Available Online through
www.ijpbs.com (or) www.ijpbsonline.com

IJPBS |Volume 3| Issue 4 |OCT-DEC|2013|224-228

Research Article
Pharmaceutical Sciences

DEVELOPMENT AND VALIDATION OF SPECTROPHOTOMETRIC METHOD FOR DETERMINATION OF METOPROLOL SUCCINATE

S. A. Pagar*, D.M.Shinkar[1], R.B.Saudagar[2]

*,1Department of Pharmaceutics, KCT'S RGS College of Pharmacy, Anjaneri, Nashik, 422 213. Maharashtra, India.

[2]Department of Pharmaceutical Chemistry, KCT'S RGS College of Pharmacy, Anjaneri, Nashik, 422 213. Maharashtra, India.

*Corresponding Author Email: Swati.pagar2210@gmail.com

ABSTRACT

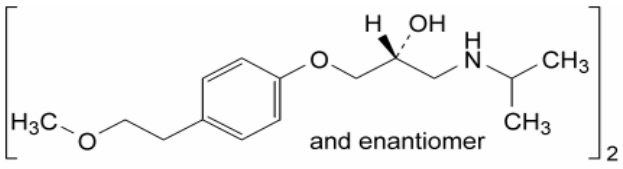
In this study, a simple, sensitive and highly accurate ultraviolet spectrophotometric method has been developed and validated for determination of metoprolol succinate in bulk and pharmaceutical formulations. The method is based on the measurement of the absorbance of metoprolol succinate solution in distilled water and phosphate buffer pH 6.8 at 221 nm and 223nm respectively in the wavelength range of 200 - 400 nm. Beer's law was obeyed in the concentration range of 5-25 µg/ml. The slope, intercept and correlation coefficient were also calculated. Results of percentage recovery shows that the method was not affected by the presence of common excipients in tablets. The developed method was validated in terms of accuracy, precision, linearity, limit of detection, limit of quantification which proves suitability of proposed method for routine estimation of metoprolol succinate in bulk and pharmaceutical formulations.

KEY WORDS

Metoprolol succinate, Spectrophotometry, Estimation, Tablets.

INTRODUCTION

Metoprolol is cardio selective β1 adrenergic receptor antagonist mainly used in hypertension, angina pectoris, cardiac arrhythmia, congestive heart failure and myocardial infarction.[1,2,3] Chemically Metoprolol is (RS)-1-(Isopropylamino)-3-[4-(2-methoxyethyl) phenoxy] propan-2-ol with molecular weight 652.81. Freely soluble in water and elimination half life of 3-7 hrs [4]. Mode of action of metoprolol is by reducing agonistic effect of catecholamines on the heart (which is released during physical and mental stress). This means that the usual increase in heart rate, cardiac output, cardiac contractility and blood pressure, produced by the acute increase in catecholamines is reduced. [5]



[6]

The drug is quite sensitive, even small amount of drug doses giving significant blockade of B_1 adrenoreceptors [7, 8]. Thus the quantitative determination of drug would be important. Literature survey reveals that several spectrophotometric, LC, HPTLC, HPLC, RP-HPLC, LC-MS methods have reported for the estimation of metoprolol succinate in pure and tablet dosage form.[9] The scope of present investigation was to develop and validate UV spectrophotometric method for the quantification of metoprolol succinate in bulk and pharmaceutical formulation.

MATERIALS

Metoprolol succinate was obtained as a gift sample from Ipca laboratories ltd Mumbai (India). All analytical grade chemicals and solvents were supplied by S.D. Fine Chemicals, Mumbai, India. Distilled water was used to prepare all solutions. Freshly prepared solutions were always employed.

Equipment

The UV-Visible Spectrophotometer (Jasco-V630) with data processing system was used. The sample solutions were recorded in 1cm quartz cells against solvent blank over the range 200-400nm. A Citizen electronic analytical balance was used for weighing the samples. An ultrasonicator bath (PCI Analytics Pvt. Ltd.) was used for sonication of the drug solution.

