

# NEW ANALYTICAL METHODS AND THEIR VALIDATION FOR THE ESTIMATION OF METOPROLOL SUCCINATE IN BULK AND MARKETED FORMULATION

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## ABSTRACT

Metoprolol succinate is cardiovascular agent. Mainly used for the treatment of hypertension, heart failure, and cardiovascular diseases.

**Purpose:** Analytical methods are required to characterize drug substances and drug products composition during all phases of pharmaceutical development. Development of methods to achieve the final goal of ensuring the quality of drug substances and drug products must be implemented in conjunction with an understanding of the chemical behavior and physicochemical properties of the drug substance. This determination requires highly sophisticated instruments and methods like HPLC, HPTLC and Spectrophotometer. Hence there was a need for the development of newer, simple, sensitive, rapid, accurate and reproducible analytical methods for the routine estimation of metoprolol succinate in bulk and pharmaceutical dosage form.

**Methods:** The present work describes two new spectrophotometric methods for the determination of metoprolol succinate in bulk and marketed formulations. Method A is based on oxidation reaction. Metoprolol succinate in presence of acidic medium reacts with excess amount of chloramine-T and remaining chloramine-T react with malachite green to produce orange colour chromogen which showed  $\lambda_{\max}$  at 516 nm. In Method B, the drug was diazotised with sodium nitrite in presence of hydrochloric acid and then it was coupled with  $\beta$ -naphthol in alkaline medium. Which produce red colour chromogen which showed  $\lambda_{\max}$  at 688 nm.

**Results:** The linearity was found in concentration range of 5-30 $\mu$ g/ml for both method A and method B. The correlation coefficient was found to be 0.9983 and 0.9993 for method A and method B respectively. The methods were validated as per ICH guidelines. The LOD and LOQ for estimation of Metoprolol succinate were found as 0.0773, 0.2343 for method A and 0.0667, 0.2021 for method B respectively.

**Conclusion:** Proposed methods were successfully applied for the quantitative estimation of Metoprolol succinate in marketed formulations.

**KEY WORDS** Metoprolol succinate, Malachite green,  $\beta$ -naphthol, validation and colourimetry.

## INTRODUCTION

Metoprolol succinate is a  $\beta_1$ -selective (cardioselective) adrenoceptor blocking agent. several possible mechanisms have been proposed: (1) competitive antagonism of catecholamines at peripheral (especially cardiac) adrenergic neuron sites, leading to decreased cardiac output; (2) A central effect leading to reduced sympathetic outflow to the periphery (3) suppression of renin activity. Several methods have been reported in the literature for analytical determination of this substance. It has been determined by different techniques including simultaneous estimation<sup>[1]</sup>, Reverse-Phase HPLC method<sup>[2]</sup>, RP-HPLC method for simultaneous determination<sup>[3]</sup>, spectrophotometric method<sup>[4]</sup>, UV Spectroscopy determination<sup>[5,6,7]</sup>.

In the present work, a simple, accurate and sensitive method for determining metoprolol succinate in pure form and pharmaceutical formulations was introduced.

The literature survey on the analytical applications of malachite green and  $\beta$ -naphthol indicates that these compounds have not been earlier reported as reagents for the spectrophotometric determination of metoprolol succinate in either biological fluids or pharmaceutical formulations. Hence the author has made an attempt to develop simple and rapid methods for the estimation of the sited drug in bulk and pharmaceutical formulations.

## MATERIALS AND METHODS

Metoprolol succinate was obtained in highly pure form (pharmaceutical grade) from the local pharmaceutical industry. Its pharmaceutical preparations obtained from different commercial sources. All other reagents were of analytical grade. Distilled water was used for preparation of all solutions. Ultraviolet and visible spectrophotometry were carried out through Systronics PC based Double Beam Spectrophotometer 2202 and JascoV-630 spectrophotometer.

### Standard drug solution:

Accurately weighed 100mg of metoprolol succinate was dissolved in 100ml distilled water to give a concentration of 1000  $\mu\text{g/ml}$ . The final concentration was brought to 50  $\mu\text{g/ml}$  for Methods A and B.

### Reagents:

#### Method A:

- 0.15% malachite green solution
- 0.02M Chloramine-T solution
- 2M  $\text{H}_2\text{SO}_4$  solution

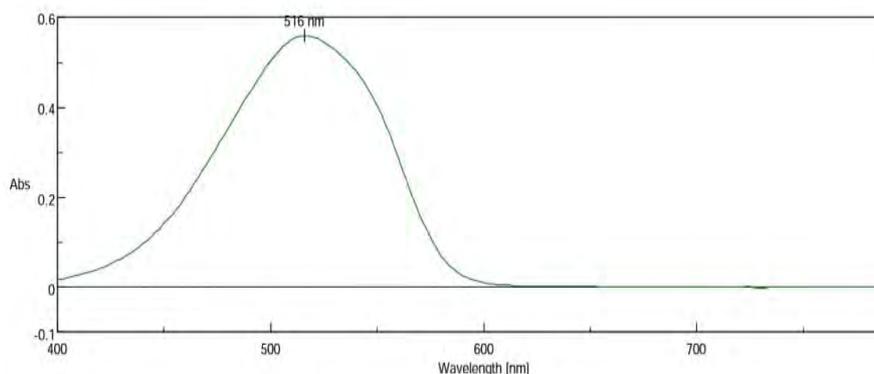
#### Method B:

