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Der Pharmacia Lettre, 2012, 4 (3):763-767
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ISSN 0975-5071
USA CODEN: DPLEB4

Quantitative Determination of Metoprolol Succinate in bulk and tablet Dosage form through comparative study of UV and derivative Spectroscopy

Jadhav A. S*., Tarkase K. N. and Deshpande A.P.

Department of Quality Assurance, P.D.V.V.P.F's College of Pharmacy, Vilad Ghat, M.I.D.C., Ahmednagar (M.S.)

ABSTRACT

Metoprolol succinate is a selective β_1 receptor blocker drug used in hypertension and other cardiac diseases. Various methods for analysis of the same are available but are time consuming and expensive. Here we have developed a new, precise and simple UV spectrophotometric methods for estimation of Metoprolol Succinate from bulk and tablet formulation in phosphate buffer 6.8. The drug obeyed the Beer's law with correlation coefficient 0.9999 and 0.9979 respectively for Method I and Method II. It showed absorption maxima at 223 nm and 226 nm respectively for method I and Method II; in phosphate buffer 6.8. The linearity was observed between 5 – 25 µg/mL. The results of analysis were validated by recovery studies, accuracy, precision, LOD, LOQ and ruggedness. The method was found to be simple, accurate, precise, economical and robust.

Key words: Metropolol Succinate, Phosphate buffer 6.8, Zero order spectra and second order spectra.

INTRODUCTION

Metoprolol is chemically (*RS*)-1-(Isopropylamino)-3-[4-(2-methoxyethyl)phenoxy]propan-2-ol. It is a white crystalline powder with formula $C_{15}H_{25}NO_3$ and molecular mass 267.364 g/mol. It is used as a selective β_1 receptor blocker used as an antihypertensive i.e., used at high BP Conditions and also can be used in treatment of congestive heart failure (CHF) Post myocardial infarction.

Analysis is an important component in the formulation and development of any drug molecule. A suitable and validated method has to be available for the analysis of drugs in bulk, in drug delivery systems, release dissolution studies and in biological samples. If a suitable method for specific need is not available then it becomes essential to develop simple sensitive, accurate, precise reproducible method for the estimation of drug samples. Methods such as HPLC, Capillary Electrophorsis and simultaneous UV-spectroscopic methods of Metoprolol succinate are reported for estimation of Metoprolol Succinate alone or in combination with other drugs.

MATERIALS AND METHODS

Instrumentation, Reagents &Chemicals:
Instruments used were UV-Visible spectrometer**,** model *JASCO* 1505 Instrument and Shimadzu ELB 300 analytical balance, Metoprolol succinate pure drug (99.99%) was obtained as a gift sample from Zydus Cadila Ahmadabad. All chemicals and reagents used were of analytical grade.

Selection of media:
Main criteria for selection of media solubility and stability i.e., drug should be soluble as well as stable for sufficient time in selected media. Metoprolol Succinate is soluble in distilled water and was soluble in di-chloromethane,

methanol, chloroform and ethanol-water mixture. It was freely soluble in phosphate buffer 6.8 and was considerably stable.

Preparation of standard stock solution:
Standard drug solution of Metoprolol Succinate was prepared by dissolving 10mg pure Metoprolol Succinate in phosphate buffer 6.8 and transferred into 100ml volumetric flask to obtain 10µg/ml of stock solution from which desired concentrations 5, 10, 15, 20, 25, 30 µg/ml of solutions were prepared.

Preparation of sample solution
Twenty tablets were weighed; average weight was determined and finely powdered. An accurately weighed quantity of tablet powder equivalent to 10mg of Metoprolol Succinate was transferred to 100 mL volumetric flask and dissolved by sonication with sufficient quantity of phosphate buffer 6.8, volume was made upto mark. The solution was then filtered through whatman filter paper no.41. A 1 mL portion of the filtrate was further diluted with phosphate buffer 6.8 in a 10 ml volumetric flask upto mark (10µg/mL) on label claim basis. The absorbance of the resulting solution was measured at 223 nm (method I) and 226 nm (method II) against solvent blank. The results of estimation by proposed methods are shown in Table**.**

Determination of λmax:
A 10 µg/ml solution of Metoprolol Succinate was prepared and scanned in UV range of 200-400nm and spectrum was obtained. The λmax was found to be at 223 nm wave length where absorbance was maximum at this wavelength for Method I, and the λ_{max} for Method II was found to be 226 nm. Hence these are considered as absorbance maxima(λmax**)** shown in fig 1,3.

Preparation of calibration curve:
Standard stock solution was suitably diluted with phosphate buffer 6.8 to obtain concentrations ranging from 5-25 µg/ml. Absorbance of these solutions was measured at 223nm for Method I and at 226 nm for Method II using UV. The calibration curve was plotted as concentration versus absorbance over the range of 5-25 µg/mL with correlation coefficient of 0.9995 and 0.9979 for the proposed method I and method II.

Validation
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, absorbance was recorded. The % recovery was then calculated as
% Recovery = [(A – B) / C] x 100,
Where A is total amount of drug estimated;
B is amount of drug found on preanalyzed basis;
C is amount of pure drug added to formulation.