Preparation of stock solutions:

1] In distilled water: 1000 ppm of stock solution was prepared by dissolving 10 mg of metoprolol succinate in 10 ml of distilled water; wavelength was determined and found to be 221nm.

2] Phosphate buffer pH 6.8: 1000 ppm of stock solution was prepared by dissolving 10 mg of metoprolol succinate in 10 ml of phosphate buffer pH 6.8; wavelength was determined and found to be 223nm.

Stock solution was further diluted to obtain 5-30µg/ml with distilled water and pH6.8 buffer respectively. Standerd solutions of Metoprolol succinate (10 microgram per ml) were scanned in 200-400 nm range to determine the maximum absorbance. The absorbance was measured at 221nm for distilled water and 223 nm for phosphate buffer pH6.8 buffer. The calibration curve was plotted in the concentration range of 5-30 µg/ml of metoprolol succinate using distilled water and pH 6.8 buffer as blank respectively.

Validation of the proposed method [10, 11, 12]

The proposed method was validated according to the International Conference on Harmonization (ICH) guidelines.

Linearity (Calibration curve): the developed method validates as per ICH guidelines. The plot of absorbance verses concentration is shown in fig1and fig 2 for distilled water and phosphate buffer pH 6.8.It can be seen that plots are linear in the concentration range of 5-25 µg/ml with correlation coefficients (r^2) of 0.995 and 0.992

Precision (repeatability): Intraday and interday precision was determined by measurement of the absorbance for three times on same day and on three different days. The relative standard deviation for replicates of sample solutions was less than 2 % which meet the acceptance criteria for established method.

Accuracy (recovery study): Recovery studies were carried out by adding a known quantity of pure drug to the preanalysed formulations and the proposed method was followed. From the amount of drug found, percentage recovery was calculated as per ICH guidelines.

Sensitivity: Sensitivity studies were carried out where limit of detection (LOD) and limit of quantification (LOQ) were determined using following equation.

$$\textbf{LOD} = 3.3\,\sigma/S \qquad \textbf{LOQ} = 10\,\sigma/S$$

Where, σ = the standard deviation of the response.

S = slope of the calibration curve.

RESULTS AND DISCUSSION

The maximum absorption for metoprolol succinate in distilled water and phosphate buffer PH6.8 were observed at 221nm and 223 nm respectively. The high values of correlation coefficient in distilled water and phosphate buffer pH 6.8 indicate linearity for metoprolol succinate in both solvents. Beer's law was obeyed for distilled water and phosphate buffer pH6.8 in the range of 5-30 µg/ml the accuracy of method was determined by calculating mean percentage recovery and %relative error. The Percentage recovery ranges from 99.53 to 100.80 and % relative error was within 2% both solvents and are

presented in Table **4**. Precision was calculated as repeatability , inter and intraday variations for metoprolol succinate, %RSD was found to be less than 1.The repeatability data are presented **In Table 2 and Table 3**. LOD was found to be 1.389 µg/ml for detection of metoprolol succinate in water and 0.1399 µg/ phosphate buffer 6.8. LOQ was found to be 4.2084 µg/ml in distilled water and 0.4240 µg/ml in phosphate buffer pH 6.8. The proposed methods were found to be simple, accurate, precise and rapid for the routine determination of Metoprolol succinate in bulk and combined dosage form.1

Table 1: Optical parameters for determination of Metoprolol succinate

Data	Results	
	Distilled water	Phosphate buffer pH 6.8
Wavelength (nm)	221	223
Slope	0.019	0.027
correlation coefficient	R2= 0.995	R2= 0.992
Intercept	0.015	0.009
LOD(mcg/ml)	1.389	0.1399
LOQ(mcg/ml)	4.2084	0.4240

