Spectrophotometric Determination of Betaxolol Hydrochloride and Metoprolol Tartrate

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A simple, sensitive and accurate spectrophotometric method has been developed for the determination of betaxolol hydrochloride and metoprolol tartrate in bulk and from pharmaceutical dosage forms. This is an indirect method for the estimation of betaxolol hydrochloride and metoprolol tartrate, which involves oxidation of drug by N-bromosuccinimide and estimation of unreacted N-bromosuccinimide with metol-sulphanilamide reagent. The charge transfer complex so formed is estimated at 520 nm. Both the drugs obey Beer's law in the concentration range of 4-40 mg/ml.

Betaxolol hydrochloride (BX) is a cardioselective β_1-adrenergic blocker used in the management of glaucoma and ocular hypertension[1]. Chemically it is 1-{4-[2-(cyclopropyl methoxy) ethyl] phenoxy}-3-isopropylaminopropan-2-ol hydrochloride. Metoprolol tartrate (MT) is a b-adrenoreceptor-blocking agent used in the management of angina pectoris, cardiac arrhythmia and hypertension[2]. Chemically it is, 1-[4-(2-methoxy ethyl) phenoxy]-3-[1-methylethylamino]-2-propanol][3]. Both are official in USP[3,4] and MT is also official in IP[5]. Literature survey revealed few spectrophotometric methods[5-7] for MT only and none were reported for BX.

All the reagents used in the current investigation were of analytical grade. Aqueous solutions of acetic acid (3.5x 10^{-1}M), N-bromosuccinimide (NBS) (2.53x10^{-3}M) and metol (8.71x 10^{-3}M) were prepared in double distilled water. Sulphanilamide (SA) (1.16x10^{-3}M) was prepared by dissolving in 5 ml of 0.1N HCl and diluted with double distilled water. Spectral and absorbance measurements were made on an Elico SL 159 UV/Vis spectrophotometer using 1-cm quartz cells at 27±3°. Afcoset ER-200A electronic balance was used for weighing the samples.

Twenty five milligrams of each drug was weighed accurately and dissolved in 25 ml distilled water separately to give stock solutions of concentration 1 mg/ml. From this stock solution, suitable dilutions made with distilled water to get working standard solution of 200 mg/ml.

Commercially available ophthalmic solutions containing BX and tablets and injection containing MT were procured from local market. Five milliliters of eye drops was dissolved in 100 ml of distilled water and used for analysis. Twenty MT tablets were taken and powdered. From this, powder equivalent to 100 mg of MT was weighed accurately and dissolved in 70 ml of distilled water. Then it was heated on water bath for 20 min and filtered. The filtrate was diluted up to 100 ml with distilled and further dilutions were made with distilled water to get the concentrations in the linearity range. One milliliter of injection containing MT was dissolved in distilled water and diluted with distilled water to 25 ml and estimated.

Aliquots of the working standard solution of BX and MT (0.5-5 ml; 200 mg/ml) were transferred into a series of 25-ml volumetric flasks. Then 5 ml of acetic acid solution and 2.5 ml of NBS solutions were added to each flask. The volume was made up to 15 ml with distilled water in each flask and kept aside for 20 min. Then 1.5 ml of metol solution and after 2 min, 1.5 ml of sulphanilamide solution was added. The volume was made up to 25 ml with distilled water and absorbance was measured after 10 min and before 30 min

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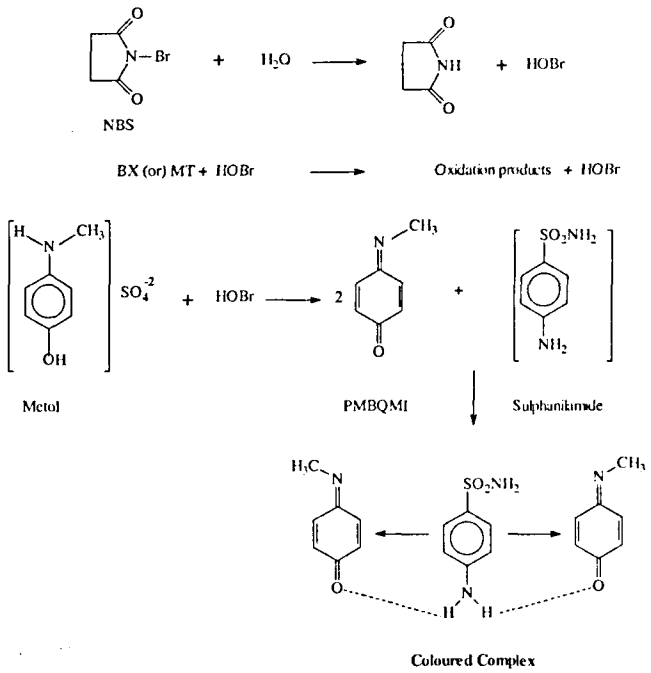
at 520 nm against distilled water. A blank experiment was also performed omitting the drug solution. The decrease in absorbance corresponding to the respective drug was obtained by subtracting the absorbance of test solution from that of the blank solution. The amount of BX and MT present in formulations was calculated from the respective calibration curves.

