of 1000µg/mL. Further, 10 mL was diluted with distilled water (100 µg/mL).

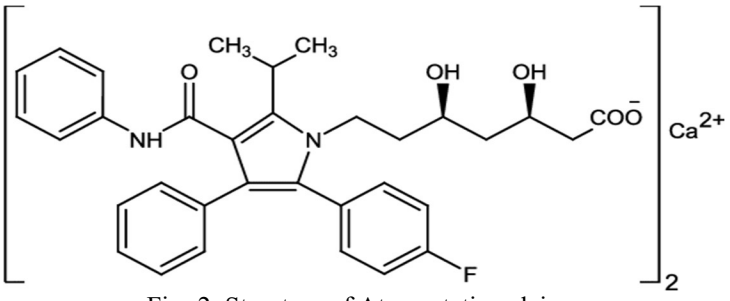

Fig.-2: Structure of Atorvastatin calcium

Preparation of Blank
Distilled water was used to dilute 10 mL of methanol to 100 mL and used as blank.

Preparation of Placebo Blank
About 25 mg of placebo powder was transferred into a 25mL volumetric flask and mixed with 15 mL of methanol. The solution was subjected to sonication for 10 minutes. The volume was adjusted with methanol and from the filtrate 1 mL was diluted to 10ml with distilled water.

Preparation of Synthetic Mixture
About 150 mg of placebo powder, 100 mg of atorvastatin calcium and 250 mg of metoprolol tartrate were intimately mixed using a glass mortar and pestle**.**

Selection of Analytical Wavelength
Scanning of the working standard solutions of MET and ATS was performed in the Ultraviolet region against the reference solution. Analytical wavelengths were obtained from the overlain spectra as follows: λ_1 being the wavelength at which only one drug absorbs and λ_2 being the wavelength at which both the drugs absorb.

Determination of Absorptivity
Absorptivity values for the drugs were calculated from the calibration curves recorded at predetermined wavelengths.

Method Validation
Validation of the developed analytical method was performed following the ICH guidelines.[23]

Assay of Synthetic Mixture
A synthetic mixture equivalent to 25 mg of metoprolol tartrate was weight into a volumetric flask of 25 ml capacity. Methanol (15 mL) was added and the solution was subjected to sonication for 10 minutes. Methanol was added to adjust to volume, mixed, and filtered. 10 ml of filtrate was diluted to 100 mL with distilled water. Further 2 mL of solution was diluted to 10 mL using distilled water. The absorbance of the resultant solution was recorded at predetermined wavelengths. The percent purity of drugs in a synthetic mixture was calculated by the absorbance correction method.

The Concentration of Each Drug Was Determined By Following Equation
$A_1 = a_{x1}C_x$,
$A_2 = a_{x2}C_x b + a_{y2}C_y$,
Where, C_x is the concentration of ATS in g/1000 mL and C_y is the concentration of MET in g/1000 mL.
A_1 signifies the absorbance of the sample solution at λ_1 and A_2 signifies the absorbance of the sample solution at λ_2. a_{x1} is the absorptivity of ATS at λ_1, a_{x2} is the absorptivity of ATS at λ_2 and a_{y2} is the absorptivity of MET at λ_2.

RESULTS AND DISCUSSION

Diluent was chosen based on the solubility of the drugs. As both MET and ATS were soluble in methanol, methanol was used to prepare standard stock solutions while further dilutions were done in distilled water. The choice of analytical wavelengths was by scanning working standard solutions of MET and ATS in UV range against blank. The spectra showed λ_{max} at 221.4 nm for MET and 244.8 nm for ATS. The spectra were overlain (Fig.-5), and analytical wavelengths were chosen as follows: λ_{max} of ATS, 244.8 nm was chosen as λ_1 (as MET showed nil absorbance at this wavelength) and 221.4 nm (λ_{max} of MET) as λ_2 as both the drugs showed satisfactory absorbance at this wavelength. Absorptivity values for both drugs were calculated by recording the absorbance of working standard solutions at predetermined wavelengths. The mean absorptivity for ATS was found to be 30.989 L/g/cm at 244.8 nm and 19.809 L/g/cm at 221.4 nm respectively, whereas for MET it was 23.949 L/g/cm at 221.4 nm.

