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Spectrophotometric determination of metoprolol by charge-transfer complexation

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ABSTRACT

This paper presents a simple, sensitive and accurate spectrophotometric method for the determination of metoprolol tartrate in dosage forms and in biological fluid samples. The method is based on the reaction of the drug as n-electron donor with the pi-acceptor Folin Reagent (NQS). The obtained charge transfer complex was measured at 469 nm. Beer's law is obeyed in the concentration range of 7.6-26.2 μg ml^{-1} with correlation coefficient 0.9995. Molar absorbance, Sandell sensitivity, limit of detection and limit of quantification were calculated. The results obtained by proposed method were statistically validated. This method was successfully evaluated for the estimation of drug in commercially available formulations and in biological fluid samples with good recovery and reproducibility.

KEYWORDS

Metoprolol;
Folin Reagent (NQS);
Spectrophotometric method;
Charge transfer complex;
Correlation coefficient;
Sandell's sensitivity;
Biological fluid samples.

INTRODUCTION

Metoprolol is a white crystalline powder with chemical formula $C_{15}H_{25}NO_3$ and molecular weight 267.364 g/mol. Chemically, it is (*RS*)-1-(isopropylamino)-3-[4-(2-methoxy-ethyl) phenoxy] propan-2-ol[1]. This drug is used as beta blocker. Clinically, beta blockers are important drugs used in the treatment of disorders like hypertension, angina pectoris and arrhythmia[2]. They are also used in the treatment of Congestive Heart Failure (CHF) and myocardial infraction[3]. Metoprolol has been determined by several analytical methods such as thin layer chromatography[4,5], Infrared spectroscopy[6], gas chromatography[7], and spectrophotometric method[8]. These methods, however, suffer from disadvantages such as lack of sensitivity, accuracy and selectivity.

Hence, in the present investigation, an attempt has been made to develop a new spectrophotometric method which is simple, low cost, selective and more accurate than the existing methods for the determination of metoprolol in pharmaceutical formulations and in biological fluid samples. This method is based on the reaction of the drug with folin Reagent (NQS) and measuring the obtained charge

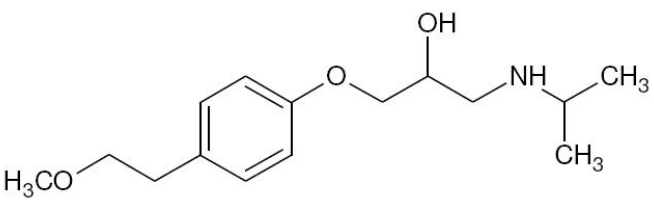


Figure 1 : Structure of metoprolol

transfer complexes.

EXPERIMENTAL

Apparatus

Schimadzu UV-visible double beam spectrophotometer (model 2450) with 1 cm matched quartz cells was used fo all the spectral measurements.

Materials and reagents

All chemicals and reagents used were of analytical grade and procured from S.D. Fine Chem, Mumbai, India. Double distilled water was used for all the experimental studies. Pharmaceutical grade metoprolol was procured from Sigma Aldrich. Pharmaceutical formulations metolar and betaloc were procured from local market. From the above stock solutions, required solutions were prepared by dilution with double distilled water.

Preparation of standard solutions

The standard stock solution of metoprolol was prepared by taking accurately weighed sample of 100 g of metoprolol in100 ml standard flask, from this stock solution 10 ml was pipetted out into a 100ml standard flask and made up the mark with methanol to get 100 µg/ml concentration. This solution was further diluted to get appropriate concentrations of 5-50 µg/ml for the current investigations.

Procedure

Different aliquots of standard metoprolol solution ranging from 1.0 – 1.8 ml (10 - 18µg/ ml) were taken in series of 10 ml of volumetric flasks. To each flask 1 ml of folin reagent (1.092×10^{-2} M) was added and the entire contents were diluted with distilled water by adjusting the volume to 8 ml with help of a micro burette and the entire contents are kept aside at laboratory temperature for 15 – 20 min, which results in the formation of yellowish brown colour. Now, the volume is made to 10 ml and stirred well. The absorbance of was measured at 469 nm against the blank and the amount of drug in the solution was computed from the calibration graph.

