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UV spectrophotometric method development and validation for the determination of metoprolol succinate in bulk and its pharmaceutical dosage form

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Abstract

A simple, economical determination of metoprolol succinate based on the UV spectrophotometric with methanol reagent. The maximum absorbance intensity of metoprolol succinate was found to be 275 nm. The achieved linearity over the concentration range with a good correlation coefficient (R^2), as well as the limit of detection (LOD) and limit of quantification (LOQ), which were obtained as 0.098 µg/ml and 0.297 µg/ml, respectively. As per International Conference on Harmonization (ICH) guidelines, all parameters have been calculated. The spectrophotometric method determination is successfully applicable to pharmaceutical dosage formulations. In the laboratories quality control test can be done. Since it is economical, perceptive and clear.

1. Introduction

It is possible to treat hypertension and lower blood pressure with beta-adrenergic blockers, such as the extended-release tablets of metoprolol succinate. Bringing down blood pressure reduces the risk of both fatal and non-fatal cardiovascular events, particularly strokes and myocardial infarctions. Its chemical name is 1-(isopropyl amino)-3-[p-(2-methoxyethyl) phenoxy] succinate of -2-propanol (Moreshwar and Rajeshwar, 2009). Metoprolol works by lessening the agonist effect that catecholamines have on the heart (Pagar *et al.* 2013). As a result of the medication's high sensitivity, even a tiny dose can effectively block beta-adrenergic receptors. The medication also has benefits that are cardioprotective, insulin resistance-improving, cerebroprotective, and anti-atherosclerotic, as well as reno protective properties (such as lowering proteinuria *via* dilatation efferent arterioles). Azelnidipine has two enantiomers because the 1, 4-dihydropyridine ring has an asymmetric carbon at position four. Azelnidipine has two enantiomers because the 1, 4-dihydropyridine ring has an asymmetric carbon at position four (Dhruvin *et al*., 2022).

A survey of literature revealed that two UV spectrophotometric methods (Moreshwar and Rajeshwar, 2009; Pagar *et al.,* 2013) were reported for the estimation of metoprolol in its pharmaceutical dosage form. There were few UV spectrophotometric (Ekta Patel *et al.* 2016; Tushar *et al.,* 2014), RP-HPLC (Mihir *et al.,* 2012; Patel *et al.,* 2019) and HPTLC (Mital *et al.,* 2012) methods have been developed for simultaneous estimation of metoprolol succinate with other drug combination. For the purpose of determining the presence of metoprolol succinate in bulk samples; a accurate, affordable, and sensitive spectrophotometric approach has been devised and is described in the current paper.

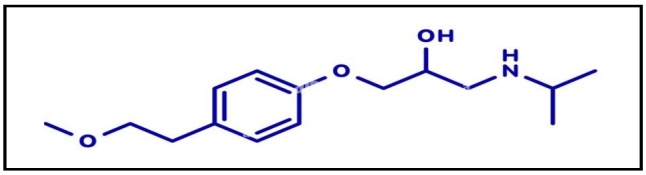

Figure 1: The structure of metoprolol succinate.

2. Materials and Methods

2.1 Instruments

The study was performed using a Shimadzu UV-visible spectropho tometer (UV-1800 series), which features a double beam and double detector arrangement with a 1 cm matched cell. The mobile phase was degassed using an ultrasonicate cleaner. Electronic balance (Sansui Vibra DJ -150S-S) was used for the weighing.

2.2 Materials

Indian company Yarrow Chemicals Private Limited supplied the metoprolol succinate standard medication. All of the chemical and reagent materials of analytical grade were purchased. Calibrated glassware was used all throughout the analysis.

2.3 Selection of suitable solvent

Based on solubility property, methanol is selected for proper dissolving of metoprolol succinate.

2.4 Standard stock solution preparation

20 mg of metoprolol succinate that had been precisely measured was transferred to a 10 ml volumetric flask and then dissolved in methanol. To get the necessary final concentration of 2000 µg/ml, the final volume was then modified using the same amount of methanol.

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2.5 Working standard solution preparation

To achieve the desired concentration of 100 µg/ml, the standard stock solution was diluted accordingly.

2.6 Determination of λmax for analysis

The UV spectrum's wavelength was chosen for the study of metoprolol succinate. Metoprolol succinate was synthesized at a concentration of 100 µg/ml, and its UV spectra was scanned between 200 to 400 nm to identify the wavelength maximum. The absorbance maximum against methanol was discovered to be 275 nm.

3. Results

3.1 Validation Parameters

3.1.1 Linearity

The absorbance of each concentration was measured at 275 nm using this approach using methanol as a blank. New aliquots were made from standard stock-2 solution ranging from 50-250 µg/ml.The value of the regression coefficient (R^2) from linearity curve was found to be 0.999.Table 1 displays the outcomes of linearity.

