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Method Development, Validation & Forced Degradation Studies For The Determination Of Metoprolol Succinate In Bulk & Pharmaceutical Dosage Form Using Uv Spectroscopy

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ABSTRACT

Metoprolol succinate is beta1-selective (cardioselective) adrenoceptor blocking agent approved by the US Food and Drug Administration (FDA) for the treatment of high blood pressure. The UV spectroscopic method has been developed for the determination of Metoprolol succinate at the wavelength range between the 200-400 nm. Metoprolol succinate showed an absorption peak at 223 nm. Linearity ranges were found as 2-50 microgram. Developed method was found to be validated and showed good precision and reproducibility. Forced degradation studies were performed by subjecting Metoprolol succinate to stress conditions such as acid & base hydrolysis, oxidation, thermal degradation and photolysis. The degraded samples were further analysed by using the developed method to determine the degradation behaviour and the amount of Metoprolol succinate degraded.

INTRODUCTION

Metoprolol is in a class of medications called beta blockers. It works by relaxing blood vessels and slowing heart rate to improve blood flow and decrease blood pressure.

Drug Profile:

PARAMETERS	DESCRIPTION
CHEMICAL NAME	(±)1- (isopropylamino)-3-[p-(2-methoxyethyl) phenoxy]-2-propanol succinate (2:1) (salt)[1]
MOLECULAR FORMULA	C34H56N2O10
MOLECULAR WEIGHT	652.8
PHYSICAL APPEARANCE OF DRUG	A white powder with crystals or colourless crystals [19]
CLASS	Antagonist of beta-adrenoceptors
DOSE	100 to 450 mg daily in split doses; the first dose should not exceed 100 mg
SOLUBILITY	It is soluble in methanol, easily soluble in water, sparingly soluble in ethanol (95 percent), and slightly soluble in isopropyl alcohol. [2]
MELTING POINT	135^0C
λmax	223 nm
PH LEVEL	6.8
HEAVY METALS	2.0 g is incompliance with Method 10ppm, the heavy metal limit test.
SULPHATE ASH	In no event exceed 0.1 percent
LOSS DURING DRYING	Not more than 0.2%, ascertained after four hours of drying at 60° in a vacuum.
ACTION MECHANISM.	Metoprolol is a drug that blocks beta1- picky (cardioselective) adrenergic receptors. This picky impact isn't absolute, however, as metoprolol also blocks beta2- adrenoreceptors, which are substantially set up in the vascular and bronchial musculature, at lesser tube attention. Metoprolol lacks natural sympathomimetic action, and at tube attention significantly advanced than those demanded for beta- leaguer, membrane- stabilizing exertion can only be observed. Studies on humans and creatures show that metoprolol reduces AV nodal conduction and detainments the sinus rate. [2]

UV Spectroscopic Method Instrumentation

A UV-Visible Spectrophotometer with 10 mm matched quartz cells was used for Spectrophotometric method. All weighing was done on electronic balance.

Reagents and chemicals

Metoprolol succinate was received as gift sample from Miss. Smita A. Navale Assistant professor (Dept. of Quality Assurance) VNCOP Lakhewadi. Tablet formulation manufactured

by USV Private limited was purchased from local market METOZOK-50 containing metoprolol succinate 50 mg per tablet**.**

Preparation of standard stock solution

Standard drug solution of metoprolol succinate was prepared by accurately weighing 10 mg of the drug, and dissolved in phosphate buffer pH 6.8 and the volume was made up to 100 ml to obtain stock solution (100 µg/ml).

Determination of Analytical Wavelength

From the standard stock solution 1 ml was pipette out into 10 ml volumetric flask. The volume was made up to 10 ml with phosphate buffer. The resulting solution containing 10 µg/ml was scanned between 200-400 nm.

