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Analytical Method Development and Validation of Spectroscopic Method for Estimation of Metoprolol Succinate

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ABSTRACT

A Simple, specific, rapid, precise and accurate UV Spectrophotometric method have been developed and Validated for determination of Metoprolol Succinate. Drug Metoprolol Succinate showed the absorption maxima in at 222 nm and was linear for a range of 5 µg/ml –25 µg/ml with correlation coefficient of 0.9993. The validation of the above proposed method was done by carrying out precision and accuracy studies. The percentage recovery at three different levels i.e. 50%, 100% and 150% was found to be 49.8%, 99.5% and 151.5% respectively. The analytical method showed good Intra precision (Repeatability) with relative standard deviation 0.672 % and Inter precision with relative standard deviation is 0.685% which is less than 2. The proposed method was validated for the parameter Specificity, Precision, Linearity and range, Ruggedness, Accuracy and recovery. Hence proposed analytical method for estimation of Metoprolol Succinate formulation drug by UV spectrophotometer in pharmaceutical can be applied for the routine quality control analysis.

Keywords: Validation, Metoprolol Succinate, UV Spectrophotometer.

INTRODUCTION

Metoprolol Succinate is an Anti-hypertensive drug belongs to cardio selective β1 adrenergic receptor antagonist[1] used in hypertension, angina pectoris, cardiac arrhythmia, congestive heart failure and myocardial infarction the IUPAC name is 2-Propanol,1-[4-(2-Methoxyethyl)Phenoxy)-3-[(1-Methylethyl)amino]-,(+)-,Butanediote (2:1) Salt. Metoprolol Succinate having molecular formula $(C_{15}H_{25}NO_3)_2.C_4H_6O_4$ and molecular weight 652.82g/mol. It is official in United States [2] and

European/British pharmacopoeia[3] with Potentiometric titration method. Literature survey reveals that few analytical methods are available including HPTLC [4-7], HPLC [8-16] and UV Spectrophotometry [17-30].

In the present work, a simple, accurate and sensitive method for determining Metoprolol Succinate in pure form was introduced. No simple and rapid work has been reported for the estimation of Metoprolol Succinate. All these reported methods either took a long time for analysis or employ mobile phases with pH adjustment of Buffer solutions which is tedious and anomalous, especially for routine testing of quality control samples of assay content study. Hence it was felt necessary to build up a simple, rapid, economical and precise Spectrophotometric method for the direct quantitative determination of Metoprolol Succinate. The current research work deals with the development of UV Spectrophotometric method and its validation as per International Conference on Harmonization (ICH) guideline [31-32]. The developed method was found to be simple, specific, stable, rapid, accurate, precise, reliable, less expensive and time saving by UV Spectrophotometric method for the estimation of Metoprolol Succinate formulation drug (Figure1).

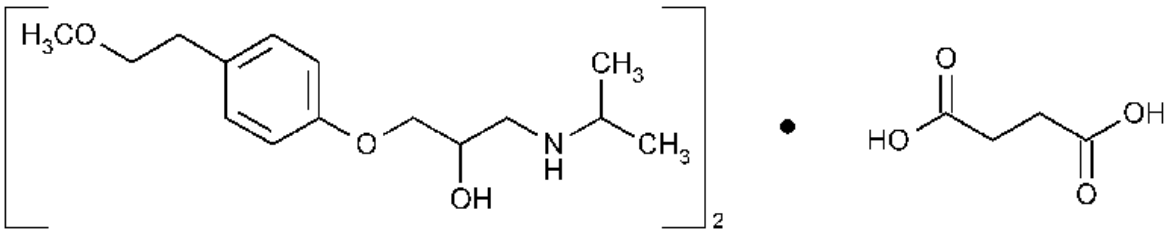

Figure 1: Chemical structure of Metoprolol Succinate.

MATERIALS AND METHODS

Instrumentation and Materials

U.V. visible double beam spectrophotometers SL 210 Elico with Spectra treat software having path length 1cm U.V. matched quartz cells were used. Metoprolol Succinate was a gift sample and Standard from Omicron Pharmaceuticals Surat Gujarat. All chemicals, solvents and reagents i.e. Hydrochloric acid, Water and Methanol used, were analytical grade and purchased from PCL/Merck Ltd, India, S.D. Fine Chem Ltd/Qualigens.

Method Development

Preparation of Diluent Solution

Transfer about 700 ml of water to the 1000 ml volumetric flask, then slowly add about 3.0 mL of Hydrochloric acid with stirring and, mix well, then with constant stirring slowly add Methanol up to mark to make volume 1000 ml. use this solution as diluent.