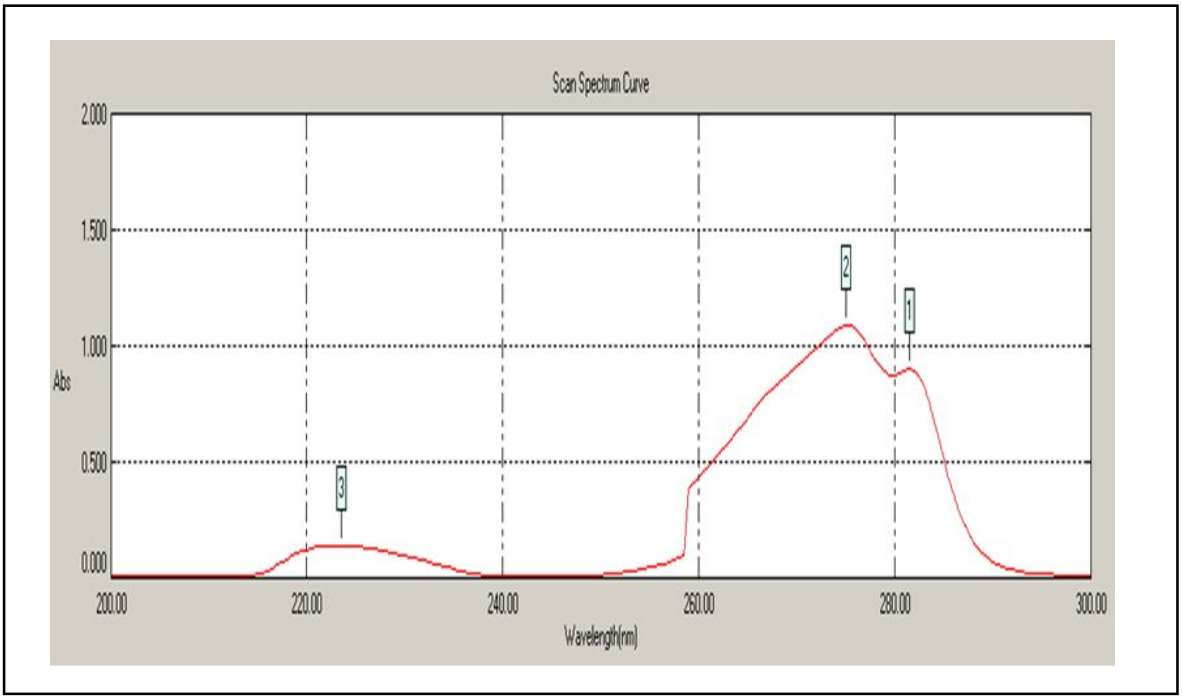

Figure 2: UV spectra of metoprolol succinate.

Table 1: Linearity results

Concentration (µg/ml)	Absorbance
50	0.233
100	0.442
150	0.653
200	0.871
250	1.083

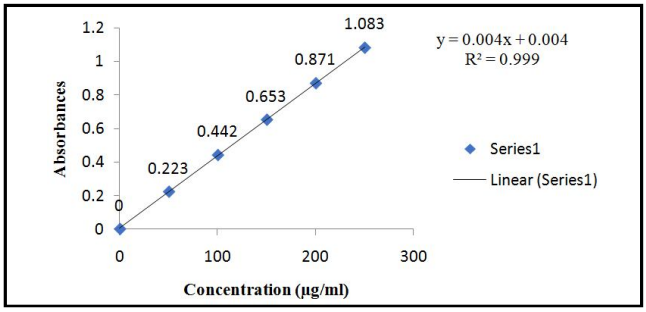

Figure 3: Linearity curve for metoprolol succinate.

3.1.2 Accuracy

By conducting recovery trials in triplicate at different concentration ranges such as 50 %, 100%, 150% and new method's accuracy was proven. Since the statistical results fell within the acceptable range, it was evident from the recovery experiments that the method is quite accurate for quantitative estimation of tablet. The results are displayed in Table 2.

Table 2: Results for accuracy

% level of accuracy	Amount added (µg/ml)	Amount found (µg/ml)	% recovery	% mean recovery
50%	50	0.438	98.21	98.88
50%	50	0.440	98.65	
50%	50	0.445	99.78	
100%	100	0.448	101.35	100.3
100%	100	0.436	98.64	
100%	100	0.446	100.90	
150%	150	0.435	99.92	100.68
150%	150	0.438	100.61	
150%	150	0.442	101.53	

3.1.3 Precision

Within the same day, twice, the drug's duplicate concentration was calculated for intraday study. In an inter-day research, the drug's concentration was determined over the course of two consecutive days, expressing the laboratory's variability over the course of several days. Results are displayed below Tables 3 and 4 are representing inter-day precision and the intra-day precision, respectively.

