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Spectrophotometric Estimation of Metoprolol Succinate by using different Hydrotropic agents

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ABSTRACT

The present study describes simple, sensitive, rapid, accurate, precise and economical spectrophotometric method for determination of Metoprolol Succinate. The spectrophotometric estimation and area under curve method is used for the analysis of the Metoprolol Succinate using an hydrotropic agent as a solvent. Metoprolol Succinate has absorbance maxima at 272 nm. Area under curve method was based on measurement of area under curve (AUC) in the wavelength range 262nm to 282nm. In both spectrophotometric methods, linearity of Metoprolol was found in the concentration range 5 to 30µg/ml by using various hydrotropic agents. The concentrations of the drugs were determined by using simultaneous equations method. The mean recovery was 99.63 ± 0.47 for Metoprolol Succinate. The method was found to be simple, sensitive, accurate and precise and was applicable for the determination of Metoprolol Succinate using hydrotopic agents. The results of analysis have been validated statistically and by recovery studies. Limit of detection and quantization in all methods were found laser in potassium acetate as compared to other hydrotropic agents used in studies. The objective of the present study is to explore the application of hydrotropy in spectrophotometric analysis of Metoprolol to replace the use of organic solvents which may be costlier, toxic and pollutant.

Keywords: Metoprolol Succinate, Hydrotropic agents, Area under Curve method.

INTRODUCTION

Metoprolol Succinate is chemically bis-[(2RS)-1-[4-(2-methoxyethyl) phenoxy]-3-[(1-methylethyl)amino]propan-2-ol] butanedioate (2:1) (salt). It is a white crystalline powder with formula $(C_{15}H_{25}NO_3)_2 \cdot C_4H_6O_4$ and molecular mass 652.81 g mol^{-1}. It is used as a selective β1 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). It acts by blocking ß1 the adrenoreceptors and is almost completely absorbed (95%) after oral administration, although the systemic bioavailability varies widely owing to extensive presystemic metabolism (40–60%). Peak plasma concentrations are achieved after 2–3 hours. The plasma half-life is about four hours [1-4].

Metoprolol is official in Indian Pharmacopoeia (IP), British Pharmacopoeia (BP) and United States Pharmacopoeia (USP). IP, BP and USP describe potentiometric method for its estimation. Various methods like UV Spectrophotometry, HPTLC, and RP-HPLC method for simultaneous determination of

Metoprolol with other drug are reported in literature for estimation of Metoprolol in pharmaceutical dosage forms as well as in biological fluids using methanol [3,4,6].

Metoprolol is freely soluble in alcohol and solubility in water is 16.9 mg/ml. Special techniques are required to solubilize poorly water-soluble drugs; Hydrotropy is one of such technique. The proposed method utilize solutions of non-toxic, non-volatile hydrotropic agents which are the substitutes and minimizes the use of organic solvents which are costlier, toxic and source of pollutant[5]. The term hydrotropic agent was first introduced by Newberg (1916) to designate anionic organic salts which, at high concentrations, considerably increase the aqueous solubility of poorly soluble solutes. Hydrotropic compounds are compounds that at high concentration solubilize poorly soluble molecule in water. The self- aggregation of hydrotropic agents is different from the surfactant self assemblies in that, hydrotropes form planar or open layer self assemblies instead of compact spheroid assemblies. Hydrotropic agents are characterized by a short, bulky compact moiety while surfactants have long hydrocarbon chain. In general, hydrotropic agents have a shorter hydrophobic segment, leading to high water solubility than surfactants. The hydrotropy is suggested to be superior to other solubilization methods such as micellar solubilization, co solvency, miscibility and salting in, because the solvent character is independent of pH, has high selectivity and does not require emulsification [7].

Concentrated aqueous solutions of large number of hydrotropic agents have been employed to enhance the aqueous solubility of many poorly water soluble drugs. Hydrotropic solutions can also be used as co-solvents, in solid dispersion technology, nanotechnology and parenteral Preparations[8,9]. Sodium benzoate, sodium salicylate, sodium acetate, sodium ascorbate, niacinamide, sodium citrate, urea are the most popular examples of hydrotropic agents which have been used to solubilize a large number of poorly water-soluble compounds [10].

MATERIALS AND METHODS

A shimadzu model 1800 (Japan) double beam UV/Visible spectrophotometer with spectral width of 2 nm, wavelength accuracy of 0.5 nm and a pair of 10 mm matched quartz cell was used to measure absorbance of all the solutions. Spectra were automatically obtained by UV-Probe system software (UV Probe version 2.10). A Sartorius CP224S analytical balance (Gottingen, Germany), an ultrasonic bath (Frontline FS 4, Mumbai, India) was used in the study.