Precision:
Precision of the method is studied as intra-day and interday precision. Intra-day and Inter-day precision was determined by analyzing the same concentration of the solutions daily for three days. In intermediate precision study, % R.S.D. values were not more than 1.0 % in all the cases.

Limit of detection and Limit of quantitation:
Limit of detection (LOD) and Limit of quantitation (LOQ) were determined by using the formula based on the standard deviation of the response and the slope.
Limit of detection (LOD) and Limit of quantitation (LOQ) were calculated by using the equations
LOD = 3 × s/S
and LOQ = 10 × s/S,
where s is standard deviation of intercept,
S is the slope of the line.

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

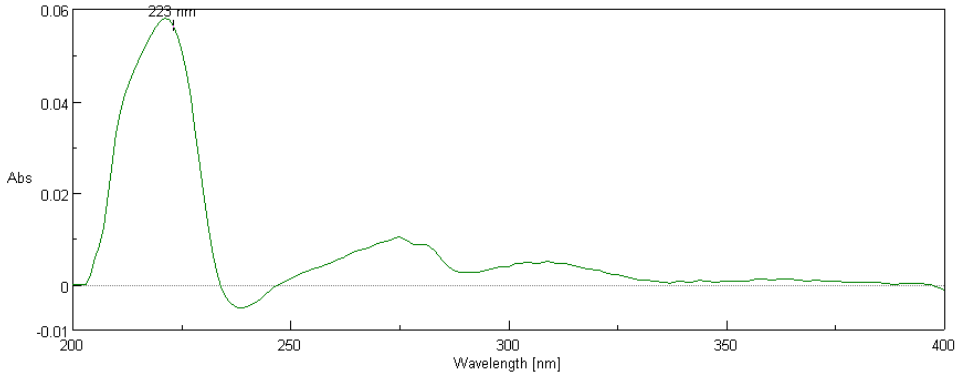

Fig.1 Absorbance maxima of Metoprolol Succinate

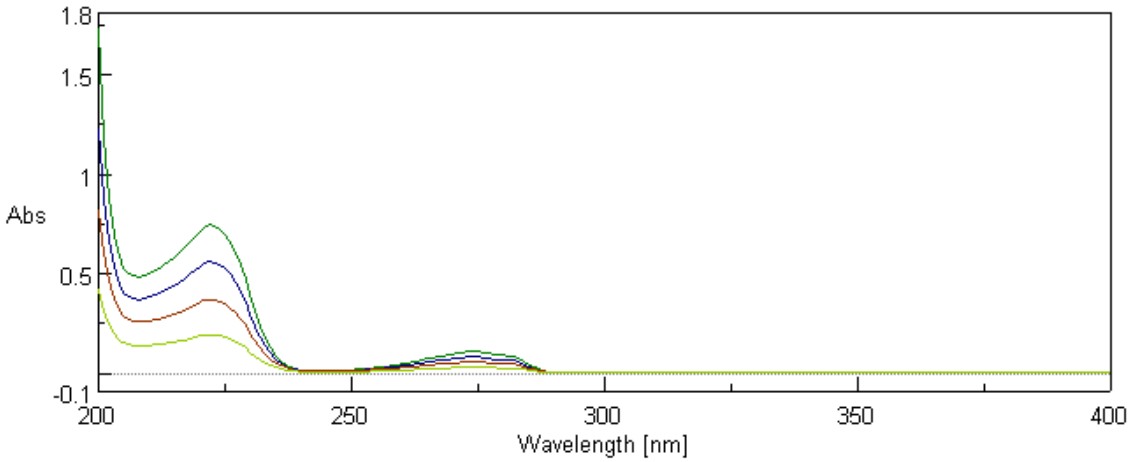

Fig.2 Overlay spectra at different concentrations of Metoprolol Succinate

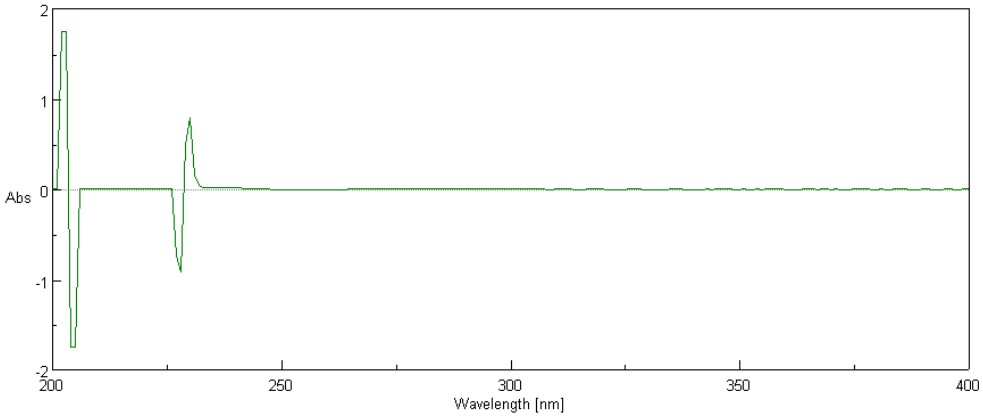

Fig.3 Second order derivative spectra of Metoprolol Succinate

Table No.1: Optical Parameters

Sr. No.	Parameters	Observations Method I	Observations Method II (Derivative)
1	λmax	223 nm	226 nm
2	Beers range	5-25 µg/ml	5-25 µg/ml
3	Correlation coefficient	0.9999	0.9979
4	Intercept	0.0349	0.0892
5	Slope	27.51	24.15