Preparation of Standard Solution

Weighed accurately about 120 mg of Metoprolol Succinate and transferred to 200 ml volumetric flask. Dissolved in diluent and made up the volume to 200 ml, further transferred 5 ml of solution to 200 ml volumetric flask up to mark to get a concentration 15 µg/ml.

Selection of wavelength for analysis of Metoprolol Succinate

The standard solution having concentration 15µg/ml was scanned at 200 nm to 400 nm with diluent as the blank to detect maximum wavelength (Figure-2).

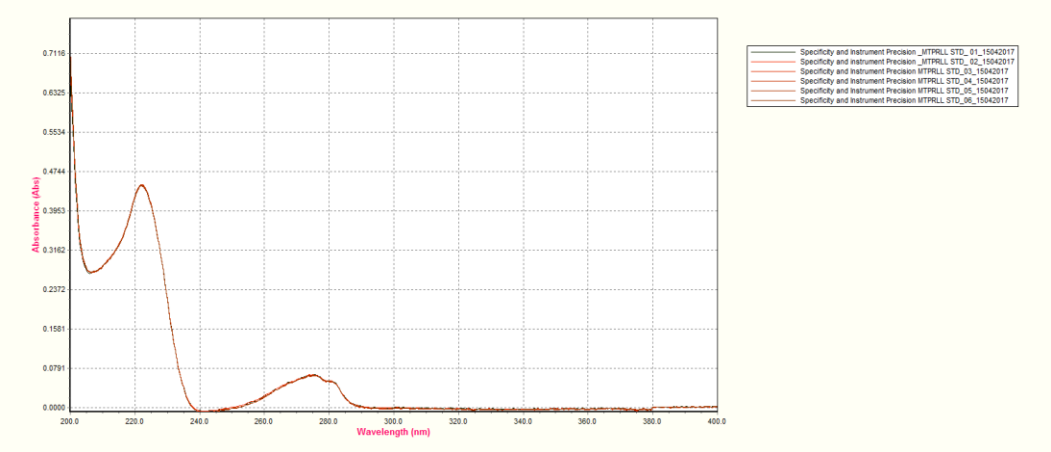

Figure 2: Estimation of Maxima of Metoprolol Succinate

From the above (Figure-2) spectra of Metoprolol Succinate wavelength maxima identified for quantification were 222 nm (λmax).

Validation of proposed Analytical Method

The proposed method was validated according to International Conference on Harmonization (ICH) guidelines for validation of analytical procedures [42-43]. Analysis of variance (ANOVA) was used to verify the validity and performance effectiveness of the proposed analytical methods.

Specificity

Specificity is the ability to assess unequivocally the analyte in the presence of components which may be expected to be present. Typically these might include impurities, degradants, matrix, etc. Specificity was done by scanning of Diluent solution and Standard solution of Metoprolol Succinate having concentrations 15 µg/ml in Spectrophotometric range from 200 nm to 400 nm to check specific absorption maxima at predefined wavelength i.e. 222 nm and Standard solution stability study done to evaluate the solution stability at different time interval up to 24 hrs.

RESULTS AND DISCUSSION

The method discussed in the present work provides a simple, stable, rapid, accurate, precise, reliable, less expensive (Economical), time *saving* and convenient method for the analysis of Metoprolol Succinate using U.V. Spectrophotometry. λ max selected for quantization was 222 nm. In the developed analytical method, the linearity was observed 0.9993 in the concentration range of 5 µg/ml -25 µg/ml.

Method precision for the Metoprolol Succinate at concentrations level 15µg/ml was found in the range of 98.9%-100.7%. Accuracy of the proposed method was ascertained by recovery studies and the results were expressed as percent recovery and were found in the Range of 99.5%-101.0%.Values of standard deviation and coefficient of variance was satisfactorily indicating the accuracy of both the methods. Intra-day and Inter-day precision studies were carried out by analyzing the sample of Metoprolol Succinate at different time interval on the same day and on different days respectively. Standard deviation and coefficient of variance for Intra-day and Inter-day precision studies was found to be less than 2 indicating precision of the proposed method.

Based on the outcome of analytical method development and analytical validation study test results, it was found that, the proposed analytical method for estimation of Metoprolol Succinate by UV Spectrophotometry is Accurate, Precise, Reproducible, Stable, Simple, Rapid Time saving and less expensive (Economical). The analytical method can be employed for routine quality control of Metoprolol Succinate in pharmaceutical analysis.