RESULTS AND DISCUSSION

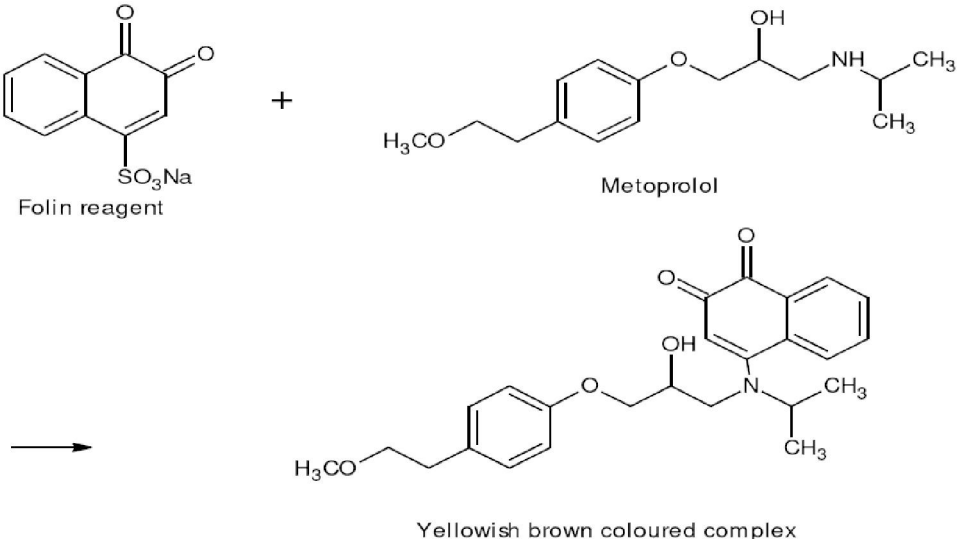
Absorption spectrum

Metopropol was spectrophotometrically determined by the reaction of NQS (1, 2 Napthaquinone 4-sulphonic acid) with metoprolol. A maximum absorbance of 469 nm was observed against the blank regent with the formation of yellowish brown complex. Based on reaction stoichiometry, a probable reaction scheme has been proposed (Scheme-III)[9].

Method validation

Linearity

The linearity of calibration graphs are proved by high values of correlation coefficient and small values of y- intercept of the regression equation. The molar



Scheme I : Path way for the reaction of metoprolol with NQS

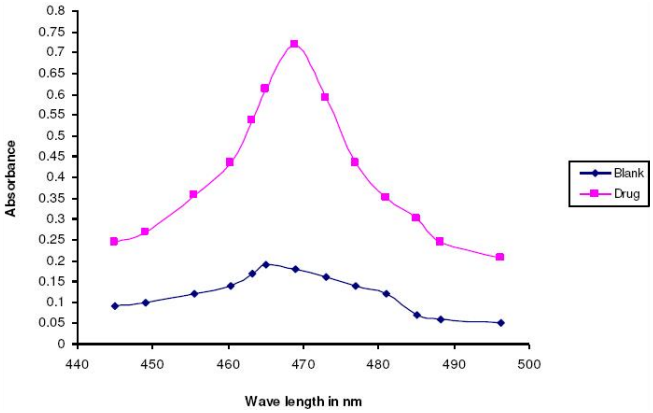


Figure 2 : Absorption spectrum of metoprolol with folin reagent

absorbtivities of the colored complexes and relative standard deviation for the proposed spectrophotometric method were also calculated and shown in table 1.

TABLE 1 : Optical characteristics of proposed method

Parameter	value
λ_{max} (nm)	469
Beer's law limit (µg/ml)	7.6-26.2
Molar absorbance ($L.mol^{-1}$ cm^{-1})	0.66
Sandell's sensitivity ($\mu g.cm^{-2}$/0.001 A.U)	0.0015
Correlation coefficient (r^2)	0.9995
Slope (m)	0.0253
Intercept (c)	0.0104
%RSD	0.1515
Colour	Yellowish-Brown
LOD	0.1182
LOQ	0.3936

Robustness and ruggedness

In the study of robustness, some parameters like pH range, concentrations of the drug and reagents, shaking time were interchanged. Even after that, the results were unaffected by small deliberate and shaking time.

The percentage of relative standard deviation for the proposed method developed by two analysts in two

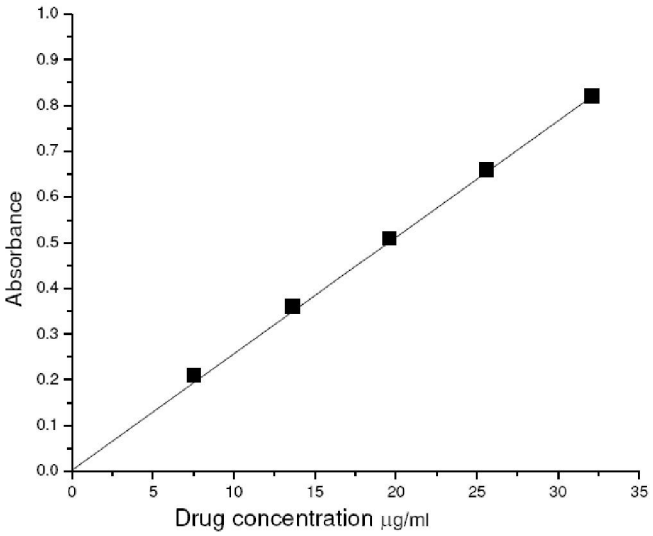


Figure 3 :Calibration plot of metoprolol

different instruments in two different days proved that there is no statistical difference between the above said two analysts and instruments which concludes the developed analytical method was robust and rugged.