Precision

Table 2: Intraday variability

Conc (mcg/ml)	Absorbance			Mean	Standard deviation	% RSD
mcg/ml	Trial I	Trial II	Trial III			
5(Water)	0.51	0.50	0.52	0.51	0.01	1.9607
5(pH 6.8 buffer)	0.1693	0.1663	0.1695	0.1683	0.001793	1.0646
10(water)	0.1584	0.1596	0.1577	0.1585	0.000961	0.6059
10(pH6.8 buffer)	0.3487	0.3466	0.3462	0.3471	0.001343	0.3868
15 (water)	0.2622	0.2654	0.2635	0.2636	0.001617	0.6131
15(pH6.8 buffer)	0.4491	0.4488	0.4493	0.4490	0.000252	0.05604

Table 3: Interday variability

Conc (mcg/ml)	Absorbance			Mean	Standard deviation	% RSD
mcg/ml	Trial I	Trial II	Trial III			
5(Water)	0.49	0.5	0.51	0.50	0.008165	1.6329
5(pH 6.8 buffer)	0.1693	0.1649	0.1678	0.1673	0.002237	1.3367
10(water)	0.1584	0.1581	0.1564	0.1573	0.001021	0.6480
10(pH6.8 buffer)	0.3487	0.3452	0.3448	0.3462	0.002146	0.6198
15 (water)	0.2622	0.2643	0.2645	0.2636	0.00104	0.3945
15(pH6.8 buffer)	0.4491	0.4478	0.4465	0.4478	0.0013	0.2903

Table 4: Results of assay:

Formulation	Label claim, mg/tablet	Amount found* Mg/tablet	% Amount found	% C. V.
Brand I (LOPRESOR)	23.75	23.64	99.53	0.3181
Brand II (METSCORE)	23.75	23.85	100.42	1.646

***Mean of three determinations.**

Table 5: Recovery study

Sr.No.	Label claim, Mg/tablet	Amount of standard added,mg	Total amount recovered/mg	% recovery	Standard Deviation	% relative standard deviation
1	25	5	29.37	97.66 %	0.0002	0.02527
2	25	10	34.36	98.94%	0.000737	0.0782
3	25	15	37.02	93.55%	0.000351	0.0351

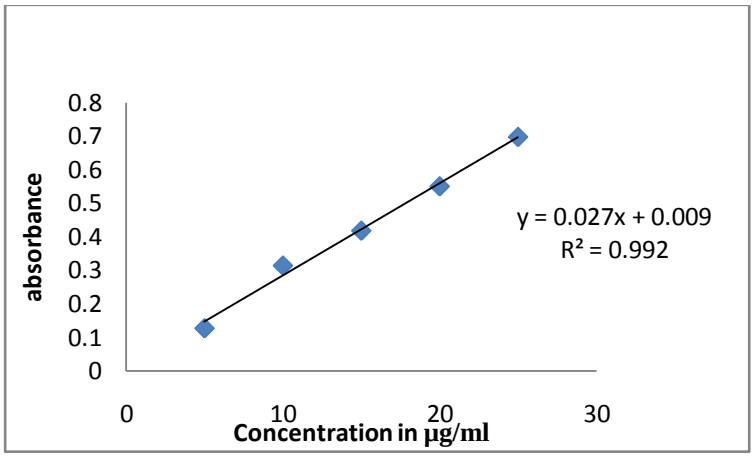


Fig.1: Calibration curve of metoprolol succinate in pH 6.8 phosphate buffer.