This is an indirect method for the estimation of BX and MT, which involves two stages, oxidation of drug by NBS (first stage) and estimation of the unconsumed NBS with metol-SA reagent (second stage). In the first stage the volume of NBS required for oxidation of BX and MT, the time and temperature for the oxidation, volume of acetic acid and effect of KBr on the oxidation were established through controlled experiments. The volume of NBS above 3 ml gave high optical density in blank, which resulted in erroneous results. The minimum time required for complete oxidation was found to be 15 min. At higher temperatures the results were found to be inconsistent and no additional advantage was observed. Presence of KBr did not catalyse the reaction between NBS and BX and MT. Therefore KBr was excluded from the method. Presence of acetic acid enhances the stability of the color from 10-30 min by lowering the pH to 2.9.

In the second stage, the volume of SA and the solvent for final dilution were found by varying one parameter at a time and the results are 2 ml of metol solution produced low absorbance and high blank values, a minimum time of 1 min was necessary for metol to undergo oxidation and beyond 3min the quinone imine formed *in situ*, undergoes hydrolysis slowly to quinone which resulted in low sensitivity and a minimum of 1.5 ml of SA (1.16×10^{-2} M) was necessary for charge transfer complex formation with p-N-methyl benzoquinone monoimine (PNBM) formed *in situ*. Final dilution with other water miscible solvents did not enhance the intensity of colored species and water was found to be best for final dilution.

This method involves two steps. Initially BX and MT are oxidized with NBS, subsequently the un reacted NBS reacts with metol to form less stable PNBM. The so formed PNBM couples with sulphanilamide to give colored complex may be regarded as charge transfer type, presumed to be taking place, involving electron transfer from the highest occupied molecular orbital (π) of SA to lowest empty molecular orbitals (π^*) of the two adjacent PNBM molecules (formed *in situ*) from metol and NBS (scheme 1).



Scheme 1

TABLE 1: OPTICAL CHARACTERISTICS AND PRECISION.

Parameters	BX	MT
Beer's law limits (μg/ml)	4-40	4-40
Sandell's Sensitivity ($\mu g/cm^2$/0.001 absorbance limit)	0.0884	0.0838
Molar extinction coefficient (l/mol.cm)	3.89×10^3	8.175×10^3
% Relative standard deviation**	0.8584	0.8327
% Range of error		
0.05 confidence limits	±0.718	± 0.696
0.01 confidence limits	±1.061	±1.03
Correlation coefficient	0.9998	0.9998
Regression equation (Y*)		
Slope (a)	1.09×10^{-2}	1.097×10^{-2}
Intercept (b)	0.5×10^{-3}	5.06×10^{-3}

Y*=b+ac, where 'c' is concentration in μg/ml and Y is absorbance unit, **Calculated from eight replicate samples.

TABLE 2: ESTIMATION OF BETAXOLOL HYDROCHLORIDE BY THE PROPOSED METHOD.

Formulations	Labeled amount (%)	Amount obtained (%)		Percent recovery
		Proposed method	Reported method[2]	
Eye drops Optipres(Cipla)	0.5	0.498	0.492	99.4
Iobet (FDC)	0.25	0.249	0.245	99.7

Each value is average of four determinations; a, the amount added is 10 mg.

TABLE 3: ESTIMATION OF METOPROLOL TARTRATE BY THE PROPOSED METHOD.

Formulations	Labeled amount mg	Amount obtained mg		Percent recovery
		Proposed method	Reported method[3]	
Tablets Betaloc (Astra IDL)	100	99.89	99.24	99.19
Metolar (Cipla)	100	99.97	99.52	99.52
Lopressor (Novartis)	100	99.98	99.64	99.96
Injection Betaloc (Astra IDL)	5	4.99	4.91	99.7

Each value is average of four determinations; a is the mount added, 10 mg.

The optical characteristics such as molar absorptivity, Sandell's sensitivity, correlation coefficient, % relative standard deviation and % range of error for the proposed methods were given in Table 1. In order to determine the precision and accuracy of the proposed methods, solutions containing known amount of drug were prepared and analyzed in four replicates. The results of the analysis of formulations such as eyedrops, injections and tablets containing these two drugs by the proposed methods and reported method were given in Tables 2 and 3. The results showed that the proposed method has precision and accuracy. The results also indicated the proposed method is sensitive, accurate, precise and reproducible and may find application in the routine estimation of BX and MT in bulk and in pharmaceutical formulations. When pharmaceutical preparations were analyzed, the results obtained by the proposed method were in good agreement wits the labeled amount and are comparable with the respective reference method. The recovery in both the methods was found to be 99-100.5%.

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