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Quantitative determination of metoptolol succuinate using area under curve UV- spctrophotometric method in bulk and tablet dosage form

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ABSTRACT

A simple, precise and economical UV - spectrophotometric method has been developed for the estimation of Metoptolol succuinate in pharmaceutical dosage form. Method applied was area under curve (AUC) in which area was integrated in the wavelength range of 264.0 nm – 283.80 nm. Calibration curves were plotted for the method by using instrumental response at selected wavelengths and concentrations of analyte in the solution. Linearity for the detector response was observed in the concentration range of 40-200 µg/ml for the method. Tablet formulation was analyzed and the percentage of drug determined in the assays was 98.25% – 101.31%. Accuracy and precision studies were carried out and results were satisfactory. The results of the analysis were validated statistically. Limit of detection and limit of quantitation were determined as 3.5 and 12.5 µg/ml. The method was validated by following the analytical performance parameters suggested by the International Conference on Harmonization. All validation parameters were within the acceptable range. The developed method was successfully applied to estimate the amount of Metoptolol succuinate in pharmaceutical formulation.

KEYWORDS

Metoptolol succuinate;
UV-spectrophotometry;
Area under curve;
Validation.

INTRODUCTION

Metoptolol succuinate (AB), chemically, 1-(isopropylamino)-3-[p-(2- methoxyethyl) phenoxy]-2-propanol succinate, is an anti-hypertensive and an Adr-energic agent[1]. A detailed literature survey for Metoptolol succuinate revealed that several analytical methods such as Spectrophotometric methods were reported for the quantification of Metoptolol succuinate. There are few RP-HPLC methods were reported for the determination of Metoptolol succuinate in pharmaceutical dosage form[2-8].

The method was validated according to ICH guidelines[9]. Thus the objective of present study was to develop an applicable method for the routine analysis of Metoptolol succuinate in tablet formulations.

EXPERIMENTAL WORK

Material and method

Metoptolol succuinate working standard was obtained as gift sample from Astra Zeneca. The drug was

used without further purification. A tablet formulation containing 25 mg of Metoptolol succuinate was purchased from local market. Analytical grade solution was used for the experiment.

Instruments used

A double beam UV-VIS spectrophotometer (UV-2450, Shimadzu, Japan) connected to computer loaded with spectra manager software UV Probe 2.21 with 10 mm quartz cells was used. The spectra were obtained with the instrumental parameters as follows: wavelength range: 200-400 nm; scan speed: medium; sampling interval: 1.0 nm; band width ($\Delta\lambda$):10.0 nm; spectral slit width: 1 nm. All weights were taken on electronic balance (Model Shimadzu AUX 120).

Preparation of standard stock and working standard solution

Stock standard solution of MS was prepared by dissolving 20 mg of MS into 100 mL of water to obtain concentration 200 µg/mL. From the stock standard solution, 2 mL of MS was transferred in to 10 mL volumetric flask and the volume was adjusted to the mark with same solvent to obtain Strength 40 µg/mL. The solution was scanned in the UV- region i.e. 200 – 500 nm. Zero order spectrum, obtained using UV probe software of the instrument. The two wavelengths 264 nm and 283 nm were selected for the determination of Area Under Curve (AUC)

Method: area under curve

The AUC (area under curve) method is applicable where there is no sharp peak or when broad spectra are obtained. It involves the calculation of integrated value of area with respect to the wavelength between the two selected wavelengths 264.0 and 283.80. Area calculation 6processing item calculates the area bound by the curve and the horizontal axis. The horizontal axis is selected by entering the wavelength range over which area has to be calculated. This wavelength range is selected on the basis of repeated observations so as to get the linearity between area under curve and concentration. The spectrum obtained of zero order derivative was used to calculate AUC. The calibration curve was constructed by plotting concentration (40-200 µg/mL) versus AUC.