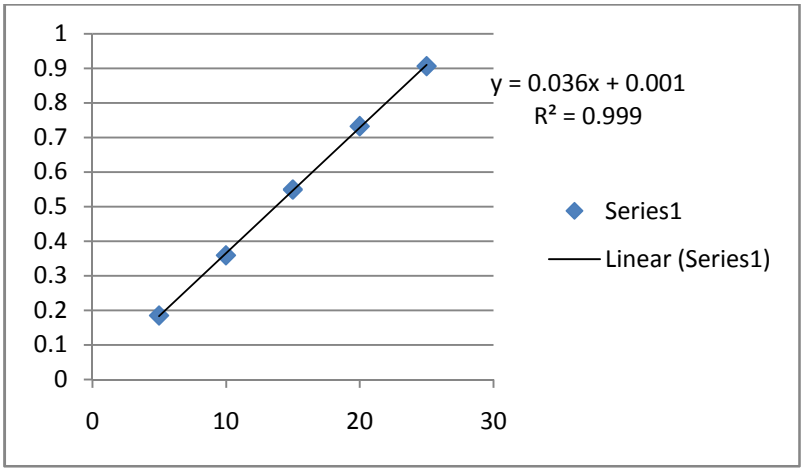

Fig.4 Calibration curve of Metoprolol succinate

Table No.2: Assay of Metoprolol Succinate 50 mg tablets (Toprol XL 40)

Sr.No.	Lable claim	% claim found*	
		Method I	Method II
Sample 1	50 mg	99.84 %	99.26 %
Sample 2	50 mg	99.97 %	99.52%

**mean of 5 determinations.*

Table No.3: Results of Recovery study of Metoprolol Succinate 50 mg tablets (Troprol XL 50):

Labelled Amount	Amount of drug Added (%)	Method I			Method II (Derivative)		
		Amount of drug Recovered(mg)	Percent Recovery (%)*	% RSD	Amount of drug Recovered(mg)	Percent Recovery (%)*	% RSD
50 mg	80	39.86	98.65	0.28	39.24	98.10	0.48
50 mg	100	49.72	99.44	0.34	49.35	98.70	0.27
50 mg	120	58.23	97.05	0.30	58.89	98.15	0.24

**mean of 4 determinations.*

Table No.4: Validation parameters:

Sr.No.	Method I		Method II (Derivative)	
	LOD	LOQ	LOD	LOQ
1	0.0498	0.232	0.765	0.280

Table No.5: Validation parameters

Sr.No.	Parameters	Method I	Method II (Derivative)
1	Intraday precision Amount found ± %RSD (n=3)	99.37 ± 0.67	98.57 ± 0.98
2	Interday precision Amount ± %RSD (n=3)	98.85 ± 0.99	97.46 ± 2.41
3	Ruggedness Amount found ± %RSD (n=3)	0.142	0.159

A validated, simple, rapid sensitive and accurate UV-Spectrophotometric methods has been developed for estimation of Metoprolol Succinate in bulk and pharmaceutical formulation. In phosphate buffer 6.8, Metoprolol succinate showed absorbance maxima at 223nm and 226nm respectively for Method I and Method II. Linearity was observed in the concentration range 5-25 µg/mL with correlation coefficient value 0.9999 and 0.9979 respectively for Method I and Method II. The proposed method was applied to pharmaceutical formulation and Percent amount of drug estimated was found in good agreement with the label claim. The recovery experiment was carried out at three different levels i.e., 80 %, 100 % and 120 %. The percentage recovery was found to be 98.38 % and 98.31 % respectively for Method I and Method II; the low values of % R.S.D. are indicative of the accuracy and reproducibility of the method. The precision of the method was studied as an intra-day and inter-day precision. Ruggedness of the proposed method was studied with the help of two analysts. The Limits of Detection and Quantitation for Metoprolol Succinate with a lower concentration were 0.0498 and 0.232 for Method I and for Method II 0.765 and 0.280 respectively, values which are under the lowest expected concentrations in the sample.

CONCLUSION

The present study was undertaken with an objective of developing simple, sensitive and reliable analytical method like UV-Visible spectrophotometry for estimation of Metoprolol Succinate in phosphate buffer 6.8 in tablet dosage form. The method has sufficiently good accuracy, precision and permitted as a cost effective as other methods. The analytical method is simple, sensitive, rapid and specific. Further it can be conveniently employed for the routine analysis and the quality control of Metoprolol Succinate in tablet formulation.

Acknowledgement
The authors are thankful to P.D.V.V.P.F's College of Pharmacy Ahmednagar (M.S.), India for providing the required facilities to carry out this research work.

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