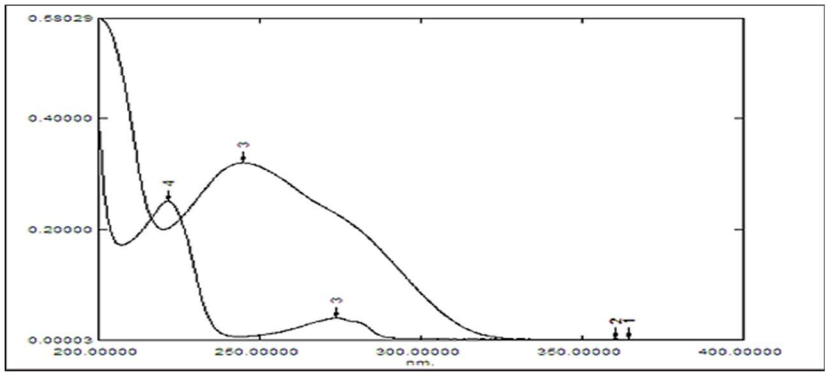

Fig.-3: Overlain Spectra of Metoprolol Tartrate and Atorvastatin Calcium

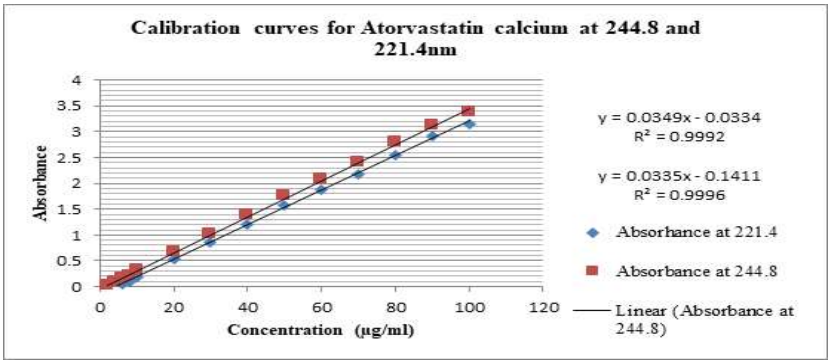

Fig.-4: Calibration Curves for Atorvastatin Calcium at 244.8 nm and 221.4 nm

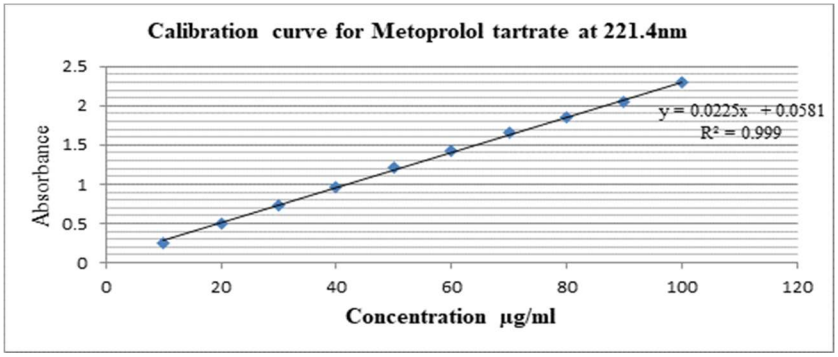

Fig.-5: Calibration Curve for Metoprolol Tartrate at 221.4 nm

Linearity

The solutions for linearity were prepared as per methodology and absorbance was measured at predetermined wavelengths. The calibration curves for the drugs are displayed in Fig.-4 and 5, and linearity data is shown in Table-1. The linear range established was 2 – 100 µg/mL for ATS and 10 – 100 µg/mL for MET respectively.