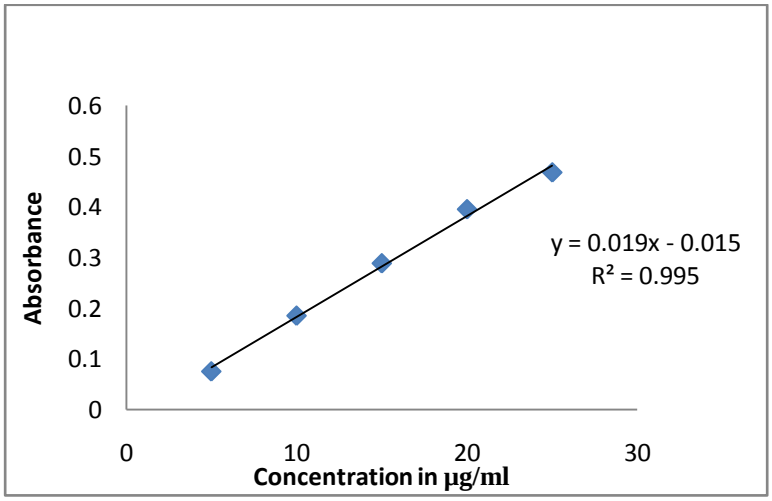


Fig.2: Calibration curve of metoprolol succinate in distilled water.

CONCLUSION

Simple spectrophotometric method for determination of metoprolol succinate have been developed and validated as per ICH guidelines. The proposed method is found to be simple, rapid, sensitive, accurate and reproducible also can be used for the routine quality control analysis of metoprolol succinate in bulk and pharmaceutical formulations.

REFERENCES

1. Jaiswal J., Anantawar S.P., Narkhede M.R., Gore S.V., And Mehta K. Formulation and evaluation of thermo reversible in situ gel of metoprolol succinate.

International journal of pharmacy and pharmaceutical sciences, 4(3): 96-102, (2012).
2. The Merck Index, , Merck Res. Lab. Division of Merck and Co. Inc, Whitehouse station, New Jersey, USA. Fourteenth edn: 6151, (2009).
3. Gaikwad V. Formulation and evaluation of In-Situ gel of metoprolol tartarate for nasal delivery. Journal of Pharmacy Research, 3(4): 788-793, (2010).
4. Moffat A.C., Osselton M.D., Widdop B. Clarke's Analysis of Drugs and Poisons in pharmaceuticals, body fluids and postmortem material.. Pharmaceutical Press, London. 3rd edn: 1275-1276, (2004)
5. http://www. Drug Bank Metoprolol (DB00264). Htm (19 November 2013).
6. Sweetman S.C., Martindale, The complete drug reference. Pharmaceutical Press, Great Britain. 34thedn: 1201, (1202 2005).
7. Q2A: Text on; Validation of Analytical Procedures. In International Conference on Harmonization. Federal Register, 60 (40): 11260–11262, (1995).
8. Q2B: Validation of Analytical Procedures: Methodology, Availability. In International Conference on Harmonization. Federal Register, 62 (96): 27463–27467, (1997).
9. Kulkarni M.N., Rajeshwar V.K., Shirsagar R.V., Sakarkar D.M., development and validation of spectrophotometric method for determination of metoprolol succinate. International Journal of ChemTech Research, 1(4):1273-1277, (2009).
10. Jadhav A. S., Tarkase K. N., Deshpande A.P., Quantitative Determination of Metoprolol Succinate in bulk and tablet dosage form through comparative study of UV and derivative Spectroscopy. Der Pharmacia Letter, 4 (3): 763-767, (2012).
11. Salem., Hesham., Abdallah., Ola M., Determination of Metoprolol and Felodipin in binary mixture using chemometric –assisted spectrophotometric and high performance liquid chromatographic –UV methods. American Journal of Applied Sciences,4(9):709-711,(2007).
12. Rahman N., Rahman. Aami S. N. validated kinetic spectrophotometric method for determination of Metoprolol Tartarate in pharmaceutical formulations. Chem. Pharm. Bull, 53(8): 942-948, (2005).

***Corresponding Author:**
S.A.Pagar*
Department of Pharmaceutics,
KCT'S RGS College of Pharmacy,
Anjaneri, Nashik, 422 213.
Maharashtra, India.
Email: swati.pagar2210@gmail.com