- 1.5%  $\beta$ -naphthol solution
- 3% Sodium nitrite solution
- 2% HCL solution

### Assay procedure for the determination of Metoprolol succinate:

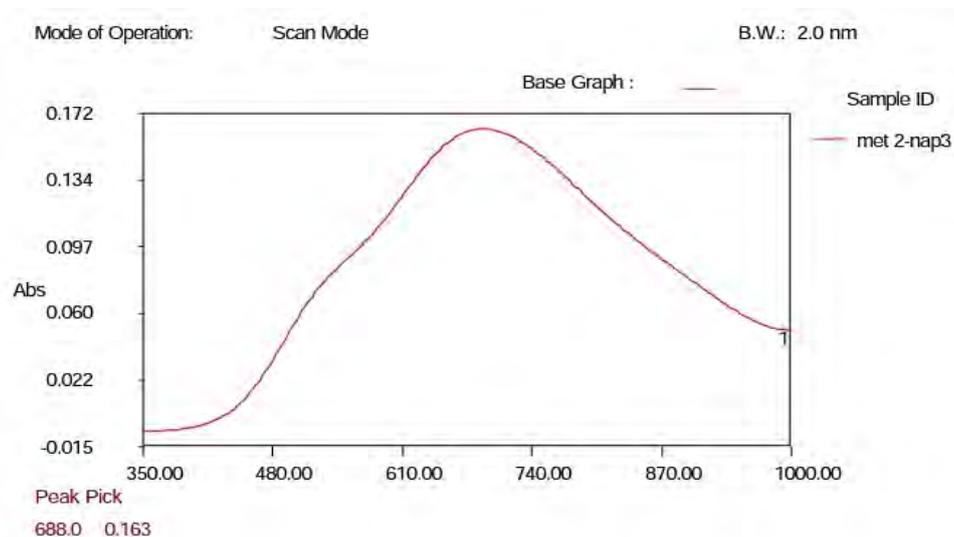
**Method A:** Seven 10 ml volumetric flasks were taken. 1.5 ml of 0.02M Chloramine-T and 2 ml of 2M  $\text{H}_2\text{SO}_4$  were added in all volumetric flasks, kept it aside for 20 minutes. Aliquots of the standard solution containing 0.5 – 3.0ml (5-30 $\mu\text{g/ml}$ ) of Metoprolol succinate were added in each volumetric flask and wait for 10 minutes. Then 0.8 ml 0.15% of malachite green solution was added and made up the volume with distilled water. Absorbance was taken against blank at 516 nm. (Fig: 1) against reagent blank which shown nil absorbance at corresponding wave length. The calibration curve was prepared to calculate the amount of the drug.

Fig: 1 Absorption spectrum of colored chromogen in method A



**Method B:** Seven 10 ml volumetric flasks were taken. In flask 0.5-3 ml (5-30 $\mu\text{g/ml}$ ) of working standard of Metoprolol succinate were added. Then 1 ml of 2% HCL and 0.6 ml of 3% sodium nitrite solution was added and kept aside for 5 minute to complete the reaction. Then add 2 ml of 1.5%  $\beta$ -naphthol solution to each volumetric flask and made up the volume with distilled water. Absorbance was taken against reagent blank at 688 nm. (Fig: 2) at which the reagent blank has no absorbance and the calibration curve was prepared.

Fig: 2 Absorption spectrum of colored chromogen in method B



### Assay of pharmaceutical formulations

Tablet powder equivalent to 100 mg was accurately weighed and dissolved in water and filtered. The filtrate was made up to 100 ml and appropriate aliquots of the drug solution were treated as described above and the results were tabulated.

### RESULTS AND DISCUSSION

Method A is based on oxidation reaction. Metoprolol succinate in presence of acidic medium reacts with excess amount of chloramine-T and remaining chloramine-T react with malachite green to produce orange colour chromogen which showed  $\lambda_{\max}$  at 516 nm. In Method B, the drug was diazotised with sodium nitrite in presence of hydrochloric acid and then it was coupled with  $\beta$ -naphthol in alkaline medium. Which produce red colour chromogen which showed  $\lambda_{\max}$  at 688 nm.