Table-1: Linearity Study Data

Parameters	Atorvastatin calcium		Metoprolol tartrate
	At 244.8 nm	At 221.4 nm	At 221.4 nm
Linearity and range	2 – 100 µg/mL	2 – 100 µg/mL	10– 100 µg/mL
Regression equation	Y = 0.0349x - 0.0334	Y = 0.0335x - 0.1411	Y = 0.0225x + 0.0581
Slope	0.0349	0.0335	0.0225
Intercept	0.0334	0.1411	0.0581
Correlation coefficient	0.9992	0.9996	0.9990
Mean absorptivity	30.9890 L/g/cm	19.8095 L/g/cm	23.9490 L/g/cm

Precision

Solutions were prepared as per methodology and absorbance was recorded at predetermined wavelengths. The results of precision studies are displayed in Table-2. The % RSD of precision study for MET and ATS was found to be within the acceptable limits of less than 2 %.

Table-2: Precision Study Data

Drug	Mean % assay ± SD	% RSD
Repeatability (n=6)		
ATS	99.58 % ± 1.2206	1.2257
MET	98.78 % ± 1.0492	1.0622
Intra Day Precision (n=3)		
ATS	99.93 % ± 0.2013	0.20150
MET	99.48 % ± 0.6087	0.61186
Inter Day Precision (n=3)		
ATS	99.98 % ± 1.11380	1.11390
MET	100.27 % ± 1.04115	1.03836

Accuracy

The results of the accuracy study are shown in Table-3. The % recovery at 80%, 100%, and 120% for MET and ATS was found to be within the acceptable criteria of 95 % - 105 % establishing the accuracy of the developed method.

Table-3: Accuracy Study Data

Level of addition (%)	% Recovery		Mean % Recovery	
	ATS	MET	ATS	MET
80 %	102.40 103.00 103.46	102.56 99.55 103.50	102.95	101.87
100 %	100.15 99.49 102.39	100.26 101.09 99.28	100.68	100.21
120%	100.49 101.10 101.40	100.03 100.53 99.00	100.99	99.85

Limit of Detection and Quantitation

The data for LOD and LOQ measurements as shown in Table-4 proved that the developed method was sensitive.

Table-4: Results for LOD and LOQ Study

LOD (µg/mL) LOQ (µg/mL)	0.04256 0.12900	0.0814 0.2470	1.825 5.531

Robustness

The data for robustness studies for change of instrument, analyst, and sonication time is displayed in Table-5. As seen deliberate changes introduced did not adversely affect the results of the analysis. Hence, the developed UV method for ATS and MET by absorbance correction method was found to be robust.

Table-5: Results for Robustness Study

Parameters	Mean Absorbance (n=3)		Mean % assay (n=3)	
	At 244.8 nm	At 221.4 nm	ATS	MET
Change of UV instrument				
Instrument 1	0.25000	0.64900	100.72	102.11
Instrument 2	0.24959	0.63956	100.68	100.21
Change of analyst				
Analyst 1	0.25000	0.64900	100.72	102.11
Analyst 2	0.25384	0.63781	102.39	99.28
Change of sonication time				
10 minutes	0.25000	0.64900	100.72	102.11
12 minutes	0.24632	0.63104	99.36	98.87
15 minutes	0.24767	0.63821	99.90	100.18

Assay of the Synthetic Mixture

The % assay values obtained are displayed in Table-6. As seen the % assay value for the synthetic mixture was 98.18% for ATS and 99.10% for MET which was within the acceptance criteria (90 – 110%).

TABLE-6: Assay of Synthetic Mixture

Drugs	Amt. present (mg)	Mean amt. found (mg) (n=3)	Mean % assay (n=3)
ATS	10	9.82	98.18
MET	25	24.78	99.10

CONCLUSION

A novel, simple and economical UV spectroscopic method for the simultaneous analysis of metoprolol and atorvastatin has been developed and validated. In the developed UV spectroscopic method, methanol was employed as the solvent, and water was used as a diluent. ICH guidelines were followed for validation of the method. The Linear range was obtained in the concentration of 10 – 100 µg/mL for MET and 2 – 100 µg/mL for ATS respectively. The % assay value for the synthetic mixture was found to be 99.10% for metoprolol tartrate and 98.18% for atorvastatin calcium which met the acceptance criteria. The developed method can thus be a valuable quality control tool for the simultaneous analysis of the drugs.

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