Preparation of sample solution

For analysis of tablets formulation (Met XL), ten tablets was weighed, average weight determined and crushed into fine powdered. An accurately weighed quantity of powder equivalent to 20 mg of MS was transferred into 100 mL volumetric flask containing 30 mL water, shaken manually and sonicated for 10 min, volume was adjusted to mark with same solvent and filtered through Whatmann filter paper no. 41. An appropriate aliquot was transferred to 10 mL volumetric flask, volume was adjusted to the mark and AUC was recorded for each concentration. The analysis was repeated for six times

Validation of method

The proposed method was validated as per ICH-Guidelines Q2 (R1)[9].

Linearity

An appropriate volume of MS in the range of 2 – 10 mL was transferred into series of six separate 10 mL volumetric flasks and volume was made up to mark with water to obtain concentration of 40 – 200 µg/mL. These solutions were scanned in UV-region 200 - 400 nm and zero order spectrum obtained. AUC measured was measured between the chosen wavelengths and a calibration curve was constructed AUC *versus* concentration.

Precision

Precision of the method is studied as repeatability, intra-day and inter-day precision. Repeatability was determined by analyzing MS (80 µg/mL) for six times. Intra-day precision was determined by analyzing the 80, 120, 160 µg/mL of MS for three times in the same day. Inter-day precision was determined by analyzing the same concentration of the solutions daily for three days.

Accuracy

To assess the accuracy of the proposed method, recovery studies were carried out three different levels i.e. 80 %, 100 % and 120 %. To the pre- analyzed sample solution a known amount standard drug solution was added at three different levels, area under curve was recorded at selected wavelengths. The % recovery was then calculated by using formula.

Specificity

Results of tablet solution showed that there is no

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interference of excipients when compared with the working standard solution. Thus, the method was said to be specific.

Ruggedness

Ruggedness of the proposed method is determined by analysis of aliquots from homogenous slot by two analyst using same operational and environmental conditions

RESULTS AND DISCUSSION

The molecular structure of the Metoptolol succuinateis presented in Figure 1. Methanol was selected as the solvent for Metoptolol succuinate because provides good solubility and other characteristics for AUC measurements. The absorption spectrum of Metoptolol succuinate in methanol is indicated in Figure 2. Optical characteristics of Metoptolol succuinate were calculated by the proposed method and are presented in TABLE 1. The percentage content of drug in