Preparation of Calibration Curve

portions of stock solutions were transferred to a series of 10 ml volumetric flasks and volume made up to the mark with phosphate buffer. The serial dilutions in the range of 2, 4, 6, 8, and 10 µg/ml were prepared. The absorbance was measured at λmax 223 nm

UV Method Validation

Linearity

The linearity of the response of the drug was verified at 2 to 10 µg/ml concentrations. The calibration curve was obtained by plotting the absorbance versus the concentration data and was treated by linear regression analysis. The equation of the calibration curve for metoprolol was obtained.[3-7]

Limit of Detection (LOD) and Limit of Quantification (LOQ)

LOD and LOQ were calculated by the equations;

$$LOD = 3.3\sigma / S \text{ and } LOQ = 10\sigma/S$$

Where S is the slope of the calibration curve and σ is the residual standard deviation.[3]

Precision

The accuracy of the method was determined by recovery experiments. Each solution was repeated in triplicate and the percentage recovery was calculated. The precision of the method was demonstrated by intra-day and inter-day variation studies.[3]

Accuracy

Accuracy of the method was studied by recovery experiments. The recovery was performed at three levels 80, 100 and 120% of metoprolol standard concentration. Three samples were prepared for each recovery level. The solutions were then analyzed, and the percentage recoveries were calculated from the calibration curve. The recovery value for metoprolol was 99.71 ± 0.493 and RSD was 0.495 which is less than 2, which shows that the method has good reproducibility (Table 3).

RESULTS AND DISCUSSION

Linearity

The linearity of the response of the drug was verified at 2, 4, 6, 8 and 10 µg/ml concentrations.

Concentration(mg/ml)	Absorbance (223 nm)
2	0.0630
4	0.0896
6	0.1161
8	0.1436
10	0.1706

Table 1: Result of calibration curve at 223 nm for Metoprolol succinate

Precision

Precision of the method was evaluated for metoprolol. The reproducibility (inter-day precision) of the method and repeatability (intra-day precision) was evaluated in the same laboratory. The values obtained were 0.1935 and 0.2539 respectively (Table 2).

Precision	Intra-Day Precision*	Inter-Day Precision*
Result	0.2539	0.1935

Table 2: Precision determinations

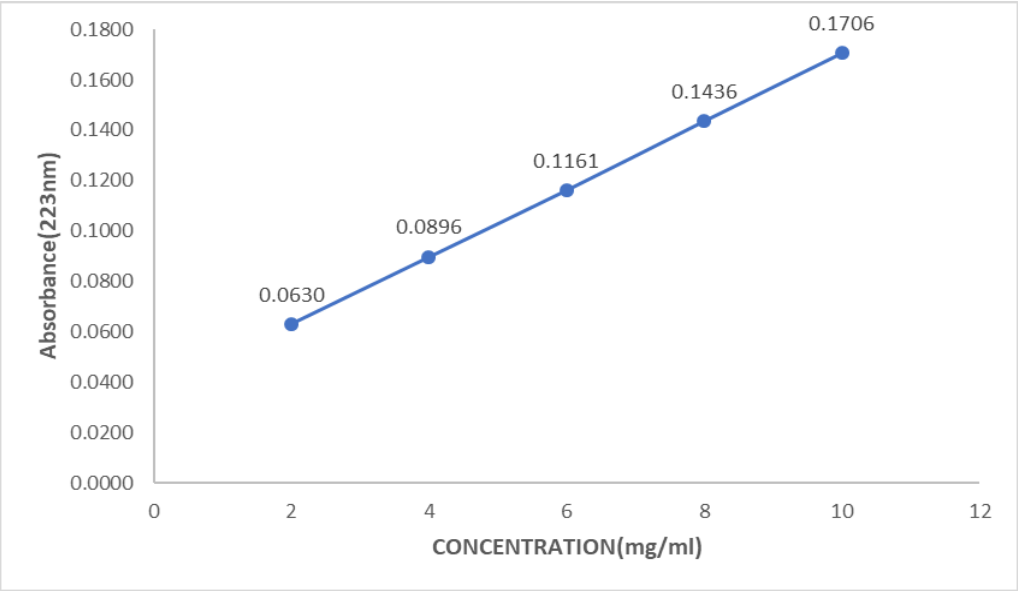

Fig.1. Linearity curve for the Metoprolol succinate at 223 nm

Drug	Pre-analyzed conc. (µg/ml)	Concentration	Wavelength (223 nm)	
			Conc.recovered	% Recovery
METOPROLOL SUCCINATE	100	80	20.03	100.15
		100	15.96	99.79
		120	19.96	99.83

Table 3: Recovery Study (UV)

