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Simple and sensitive spectrophotometric methods for the determination of acebutolol hydrochloride in bulk sample and pharmaceutical preparations

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Abstract: A direct, extraction-free spectrophotometric method has been developed for the determination of acebutolol hydrochloride (ABH) in pharmaceutical preparations. The method is based on ion-pair complex formation between the drug and two acidic dyes (sulphonaphthalein) namely bromocresol green (BCG) and bromothymol blue (BTB). Conformity to Beer's law enabled the assay of the drug in the range of 0.5-13.8 μg mL^{-1} with BCG and 1.8-15.9 μg mL^{-1} with BTB. Compared with a reference method, the results obtained were of equal accuracy and precision. In addition, these methods were also found to be specific for the analysis of acebutolol hydrochloride in the presence of excipients, which are co-formulated in the drug.

Keywords: acebutolol hydrochloride; spectrophotometry; pharmaceutical preparations.

Introduction

Chemically, acebutolol hydrochloride (Fig 1) is (N-[3-Acetyl-4-[2-hydroxy-3[(1-methylethyl)amino]propoxy]phenyl]butanamide) hydrochloride, is a cardio-selective betablocker used in the management of hypertension, angina pectoris and cardiac arrhythmias[1], which normalizes the blood pressure and prevents the occurrence of hypertensive crisis. The Official method[2] for the determination of ABH is non-aqueous titration technique detecting the end point potentiometrically in aqueous medium using 0.1M NaOH titrant. Several methods are reported in the literature for the determination of the beta-blockers including spectrophotometry [3-7], NMR[8,9], high performance liquid chromatography[10-13], thin layer chromatography[14], liquid chromatography[15,16], capillary electrophoresis[17-21], pharmacokinetics[22,23], and fluorescence[24]. The reported spectrophotometric methods [4-6] do not discuss the stability of the methods and at the same time have low sensitivity [3-6]. More over, the methods are laborious and the effects of common excipients have not been investigated [3-6]. Sungur and Yurdakul[7] have determined acebutolol by UV Spectrophotometry. When compared to this method, our method is simple and does not involve any tedious/complex reaction conditions. This prompted us to develop simple, sensitive and accurate spectrophotometric methods for the determination of ABH in pure and pharmaceutical formulations. One of the well-established spectrophotometric methods is through ion-pair complex extraction. In this case, an ion-pair is formed between a basic compound and an anionic dye (e.g., bromophenol blue, bromocresol green,

methyl orange, etc.). At a specific pH, the ion-pair, which is immiscible with water is extracted into an organic solvent and the concentration of it is determined spectrophotometrically[25-28]. The ion-pair extraction technique has some difficulties and inaccuracies arising from incomplete extraction or the formation of emulsions between the organic solvent and the basic compound, containing solution. In response to the problems resulting from extraction of the ion-pair, few articles were published for the analysis of pharmaceutical compounds through ion-pair formation without involving extraction [29-31]. In this paper, we describe the application of acidic dyes to the spectrophotometric determination of ABH without the application of buffers. The ion-pair formed between the drug and sulphonphthalein dye, BCG/BTB requires no extraction and is measured directly in chloroform. The proposed methods are applied successfully for the determination of ABH either pure or in dosage forms with good accuracy and precision. Interference from some commonly co-formulated substances is also studied.

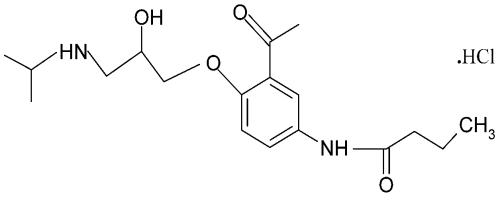

Figure 1. Structure of Acebutolol hydrochloride.

Experimental

Apparatus

The absorption spectra were recorded on a double beam CARY 50-BIO UV-Visible spectrophotometer (Varian, Australia) with 1cm matched quartz cells.

Materials and reagents

Pure ABH sample was kindly provided by HIKAL Ltd., India. Commercial dosage forms were purchased from local sources.

Stock solutions of each of 0.1% of bromocresol green (BCG), and bromothymol blue (BTB) were prepared in chloroform. Standard solution of ABH was prepared by dissolving 10 mg in 100 mL of chloroform and further diluted as and when required.

Procedures

Recommended procedure and calibration curve

Suitable aliquot volumes of ABH solution were transferred into a series of 10 mL volumetric flasks, so that the final concentration is in the range stated in Table 1. Recommended volume of the dye solution was added (Table 1), mixed well and diluted to volume with chloroform. The absorbances of the resulting colored species were measured at the specified wavelength (Table 1) against chloroform.

Table 1. Optical characteristics and Statistical Data of the Regression Equations for the Reaction of ABH with BCG and BTB.

Parameters	BCG	BTB
Volume of the dye added (mL)	5	2
λ_{max} (nm)	412	415
Beer's law limit (μg mL^{-1})	0.5-13.8	1.8-15.9
Molar absorptivity (l $moL^{-1}cm^{-1}$)	1.86 x 10^4	1.72 x 10^4
Sandell's sensitivety (ng cm^{-2})	19.667	21.692
Regression equation (Y) [a]		
Intercept, b	0.0034	0.0023
Slope, c	0.049	0.0445
Relative standard deviation (%) [d]	0.7777	1.2771
Correlation coefficient (r)	0.9928	0.9978

[a] Y = bX + c, where X is the concentration of drug in (μg mL^{-1})
[d] Average of six determinations.

Procedure for commercial dosage forms

Weighed amounts of powdered tablets equivalent to 20 mg of ABH were transferred into a 100 mL volumetric flask. The contents were shaken well with about 50 mL of chloroform for 30 min. The flask was diluted up to the mark with the same solvent. It was filtered and preceded as described above. The nominal content of the tablets was determined from the calibration curve.