Metoprolol Succinate pure drug was kindly gifted by Astron Research Centre, Ahmadabad, Gujarat, India. The commercial fixed dose combination product was procured from the local market. Methanol (AR Grade, Finar Chemicals Ltd., Ahmadabad, India) and Whatman filter paper no. 41 Millipore, USA), ammonium acetate, potassium acetate, potassium citrate, sodium acetate, sodium citrate and urea were of analytical grade.

Standard stock solution : Standard drug solution of Metoprolol Succinate was prepared by dissolving 100mg pure Metoprolol Succinate in each hydrotropic agent and transferred into 100ml volumetric flask to obtain 100µg/ml of stock solution from which desired concentrations 5, 10, 15, 20, 25, 30 µg ml^{-1} of solutions were prepared and analyzed at 272 nm.

Sample preparation : Twenty tablets were weighed; average weight was determined and finely powdered. An accurately weighed quantity of tablet powder equivalent to 100mg of Metoprolol Succinate was transferred to 100 mL volumetric flask and dissolved by sonication with sufficient quantity of each hydrotropic agent, 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 each hydrotropic agent in a 10 ml volumetric flask up to mark (10 µg ml^{-1}) on label claim basis. The absorbance of the resulting solution was measured at 272 nm (method II) against solvent blank.

Selection of scanning wavelength: After spectrophotometric method development bands where scan over the range 150- 350nm. And the spectra were obtained .it was observed that the Metoprolol Succinate showed maximum absorption at 272 isobestic point 265 nm for all the measurements.

METHOD DEVELOPMENT

Linearity: In conventional spectrophotometric method, absorbance was noted in the concentration range of 5 µg ml^{-1} to 30 µg ml^{-1}. In area under curve method, area of spectra was noted between 262 nm to 282 nm (272 nm ± 10 nm).

Limit of detection (LOD) and limit of quantization (LOQ): The detection limit and quantization limit were computed to assess quantity of analyte which can be detected and minimum quantity of analyte which can be determined quantitatively by proposed UV- spectrophotometric method.

Accuracy : To study the accuracy of the proposed methods in both Spectrophotometric recovery study were carried out by addition of known amount of standard drug in the pre analyzed tablet formulation, in 50%, 100% and 150 % of label claim. At each level of concentration, five determinations were performed. The required statistical parameters were evaluated to determine the accuracy of method.

RESULTS AND DISCUSSION

The criteria for the selection of hydrotropic agents in spectrophotometric methods include, 'sufficient concentration and volume of hydrotropic agents which completely solubilize content of drug' and these hydrotropic agents should not interfere in analyses. We have used five different hydrotropic solutions such as ammonium acetate (6M), potassium acetate (5.0 M), potassium citrate (0.5 M), sodium citrate (1.25 M) and urea (10.0 M) in distilled water. Sufficient volumes of these hydrotropic solutions were used to solubilize the content of Metoprolol completely. Hydrotropic solutions selected for this work in spectrophotometric methods have not shown any interference above 262 nm, depicted in fig. 1 and fig. 2; therefore metoprolol can be estimated by using these hydrotropic agents. The linearity was found in concentration range of 5 to 30 µg/ml for Metoprolol in all hydrotropic agents for both Spectrophotometric methods and summarized in Table 2. The limit of detection and quantization was computed for Metoprolol in all hydrotropic agents and reported in Table 1 for spectrometric methods .

Percentage recovery was found in the range of 97.4 % to 107.8 % for Metoprolol by conventional Spectrophotometric estimation and 99.50 % to 104.7 % by AUC method. The Spectrophotometric methods showed more sensitivity for Metoprolol estimation by using potassium acetate as a hydrotropic agent and minimum sensitivity observed for sodium citrate.