Instrument Precision

Instrument precision was performed to check the suitability of the developed analytical method with respect to ability of instrument consistency to provide the precise wavelength maxim when scanned the Standard solution of Metoprolol Succinate having concentrations 15 µg/ml in the UV range from 200 nm to 400 nm. To check specific absorption maxima at predefined wavelength 222 nm with reproducible absorption detection. Six separated standard preparations were scanned / analyzed according to the proposed method of analysis. The % RSD due to Metoprolol Succinate concentration for the six standards was found 0.288%. The % RSD due to Metoprolol Succinate concentration for the instrument precision meets the requirements. Results are tabulated in the (Table 1).

Table 1: Instrument Precision

Sr. No.	Standard number	Absorbance @222 nm	% RSD
1	Standard Preparation -1	0.4464	0.288%
2	Standard Preparation -2	0.4474	
3	Standard Preparation -3	0.4477	

4	Standard Preparation -4	0.4492	Limit < 2%
5	Standard Preparation -5	0.4455	
6	Standard Preparation -6	0.4465	
Average Absorbance →		0.4471	

Linearity and Range

The linearity of an assay method is its ability to elicit test results, which are directly proportional to the concentrations of drug in samples in a given range. Linearity justifies the use of single-point calibrations. The correlation coefficient of the Regression line for was found that 0.9993.

Five levels of five different concentrations Standard solution of Metoprolol Succinate having concentrations 5 µg/ml, 10 µg/ml, 15 µg/ml, 20 µg/ml and 25 µg/ml, in the range relative to the working concentrations, were prepared and read according to the method of analysis. A linear regression curve was constructed, the correlation coefficient (R2) and assessment value calculated. The correlation coefficient (R2) for Metoprolol Succinate obtained is 0.9993. The plot is a straight line and the results are tabulated in the Table 2 and Curve is shown in the Figure 3.

Table 2: Linearity and Range

Sr. No.	**Standard Concentration (µg/ml)**	**Absorbance @ 222 nm**	**Correlation coefficient**
1	5	0.1497	0.9993 Limit ≥0.999
2	10	0.3160	
3	15	0.4438	
4	20	0.5978	
5	25	0.7364	

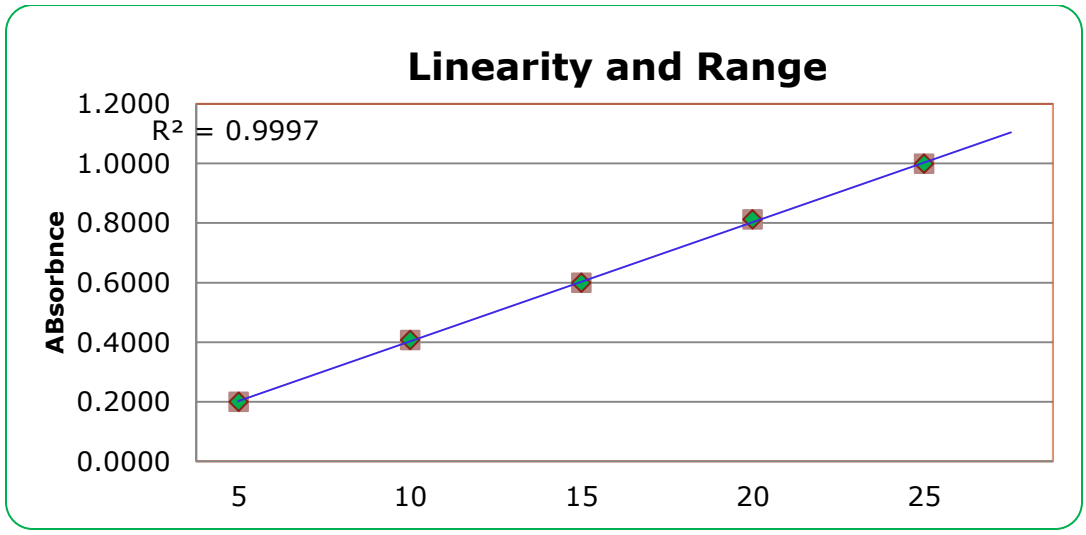

Figure 3: Linearity and Range of Metoprolol Succinate

Analytical Method Precision

The precision of an analytical procedure expresses the degree of agreement among individual test results when the method is applied to multiple sampling of a homogenous sample.

Intra Precision (Repeatability*)*

This parameter determines the repeatability of assay results under the same operating conditions over a short period of time. The % RSD due to Metoprolol Succinate concentration for the six samples was found to be 0.672%. Six separated sample preparations were analyzed according to the proposed method of analysis. The % RSD due to Metoprolol Succinate concentration for the assay meets the requirements. Results are tabulated in the Table 3.