Precision

The precision of the proposed analytical method was studied as intraday and inter day precision. Precision is to measure the ability to create reproducible results. The intraday and inter day precision was determined by analyzing the same concentration of the solutions on three different days and the obtained RSD% is less than 1 (TABLE 2) which proves that there is no considerable difference for the assay.

Analytical Applications

Assay of pharmaceuticals

For the determination of the drug metoprolol in tablet formulations, the contents of 2 tablets were weighed and finely powdered, a portion of powder equivalent to 50mg of the drug was taken into 50 ml standard flask and dissolved with small portion of methanol and made up to the mark with the same solvent. The contents in the flask are filtered on whatmann No. 41 filter

TABLE 2 : Evaluation of intra-day and inter day accuracy

Taken (mg/ml)	Intra day				Inter day			
	*Found	Recover%	± SD	%RSD	*Found	Recovery%	± SD	% RSD
	(mg/ml)				(mg/ml)			
4	3.98	99.60	0.011	0.2959	3.985	99.62	0.005	0.13
8	7.95	99.45	0.055	0.6934	7.894	98.68	0.099	1.25

*Average of five determination

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paper and washed well with methanol for the complete recovery of the drug. The resulting concentration of the solution was found to be 1 mg/ml. This solution is considered as stock solution and the required aliquots were taken from the solution for the determination of the drug metoprolol by the proposed method and these results are shown in TABLE 3. The proposed method has been applied for the determination of metoprolol in bulk samples and the obtained results were compares with official method. From the obtaines Student's t value and F values (TABLE 4), it was proved that the proposed method can be successfully applied or the determination of metoprolol with high accuracy.

Assay in serum and urine samples

TABLE 3 : Determination of metoprolol in pharmaceutical dosage

Pharmaceutical formulation	Labeled amount(mg/ml)	*Found(mg/ml)	% Recovery	± SD	%RSD
Metolar	20	19.97	99.87	0.005	0.0251
Betaloc	25	24.98	99.93	0.007	0.0310

***Average of five determinations**

TABLE 4 : Statistical analysis of the results obtained for assay of metoprolol using the proposed methods compared with the official method[11]

	Proposed Method	Official Method
Recovery percentage	99.26	99.03
±SD	0.92	1.03
N	6	6
t (2.571)[a]	0.459	
F (5.05)[a]	1.03	

[a]Values between parentheses are the tabulated t and F values, at p 0.05

TABLE 5 : Method accuracy from recovery assay

Sample	Added (mg/ml)	*Found (mg/ml)	Recovery (mg/ml)	± SD	RSD%
Serum samples	0.6	0.59	99.22	0.0055	0.92
	1	0.99	99.41	0.0026	0.26
	1.2	1.19	99.58	0.0052	0.44
Urine samples	1.6	1.59	99.58	0.0064	0.40
	1.4	1.39	99.57	0.0045	0.32
	1.8	1.78	99.20	0.0152	0.85
	2.0	1.99	99.61	0.0035	0.17
	2.4	2.39	99.83	0.0026	0.11

***Average of five determinations**

Blood and urine samples were collected from donors and were centrifuged at 3000 rpm per min. for nearly 10 min. The resulted solutions were filtered and preserved in the absence of light at a temperature of 4°C. From these solutions, various concentrations of the drug metoprolol were analyzed and these results were presented in TABLE 5. Based on the percentage of recovery, it has been proved that the proposed method can be successfully applied to determine metoprolol in biological samples viz., urine and serum.

CONCLUSIONS

In the proposed spectrophotometric method, the drug metoprolol was estimated in bulk, pharmaceutical formulations and serum samples and compared with official method[10]. The proposed analytical method is free from interference due to the excipients and other impurities present in the tablet forms. Calculated Student's t value and f value indicate that the proposed spectrophotometric method was accurate, precise, sensitive and selective and can be successfully applied for the estimation of the drug metoprolol in tablets and biological fluids.

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