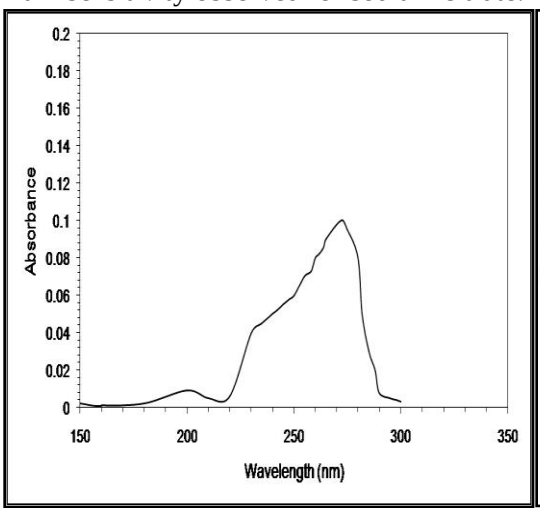

Figure 1: Spectrum of Metoprolol by using Ammonium Acetate

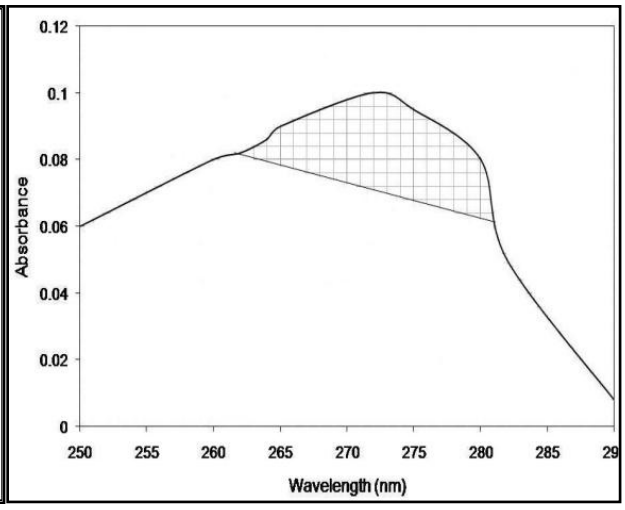

Figure 2: Area under curve between 262 to 282nm

TABLE 1: Result of recovery study for Spectrophotometric Method

Hydrotropic Agent	Volume of Hydrotropic Agent(%v/v)	Method I			Method II		
		Linearity 4-30 µg/ml	LOD µg/ml	LOQ µg/ml	Linearity 4-30 µg/ml	LOD µg/ml	LOQ µg/ml
6M AMMONIUM ACETATE	10	y=0.0407x+0.0045 r^2=0.9992	0.7	2.3	y=0.0659x+0.0476 r^2=0.9954	0.8	2.1
5M POTASSIUM ACETATE	4	y=0.0468x+0.0344 r^2=0.9991	0.5	1.2	y=0.0707x+0.0045 r^2=0.9992	0.7	2.3
0.5M POTASSIUM CITRATE	4	y=0.0459x+0.0476 r^2=0.9956	0.8	2.4	y=0.0656x+0.038 r^2=0.9995	0.9	1.8
1.25M SODIUM CITRATE	10	y=0.0456x+0.038 r^2=0.9997	0.9	2.8	y=0.0694x+0.0011 r^2=0.9993	1.1	3.2
8M UREA	10	y=0.0418x+0.0047 r^2=0.9995	0.9	2.8	y=0.0468x+0.0344 r^2=0.9991	0.5	1.2

TABLE 2: Result of Spectrophotometric Method

Hydrotropic Agent	Method	Amount of standard drug Added %	% lable claim estimated (mean + s.d)	% RSD
AMMONIUM ACETATE	I	50	100.7±1.6	1.6
		100	101.3±0.7	0.7
		150	107.8±0.5	0.5
	II	50	103.9±3.2	3.2
		100	102.7±0.4	0.4
		150	101.5±0.4	0.4
POTASSIUM ACETATE	I	50	104.8±0.5	0.4
		100	100.7±1.6	1.6
		150	104.8±0.5	0.4
	II	50	107.8±0.5	0.5
		100	102.7±0.4	0.4
		150	104.8±0.5	0.4
POTASSIUM CITRATE	I	50	107.8±0.5	0.5
		100	101.5±0.4	0.4
		150	100.7±1.6	1.6
	II	50	102.7±0.4	0.4
		100	104.8±0.5	0.4
		150	107.8±0.5	0.5
SODIUM CITRATE	I	50	100.7±1.6	1.6
		100	101.5±0.4	0.4
		150	102.7±0.4	0.4
	II	50	102.7±0.4	0.4
		100	107.8±0.5	0.5
		150	100.7±1.6	1.6
UREA	I	50	101.5±0.4	0.4
		100	100.7±1.6	1.6
		150	107.8±0.5	0.5
	II	50	100.7±1.6	1.6
		100	107.8±0.5	0.5
		150	101.5±0.4	0.4

APPLICATION

The developed method is an alternative and useful method for the estimation of poorly water soluble drugs by minimizing organic solvents. It is an eco-friendly method.

CONCLUSION

Developed spectrophotometric and chromatographic methods for estimation of Metoprolol by using different hydrotropic agents was found to be the best alternative for estimations of poorly water soluble drugs and minimize the use organic solvents. The proposed method utilizes solution of non-toxic, non-volatile hydrotropic agents which give a novel, economical and eco- friendly method for the estimation of Metoprolol in tablet dosage forms.

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