The optical characteristics such as absorption maxima and Beer's law limits for these methods are presented in Table-1. The regression analysis using the method of least squares was made for the slope (a) and intercept (b) obtained from different concentrations are summarized in Table-1. The precision and accuracy were found by analyzing six replicate samples containing known amounts of the drug and the results are summarized in Table-1

TABLE – 1 Optical Characteristics, Precision and Accuracy of Proposed Methods

Parameter	Results	
	Method A	Method B
$\lambda_{\max}$ (nm)	516 nm	688 nm
Beer's law limit	5-30 $\mu$ g/ml	5-30 $\mu$ g/ml
Regression Equation* (y)	y=bx+a: 0.0201x-0.0005	y=bx+a: 0.0233x +0.0039
Slope (b)	0.0201	0.0233
Intercept (a)	0.0005	0.0039
Correlation coefficient ( $R^2$ )	0.9983	0.9993
Limit of Detection ( $\mu$ g/ml)	0.0773	0.667
Limit of quantitation ( $\mu$ g/ml)	0.2343	0.2021
Accuracy (%Recovery $\pm$ SD)	96.95 $\pm$ 0.137	98.45 $\pm$ 0.022
Precision (Reproducibility)		
Intraday (%Recovery $\pm$ SD)	0.190 $\pm$ 0.0011	0.234 $\pm$ 0.00068
Interday (%Recovery $\pm$ SD)	0.186 $\pm$ 0.0014	0.230 $\pm$ 0.0017

$y = bx + a$ , where  $y$  is the absorbance and  $x$  is the concentration of Metoprolol succinate in  $\mu\text{g/ml}$ .

### RECOVERY EXPERIMENTS:

Weighed accurately tablet powder equivalent to 100mg and transferred into 100ml volumetric flask and dissolve in small volume of distilled water. Then filter the solution and filtrate is made up the volume with distilled water to get 1000 $\mu\text{g/ml}$  concentration. This solution was further diluted to get concentration of 100 $\mu\text{g/ml}$ . To keep an additional check on accuracy of developed assay method, analytical recovery experiments were performed. The different solutions of different concentrations like 5, 10 and 15  $\mu\text{g/ml}$  were prepared in case of both pure drug solution and the formulation extract solution and these solutions were subjected to analysis by above developed method. The six such samples were prepared and average of that readings taken for calculation of % recovery. This is reported in following table no. 2.

TABLE - 2. Assay and Recovery of Metoprolol succinate in Pharmaceutical Formulations

Method	Sample	Labeled amount (mg)	Amount found (mg)	% Recovery
A	Metapro-XL 50	50	46.7	93.4
B	Metapro-XL 50	50	47.4	94.8

### CONCLUSION

It could be concluded that the developed methods for metoprolol succinate assay is simple, sensitive, precise, accurate and can be satisfactorily applied to the analysis of metoprolol succinate in bulk and pharmaceutical formulations. The proposed methods are used for the routine analysis of the drug in the quality control.

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### REFERENCES

- [1] Modi M, Shah R, Mashru RC. Development and validation of spectrophotometric methods for simultaneous estimation of metoprolol succinate and telmisartan in combined pharmaceutical formulation. *Int J Pharm Sci Res* 2012;3(5):1348-54.
- [2] Singh B, Patel DK, Ghosh SK. Development of Reverse-Phase HPLC method for simultaneous analysis of metoprolol succinate and hydrochlorothiazide in a tablet formulation. *Tropical J Pharm Res* 2009;8(6):539-43.
- [3] Tsvetkova BG, Pencheva IP, Peikov PT. Development and validation of RP-HPLC method for simultaneous determination of metoprolol and aspirin in fixed dose combinations. *Der pharma Chemica* 2012;4(4):1512-16.
- [4] Kulkarni MN, Kshirsagar RV, Sakarkar DM. Development and validation of spectrophotometric method for determination of metoprolol succinate. *Int J Chem Tech Res* 2009;1(4):1273-7.
- [5] Shah RN, Gandhi DB, Patel MM. Simultaneous determination of amlodipine besylate and indapamide in tablet dosage form by absorption correction method and first-order derivative UV spectrophotometry. *Int J PharmTech Res* 2012;4(3):1018-24.
- [6] Kunturkar K, Jain HK. Development and validation of UV spectrophotometric method for determination of s (-) metoprolol succinate and clopidogrel bisulphate in bulk and tablet dosage form. *Int J Pharm Pharm Sci* 2013;5(3):593-98.
- [7] Dhole SM, Chaple DR, Harde MT. Validated UV spectrophotometric method for simultaneous estimation of metoprolol succinate and amlodipine besylate in their combined tablet dosage form. *Int J Ana Bio Chem* 2013;3(3):82-5.
- [8] <http://www.drugs.com/pro/metoprolol-succinate.html>
- [9] <http://www.drugs.com/sfx/metoprolol-succinate-side-effects.html>
- [10] <http://en.wikipedia.org/wiki/Metoprolol>
- [11] <http://www.webmd.com/drugs/2/drug-8814/metoprolol-succinate-oral/details>