Table 3: Results for inter-day precision

Concentration (µg/ml)	Day- 1	Day -2	Day -3
100	0.435	0.418	0.421
100	0.443	0.438	0.424
100	0.439	0.456	0.416
100	0.424	0.444	0.426
100	0.432	0.431	0.435
100	0.433	0.445	0.434
Average	**0.434**	**0.439**	**0. 426**
SD	**0.006501**	**0.0016033**	**0.007403**
% RSD	**1.498**	**0.365**	**1.738**

Table 4: Results for intra-day precision

Concentration(µg/ml)	Morning	Evening
100	0.435	0.436
100	0.443	0.433
100	0.439	0.427
100	0.424	0.438
100	0.432	0.442
100	0.433	0.429
Average	**0.434**	**0.434**
SD	**0.006501**	**0.005636**
% RSD	**1.497**	**1.298**

Table 5: Results for ruggedness

Analyst -1		Analyst-2	
Concentration (µg/ml)	Absorbance	Concentration (µg/ml)	Absorbance
100	0.433	100	0.439
100	0.435	100	0.436
100	0.432	100	0.427
100	0.427	100	0.435
100	0.424	100	0.432
100	0.436	100	0.433
Average	**0.431**	**Average**	**0.434**
SD	**0.004708**	**SD**	**0.004082**
% RSD	**1.091**	**% RSD**	**0.941**

3.1.4 Ruggedness

Two distinct analysts performed the analysis, and the absorbance of each was recorded in order to findoiut the % RSD. Results are provided in Table 5.

3.1.5 Robustness

Three separate wavelengths of analysis were used to determine the method's robustness. The relative absorbance was noted, and the findings were shown in Table 6.

Table 6: Results for robustness

Concentration (µg/ml)	Wavelength (nm)		
	274	275	276
100	0.409	0.419	0.416
100	0.411	0.421	0.417
100	0.416	0.426	0.422
100	0.419	0.429	0.425
100	0.422	0.432	0.428
100	0.426	0.437	0.433
Average	**0.417**	**0.427**	**0.423**
SD	**0.0006494**	**0.006772**	**0.006535**
% RSD	**0.156%**	**1.58%**	**1.543%**

3.1.6 Limit of detection and limit of quantification

By using a calibration curve, the suggested method's limit of quantitation and limit of detection for metoprolol were established.

$$\text{LOD} = 3.3 \times \text{Standard deviation of intercept/slope}$$

$$\text{LOD} = \frac{3.3 \times 0.00433}{0.145733}$$

$$= 0.098\ \mu g/ml$$

$$\text{LOQ} = 10 \times \text{standard deviation of intercept/slope}$$

$$\text{LOQ} = \frac{10 \times 0.00433}{0.145733}$$

$$= 0.297\ \mu g/ml$$

Table 7: Results for sensitivity

API	Limit of detection	Limit of quantification
Metoprolol succinate	0.098 µg/ml	0.297 µg/ml

3.1.7 Assay

The average weights of 10 tablets were determined after careful weighing. The tablets were crushed into a fine powder, which was then precisely weighed at about 20 mg of equivalent powder and transferred into a 50 ml volumetric flask, which had been diluted with methanol to the mark of 50 ml. Then, 2.5 ml of the above solution was pipette-out into the 10 ml volumetric flask and diluted up to the with methanol (100 µg/ml). Then, the resultant solution was scanned at 275 nm. Table 8 is representing assay results.

$$\% \text{ Assay} = \frac{\text{Test absorbance}}{\text{Standard absorbance}} \times 100$$

$$= \frac{0.436}{0.442} \times 100 = 98.64\ \%$$

$$\text{Amount found/tablet} = \frac{98.64 \times 25}{100}$$

$$= 24.66 \text{ mg/tablet}$$

Table 8: Assay results

Formulation	Brand name	Label claim	Amount found	% assay
Metoprolol succinate	Prolomet XL	25 mg/tablet	24.66 mg/tablet	98.64 %

4. Discussion

To develop the UV-spectrophotometric method for metoprolol succinate, it was scanned in the UV region between 200-400 nm against methanol as solvent and wavelength maximum was observed at 275 nm. This method is validated as per guidelines of ICH. The different parameters used for the analysis and determination of metoprolol succinate such linearity, accuracy, precision, robustness, ruggedness, LOD and LOQ. 20 mg of drug was accurately weighed and transferred in 10 ml of volumetric flask which was made up with the help of methanol as a solvent to get 2000 µg/ml concentration (stock-1). From the above stock-1 solution, 5 ml of solution was taken and transferred into 10 ml of volumetric flask which was diluted with methanol to get 1000 µg/ml. From the above solution, different concentrations in the range of 50-250 µg/ml were prepared for linearity studies and the R^2 value from linearity curve was found to be 0.999. The accuracy parameter was assessed at 50%, 100%, and 150%, and it was discovered that the mean % recovery fell within the range indicating that the method had been developed accurately. The developed method was precise since the % RSD for both the intra-day and the inter-day precision levels of the parameter were found to be < 2. The parameter LOD and LOQ were computed using linearity curve, and the results were determined to be 0.098 µg/ml and 0.297 µg/ml, respectively, so the suggested method was sensitive.

5. Conclusion

According to ICH recommendations, a simple UV-spectrophotometric method for metoprolol succinate has been developed and validated. The findings of our investigation showed that, in comparison to the previously reported methods, the proposed UV-spectrophotometric method was extremely accurate, affordable, and sensitive. The determination of metoprolol succinate in bulk was found to be feasible using the proposed UV-spectrophotometric approach.

Conflict of interest

The authors declare no conflicts of interest relevant to this article.

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