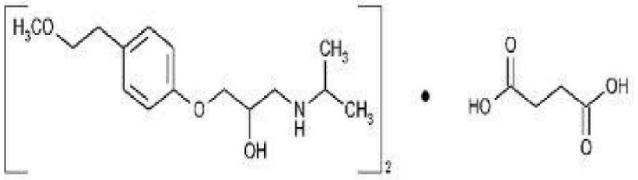

Figure 1 : Chemical structure of Metoprolol succinate

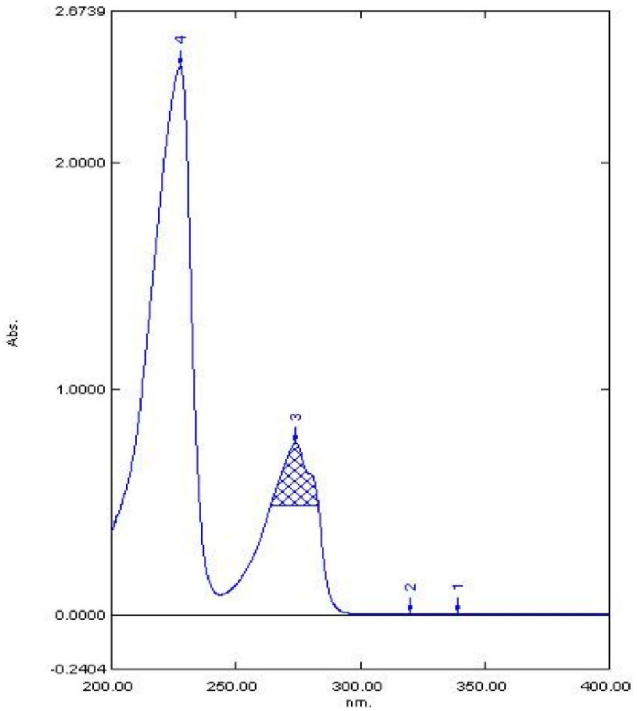

Figure 2 : Area under curve spectrum of Metoptolol succuinate in methanol

TABLE 1 : Optical characteristics of Metoprolol succinate

Parameters	Metoprolol succinate
Beer-Lambert's range(µg/mL)	40-200 ug/ml
λ max(nm)/ wave length range (nm)	239
Slope	0.020
Intercept	0.071
Correlation coefficient	0.999
Limit of detection (µg/mL)	3.5
Limit of quantitation (µg/mL)	12.8

the given tablet was found to be 98.25-101.31% (TABLE 2). The intra-day and inter-day precision values (%RSD) were calculated for Metoptolol succuinate (Results shown in TABLE 3) and the values obtained (≤2%) comply with the stated limits of the guidelines. The accuracy of Metoptolol succuinate was evaluated by the percent recovery studies at concentration levels

TABLE 2 : Assay results of commercial Metoptolol succuinate tablet.

Drug	Label Claim (mg)	Amount found (µg/mL)	%Amount found
MS	80	81.05	101.31
	80	78.60	98.25
	80	79.15	98.93
	80	80.35	100.43
	80	79.90	99.87
	80	80.55	100.68
	Mean ± SD	79.93 ± 0.91	99.91 ± 1.14
	% RSD	1.14	1.14

***Average of three determinations**

TABLE 3 : Precision

Drug	Concentration [µg/mL]	Intra-day [n = 3]	% RSD	Inter-day [n = 3]	% RSD
MS	80	100.36	1.87	100.36	1.37
	120	100.73	1.02	99.64	1.28
	160	100.72	1.28	100.11	1.17

TABLE 4 : Accuracy

Drug	Initial Amount [µg/mL]	Amount Added [µg/mL]	Amount recovered [µg/mL, n = 3]	% Recovered	% RSD
MS	80	64	143.11	99.38	0.97
	80	80	159.24	99.52	1.30
	80	96	175.43	99.67	1.21

of 80, 100, and 120% and the values obtained were found to be in the acceptable limits (≤2%) (Results pre-

sented in TABLE 4). This indicates that there was no interference from the excipients present in the dosage form. Ruggedness of proposed method was determined with the help of two different analysts, and results were evaluated by calculating the %RSD value and lying within the range (Results shown in TABLE 5).

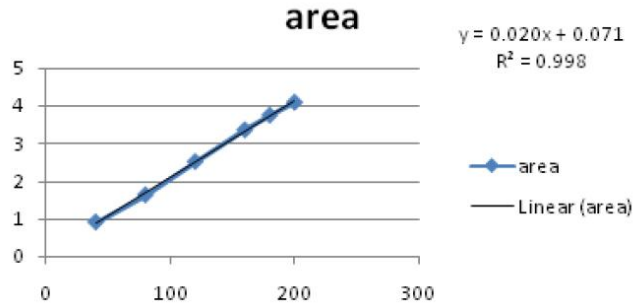

Figure 3 : Calibration curve of Metoptolol succuinate at 224nm

TABLE 5 : Ruggednes

	Analyst –I		Analyst –II	
Drug MS	% Amount found ± SD [n = 3]	% RSD	% Amount found ± SD [n = 3]	% RSD
	99.76 ± 1.09	1.09	100.03 ± 0.989	0.988

n= no. of estimations

CONCLUSION

The UV spectrophotometric AUC method developed for determination of Metoptolol succuinate was based on different analytical techniques, UV-Spectrophotometric, AUC method. The method was validated and found to be simple, sensitive, accurate, and precise in compliance to the limits stated in the ICH guidelines. Hence, we conclude that the method can be used successfully for routine analysis of pharmaceutical dosage forms containing Amlodipine besylate. The proposed spectrophotometric method will not replace the presently known methods available for the analysis of Amlodipine besylate. However, it can serve as an alternative where advanced instruments (e.g. HPLC) are not available for routine analysis.

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