Results and Discussion

Absorption spectra

The structure of ABH features its basic nature. This structure suggests the possibility of utilizing an anionic dye as chromogenic reagent. In chloroform, ABH is not an absorbing species in the visible region. The dyes employed have almost negligible absorbance (Fig 2). In contrast, when a solution of BCG or BTB in chloroform is added to the drug solution, an intense yellow colored product is produced immediately (Fig 2). This is due to the conversion of the dye into an open quinonoidal anionic derivative [32], which forms an ion-pair with ABH.

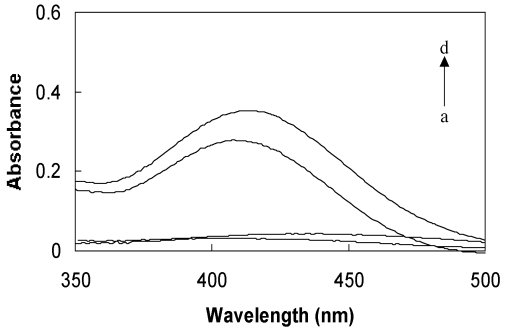

Figure 2. Absorption spectrum of reagent blanks-BCG (a) and BTB (b), and ion-pair complexes of ABH (8 µg mL^{-1}) with BCG (c) and BTB (d).

Reaction conditions

The experimental conditions were studied and it was found that 5 mL of BCG or 2 mL of BTB were sufficient to produce maximum and reproducible color. The color products were found to be stable for at least 1.5 h.

Investigation of the ABH-BCG ion-pair complex

The composition of the ion-pair complex formed between ABH and BCG/BTB was investigated by Job's method of continuous variation. It was found that the composition of drug to dye was 1:1 in both cases.

Analytical performance

Linearity of the method

Under the experimental conditions, linear correlations were obtained between the absorbances and ABH concentration over the ranges stated in Table 1 with good correlation coefficients and zero intercepts. The apparent molar absorptivities, Sandell's sensitivities and detection limits[33] were summarized in Table 1.

Interference studies

The effects of common excipients and additives were tested for their possible interferences in the assay of ABH. It was also observed that the excipients such as talc, lactose, starch and magnesium stearate did not interfere with the assay, since the formation of an ion-pair complex with anionic dyes needs a basic moiety. The results have been tabulated in Table 2 for a representative dye, BTB.

Table 2. Determination of ABH a in Presence of Excipients by BTB Method.

Material	Amount (mg)	% Recovery of ABH ± RSD[b]
Magnesium stearate	30	97.8 ± 0.72
Glucose	40	98.6 ± 0.89
Lactose	40	98.7 ± 0.93
Dextrose	40	98.8 ± 1.07
Starch	30	100.2 ± 0.88
Gum acacia	40	99.2 ± 1.10
Talc	40	99.5 ± 0.94
Sodium alginate	25	98.4 ± 0.14

[a] 5 µg mL^{-1} of ABH taken.
[b] Average of five determinations.

Precision and accuracy

In order to determine the accuracy and the precision of the method, standard solutions containing three different concentrations of ABH were analyzed in five replicates. The mean results obtained are summarized in Table 3. The small values of the standard deviation (SD), the relative standard deviation (RSD %) and the mean standard analytical error (SAE) can be considered adequate for the quality control analysis of pharmaceutical preparations.

Table 3. Evaluation of the Accuracy and Precision of the Proposed Method for ABH Determination.

Dye	ABH ($\mu g\ mL^{-1}$) Added	Found[a]	SD	RSD%	SAE
BCG	2	2.01	4.650×10^{-3}	1.7743	2.079×10^{-3}
	4	4.06	9.009×10^{-3}	1.5548	4.029×10^{-3}
	6	5.97	6.722×10^{-3}	1.2772	3.006×10^{-3}
	8	8.05	2.863×10^{-3}	0.7777	1.280×10^{-3}
BTB	4	4.12	9.167×10^{-3}	1.2625	4.099×10^{-3}
	6	6.04	3.807×10^{-3}	1.3599	1.702×10^{-3}
	8	7.95	4.690×10^{-3}	1.2770	2.090×10^{-3}

[a] Mean of five determinations
SD - standard deviation
RSD% - relative standard deviation
SAE - standard analytical error.

Pharmaceutical applications

The proposed methods are equally accurate and precise as the Official method as indicated by the % recovery. Table 4 shows the results obtained for the determination of ABH in commercial tablets by means of both the proposed methods and the Official method[2].

Table 4. Application of the Proposed Spectrophotometric Methods for the Determination of ABH in Dosage Forms.

Commercial product	% Recovery [a] ± SD		Official method
	BCG	BTB	(BP 2003)
ABH-400 mg/tablet	99.78 ± 0.81	99.68 ± 0.73	99.5 ± 1.3
t	1.15	1.92	
F	2.57	3.17	
ABH-200 mg/tablet	99.82 ± 0.78	99.85 ± 0.84	99.3 ± 0.9
t	0.89	1.65	
F	1.33	1.15	
Sectral 200 mg/tablet	99.92 ± 1.1	99.88 ± 0.96	99.5 ± 1.2
t	1.24	1.43	
F	1.19	1.56	

The theoretical values of t and F at P=0.05 are 2.31 and 6.39, respectively.
[a] Mean of five determinations.

Conclusions

The proposed methods are rapid, simple, accurate and in addition, offer advantages in determining ABH, (in pharmaceutical preparations), when extraction difficulties arise with other spectrophotometric methods. Hence, the proposed methods could be adopted routinely for quality control in pharmaceutical industries.

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