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Investigation of penbutolol–iron(III) complex and its spectrophotometric determination in tablets*

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Abstract: It has been established that penbutolol reacts with iron(III) chloride in the presence of ammonium thiocyanate to form a pink complex (2:1) that is soluble in chloroform with a maximum absorbance at 478 nm. By application of the methods of Sommer and Job involving non-equimolar solutions, the conditional stability constant ($\log k'$) of the complex at the optimum pH of 1.5 ± 0.02 and an ionic strength of (μ) 0.14 M, was found to be 5.769. The molar absorptivity at 478 nm was 136 l mol^{-1} cm^{-1} at pH 1.5 ± 0.02. The validity of Beer's law has been tested in the concentration range 3–18 × 10^{-4} M; the relative standard deviation (n = 8) was 1.52–3.21%. The proposed method was found to be suitable for the accurate, simple and rapid analysis of penbutolol in the bulk drug and in tablets.

Keywords: *Penbutolol; Fe(III) chloride; complexometry; colorimetry.*

Introduction

Penbutolol,1-(2-cyclopentylphenoxy)-3-[(1,1-dimethylethyl)amino]-2-propanol is one of the beta-adrenergic blockers. A number of analytical methods for the determination of the beta-adrenergic blockers have been described. A few reports have been published on reactions in which a coloured ion-pair is formed, the ion-pair is subsequently extracted by a suitable solvent and determined by spectrophotometry [1–7]; TLC-spectrophotometry [8] and gas chromatography (GC) [9–13] have been used for the drug in biological fluids. TLC, GC [14] and HPLC [15–19] methods have also been described for penbutolol. The aim of the present work was to study the reaction between penbutolol and Fe(III) ions as a basis for its determination in pharmaceutical preparations. This work is a continuation of the author's systematic studies on the behaviour of complexes of beta-adrenergic blockers with Fe(III) ions [20].

Experimental

Reagents

Penbutolol sulphate (Hoechst), Fe(III) chloride, ammonium thiocyanate, hydrochloric acid and chloroform were used. All chemicals were of analytical grade (Merck); double-distilled water was used.

Solutions

For analytical purposes a freshly prepared 5 × 10^{-3} M solution of pure penbutolol sulphate in 0.1 M HCl was used as the stock solution. Potassium chloride (1.0 M), 0.5 M Fe(III) chloride in 0.1 M hydrochloric acid, 1.0 M ammonium thiocyanate and 1 × 10^{-3} M HCl were prepared. The ionic strength (μ) of the final solution for spectrophotometric determination was kept constant by the addition of 1 M potassium chloride.

Apparatus

A spectrophotometer (Specord M 40, Carl Zeiss) with 10-mm quartz cells was used. A pH-meter (Beckman Zeromatic SS-3), calibrated with appropriate standard buffer solutions, was employed.

Procedure

To 2 ml of penbutolol sulphate solution in 0.1 M HCl (or an extract of penbutolol sulphate from tablets) was added 1 ml of potassium chloride solution, 1 ml of Fe(III) chloride solution in 0.1 M HCl and 2 ml of ammonium thiocyanate solution in an Erlenmeyer flask fitted with a ground-glass stopper. Finally,

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5 ml of chloroform and 1 ml of 10^{-3} M HCl were added. The Erlenmeyer flask was closed and the reaction mixture was gently shaken by means of a shaking machine for 10 min. The pink chloroformic layer was separated in a separating funnel and its absorbance was measured at 478 nm against chloroform as a blank. All measurements were made at room temperature (25 ± 0.5 C).

Preparation of calibration curve

A calibration curve was prepared with eight standard solutions of concentration 3–18 × 10^{-4} M penbutolol sulphate in 0.1 M HCl. For each solution three measurements were made at 478 nm against chloroform.

Results and Discussion

It was found that penbutolol reacts with Fe(III) chloride in the presence of ammonium thiocyanate at pH 1.5 ± 0.02 to produce a pink complex that is soluble in chloroform. Absorption spectra were recorded over the wavelength range 380–660 nm. The complex showed an absorbance maximum at 478 nm (Fig. 1, curve 1) which was therefore used for the analytical determinations.

All measurements were performed against a reagent blank, with an appropriate correction for the cell blank. pH 1.5 ± 0.02 was used as the working pH. The shape of the absorption spectrum and the position of the absorption maximum of the complex formed did not vary with pH; this result indicates that only one type of complex is formed.

Maximum absorbance was observed after 10 min. Thus measurements were made at 10 min; the ionic strength was 0.14 M. The composition and conditional stability constant of the complex were determined by Job's method of equimolar solutions; the curves obtained displayed a maximum at a molar fraction of

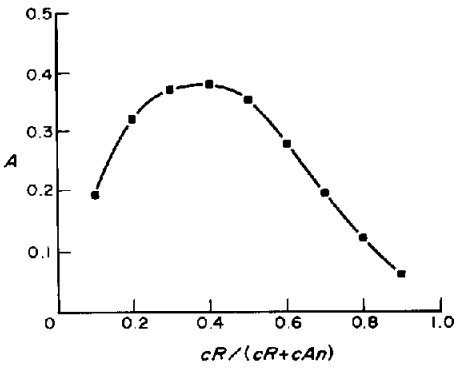

Figure 2
Job's curve of equimolar solutions at 478 nm. [Penbutolol] = [Fe(III)] = 1.2 × 10^{-2} M, pH = 1.5 ± 0.02; μ = 0.14 M.