Table 3: Intra Precision (Repeatability) Results

Sr. No.	Sample number Results	Metoprolol Succinate % Assay content	% RSD of Six Assay content
1	Sample Preparation -1	100.7	0.672% Limit < 2%
2	Sample Preparation -2	98.9	
3	Sample Preparation -3	99.3	
4	Sample Preparation -4	99.1	
5	Sample Preparation -5	99.4	
6	Sample Preparation -6	99.0	
	Average % Assay ⟶	99.4	

Inter Precision (Repeatability*)*

This parameter determines the Intermediate repeatability of assay results under the same operating conditions test performed on a different day, using different makes of reagents and solvents. The % RSD due to Metoprolol Succinate concentration for the six samples was found to be 0.685%. Six separated sample preparations were analyzed according to the proposed method of analysis. The % RSD due to Metoprolol Succinate concentration for the assay meets the requirements. Results are tabulated in the (Table 4).

Table 4. Inter Precision (Repeatability) Results

Sr. No.	Sample number Results	Metoprolol Succinate % Assay content	% RSD of Six Assay content
1	Sample Preparation -1	99.4	0.685% Limit < 2%
2	Sample Preparation -2	99.9	
3	Sample Preparation -3	100.7	
4	Sample Preparation -4	98.9	
5	Sample Preparation -5	99.1	
6	Sample Preparation -6	100.0	
Average % Assay ⟶		99.7	

Ruggedness

Ruggedness of the method was determined by carrying out the analysis on different days, different makes of reagents and solvents. The respective test assay results of Metoprolol Succinate having concentration as 15 µg/ml was illustrious. The result is expressed as shown in table 4. The developed method for estimation of Metoprolol Succinate was found to be rugged as Shown in table 5.

Table 5. Ruggedness

Sr. No.	**Precision**	**% RSD of assay of Six Preparation**	**Limit For Ruggedness**
1	Intra Precision	0.672	NMT 2%
2	Inter Precision	0.685	
% RSD of Overall 12 Assay content		0.652	

Accuracy

This parameter determines the accuracy of the assay results under the same operating conditions test.

A sample was constituted analyzed for the accuracy with known quantity of standard samples of Metoprolol Succinate at 50%, 100%, 150% concentration levels and assayed as per the method stated under analytical Methods respectively. Three determinations were performed under each concentration levels respectively. Results are shown in Tables 6, 7, 8. The % RSD due to recovery of Metoprolol Succinate at 50%,100%, 150% concentration levels was found to be 0.736%, 0.814% and 0.924% respectively. Nine sample preparations were analyzed according to the proposed method of analysis. The %RSD due to Metoprolol Succinate concentration for he assay meets the requirements and within 98.0% to 102%. Results are tabulated in the Table 6, 7, 8.

Table 6. Accuracy and Recovery Results @ 50 % Concentration level

Sr. No.	**Accuracy** @ 50% **level**	**Recovery of Metoprolol Succinate % Assay content**	**% Recovery** 98.0% to 102%	**% RSD**
1	Sample Preparation -1	50.1	99.5	0.736% Limit < 2%
2	Sample Preparation -2	49.4		
3	Sample Preparation -3	49.8		
Average % Assay →		49.8		

Table 7. Accuracy and Recovery Results @ 100 % Concentration level

Sr. No.	**Accuracy** @ 100% **level**	**Recovery of Metoprolol Succinate %Assay content**	**% Recovery** 98.0% to 102%	**% RSD**
1	Sample Preparation -1	100.1	99.5	0.814% Limit < 2%
2	Sample Preparation -2	99.9		
3	Sample Preparation -3	98.6		
Average % Assay →		99.5		

Table 8. Accuracy and Recovery Results @ 150 % Concentration level

Sr. No.	**Accuracy** @ 150% **level**	**Recovery of Metoprolol Succinate %Assay content**	**% Recovery** 98.0% to 102%	**% RSD**

1	Sample Preparation -1	152.8	101.0	0.924% Limit < 2%
2	Sample Preparation -2	151.5		
3	Sample Preparation -3	150.0		
Average % Assay →		151.5		

Solution Stability of Standard Solution

Solution stability of the standard solution performed up to 24 hrs with different time interval and found the solution is stable showing cumulative % RSD of different time interval is 0.556 which is less than the 2. Hence the Metoprolol Succinate solution is stable up to 24 hrs at room temperature.

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