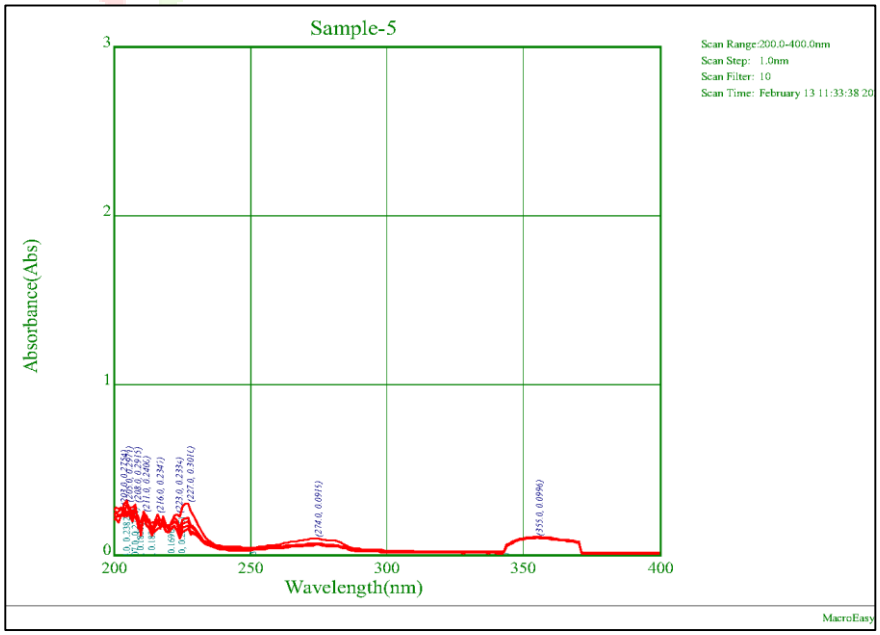

Fig.2. Absorbance (λmax)

Forced Degradation Studies

Forced degradation is the process of subjecting drug to extreme chemical and environmental conditions. Forced degradation studies show the chemical behaviour of the molecule and provide an approach to analyse the stability of drug. It provides an insight into degradation pathways and degradation products of the drug substance and helps in elucidation of the structure of the degradation products. Forced degradation studies are done as per the ICH guidelines: ICH Q1A: Stability Testing of New Drug Substances and Products and ICH Q1B: Photo Stability Testing of New Drug Substances and Products. Degradation studies are performed under acidic, basic hydrolysis, oxidation, thermal and photolytic conditions. [8,9]

Acid Degradation

From 100µg/ml Metoprolol Succinate standard solution 1 ml was pipetted out in to a 10 ml volumetric flask. To this 1 ml of 0.1 N HCl was added and allowed to stand for 24 hr. [10]

Alkali Degradation

From 100µg/ml Metoprolol Succinate standard solution 1 ml was pipetted out in to a 10 ml V.F. To this 1 ml of 0.1 N NaOH was added and allowed to stand for 24 hr. [10]

Oxidative Degradation

From 100µg/ml Metoprolol Succinate standard solution 1 ml was pipetted out in to a 10 ml V.F. To this 1 ml of 3 % H2O2 solution was added and allowed to stand for 24 hr. [10,11]

Thermal Degradation

Metoprolol Succinate drug was exposed to 40°C temperature in a hot air oven. After 4 hr required amount of drug was taken and 10µg/ml solution was prepared using ACN as diluent. Absorbance of the solution was measured at 223 nm and amount of drug degraded was calculated. [11]

RESULT:

Degradation type	Experimental conditions	Storage conditions	Sampling time (days)	Percentage Degradation (%)
Hydrolysis	Control API (no acid or base)	25 ^{0}C	1	0%
a) Acid	0.1 N HCl	37^{0}C	1	16.60%
	Acid control (With API)	37^{0}C	1	
b) Base	0.1 N NaOH	37^{0}C	1	17.12%
	Base control (With API)	37^{0}C	1	
Oxidation	3% H_2O_2	37^{0}C	1	43.49%
	Peroxide control	37^{0}C	1	
Thermal	Heat chamber	40^{0}C	4hr	8.31%
	Heat control	Room temp.	1	

Table 4: Forced Degradation

CONCLUSION

A simple, rapid, accurate and reproducible UV Spectroscopic method was developed and validated as per the ICH guidelines. The method was used for assessing the degradation behaviour of the Metoprolol succinate under different stress conditions as per ICH guidelines. Results show that the drug undergoes most degradation under peroxid conditions. All the validation parameters were found to be within the limits. Therefore, this method can be used for routine quality control tests of Metoprolol succinate in bulk drug and pharmaceutical formulation.

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