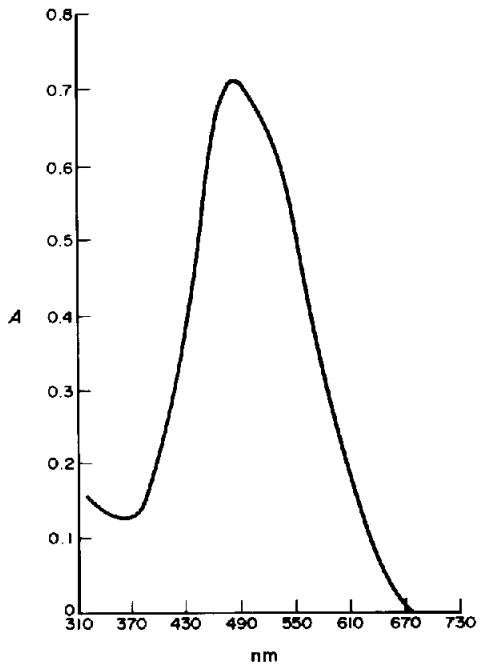

Figure 1
Absorption spectra of penbutolol–Fe(III) complex. [Penbutolol] = 4 × 10^{-3} M; pH = 1.5 ± 0.02; μ = 0.14 M.

Table 1
Conditional stability constant of the penbutolol–Fe(III) complex* calculated by Sommer's method

log K'	log K'_{min}	log K'_{max}	SD	RSD (%)
5.57	5.42	5.76	0.174	3.12

*Conditions: pH = 1.5 ± 0.02; μ = 0.14 M; T = 25 ± 0.5°C; n = 6.

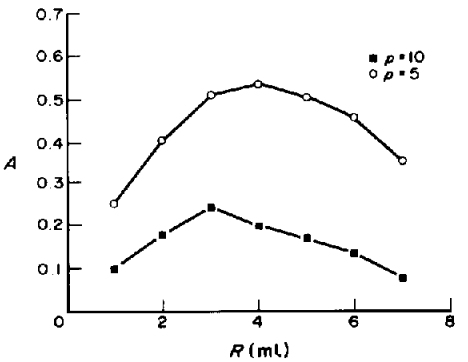

Figure 3
Job's curve of non-equimolar solutions at 478 nm. [Fe(III)] = 4 × 10^{-2} M; p = 5 (curve 1); p = 10 (curve 2). pH = 1.5 ± 0.02; μ = 0.14 M.

Table 2
Conditional stability constant of the penbutolol–Fe(III) complex* calculated by Job's method for non-equimolar solutions

[Fe(III)]	p	X_{max}	log K'†
4×10^{-2}	5	0.333	6.13
4×10^{-2}	10	0.250	5.80

*Conditions: pH = 1.5 ± 0.02; μ = 0.14 M; T = 25 ± 0.5°C.
†Mean value of log K' = 5.965.

Table 3
Results of the spectrophotometric determination of penbutolol bulk drug and penbutolol in "Paginol" tablets

Sample	Concentration (mg ml^{-1})	Found (mg ml^{-1})	SD	RSD (%)	Sx	Recovery (%)
Penbutolol bulk drug	0.680	0.680	0.003	1.52	0.0012	100.0
"Paginol" tablets 40 mg	0.680	0.669	0.007	3.21	0.025	98.5

$X_{max} = 0.33$ which indicates the formation of a penbutolol–Fe(III) complex in a ratio 2:1 (Fig. 2).

The conditional stability constant of the complex was calculated by the method of Sommer by using Job's curves of equimolar solutions.

The results are presented in Table 1. By using Job's method of non-equimolar solutions, the curves obtained for a five-fold and a 10-fold excess of reagent (p; Fig. 3) gave a value for X_{max}; this value was obtained by projecting the peak maximum onto the abscissa and dividing it by the total volume of solution used in each case (12 ml). The conditional stability constant was then calculated from the equation:

$$K' = \frac{(p-1)^2(2-3X_{max})}{(c_{penbutolol})^2 p[(2+p)X_{max}^{-2}]^3},$$

where $p = 5$ or 10, and $C_{Fe(III)chloride} = 4 \times 10^{-2}$ M. The values of logK' are presented in Table 2.

Quantification and linearity of the calibration curve

Beer's law was verified at pH = 1.5 ± 0.02. A linear relationship between absorbance and concentration was established over the range $3–18 \times 10^{-4}$ M. The molar absorptivity of the complex was 136 l mol^{-1} cm^{-1}. The regression equation was $y = -0.00593 + 0.02076x$; the correlation coefficient (r) was 0.9986 (n = 8), indicating excellent linearity. The relative standard deviation (n = 7) varied from 1.52 to 3.22%.

Application to a dosage-form

The applicability of the method for the assay of a simple dosage-form was examined by analysing Paginol (JGR/HOE) tablets. The recovery was 98.47% (n = 7). The results confirm the suitability of the proposed method for the accurate and sensitive analysis of penbutolol both in the bulk drug and in a dosage-form (Table 3).

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