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Short Communication

Investigation and spectrophotometric determination of the allprenolol hydrochloride–iron(III) complex in bulk drug and in dosage form*

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Introduction

Allprenolol, 1-(*o*-allylphenoxy-3-isopropil-amino)-2-propanol, is an adrenergic beta receptor blocking agent used in the treatment of angina pectoris, some forms of heart arrythmias and arterial hypertension.

A number of analytical methods for the determination of adrenergic beta-blockers have been described. These include a few reports on coloured reactions of amine and a corresponding indicator in which a coloured ion pair and coloured complex have been created, subsequently extracted by a suitable solvent, and determined spectrophotometrically [1–8]. TLC–spectrofluorimetry [9], HPLC [10] and gas chromatography [11–13] have also been described.

Accordingly, the aim of our work is to study the reaction between allprenolol hydrochloride and the iron(III) ion, as a basis for its determination in pharmaceutical dosage forms.

Experimental

Reagents

Allprenolol hydrochloride (Bosnalijek/Asta, Sarajevo, Yugoslavia) and iron(III) chloride (Merck) were used. All other chemicals were of analytical reagent grade purity (Merck).

Solutions

The stock solution of allprenolol hydrochloride was prepared by dissolving the compound in doubly-distilled water (2×10^{-2} mol l^{-1}). A standard solution of allprenolol hydrochloride from "Aptin" tablets (Bosnalijek/Asta, Sarajevo, Yugoslavia) containing 50 mg of allprenolol hydrochloride was prepared by the extraction of the powdered mass of tablet with water. After filtration, the extract was diluted with water to produce an allprenolol concentration of 2×10^{-2} mol l^{-1}. Seven different concentrations of both the bulk drug and tablets were prepared.

A freshly prepared 0.5 M iron(III) chloride solution was made by dissolving in 0.1 M hydrochloric acid. A 1 M ammonium thiocyanate standard solution was prepared in water. The standardization of iron(III) chloride and ammonium thiocyanate solutions is not necessary when determining allprenolol hydrochloride only.

Apparatus

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

Procedure

To 1 ml of a standard solution of allprenolol hydrochloride (2×10^{-2} M) or to 1 ml of a water extract of allprenolol hydrochloride from tablets, placed in a Erlenmeyer flask fitted with a ground glass stopper, 1 ml of 0.5 M iron(III) chloride in 0.1 M hydrochloric acid, 2 ml of

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1 M ammonium thiocyanate, 5 ml of chloroform and 2 ml of 3 M hydrochloric acid were added. The Erlenmeyer flask was stoppered and the reaction mixture was gently shaken on a shaking machine for 10 min. The pink coloured chloroformic layer was separated in a separatory funnel and absorbance was measured at 477 nm against the reagent blank.

Procedure for the calibration curve

The calibration curve was prepared with the seven standard solutions of allprenolol hydrochloride in water (0.6–2.4 mmol l^{-1}). With each solution three experiments were run following the procedure described. The measurements were performed at 477 nm, against the reagent blank.

Results and Discussion

Absorption spectra

Allprenolol hydrochloride reacts with iron(III) chloride in the presence of ammonium thiocyanate in acidic media. The reaction takes place at room temperature at pH = 1.30 and ionic strength, μ = 1, and the complex formed between allprenolol hydrochloride and the iron(III) ion was extracted with chloroform. Absorption spectra were recorded over the range 380–660 nm. The pink complex shows one absorbance maximum at 477 nm (Fig. 1).

A chloroformic extract obtained by extracting a mixture of 1 ml water, 1 ml iron(III) chloride, 2 ml of ammonium thiocyanate and 2 ml of hydrochloric acid was used as a blank. Chloroformic extracts of the blank and of the compounds which take part in the formation of the complex do not absorb in the spectral region 380–660 nm.

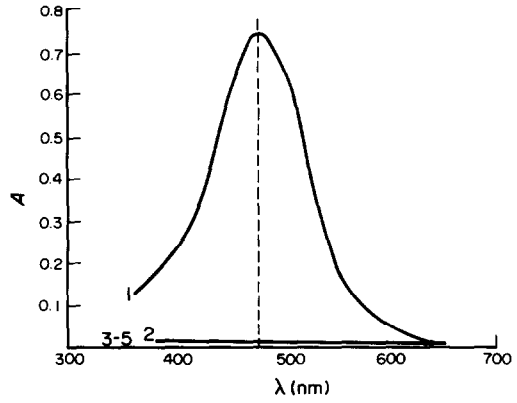

Figure 1
Absorption spectra of allprenolol hydrochloride–iron(III) complex (curve 1); iron(III) chloride and ammonium thiocyanate (curve 2); iron(III) chloride, ammonium thiocyanate and allprenolol hydrochloride (3–5): λ_{max} = 477 nm; pH 1.30 ± 0.02; μ = 1; [allprenolol hydrochloride] = 4 × 10^{-3} mol l^{-1}.

Determination of the complex composition

The composition of the complex of allprenolol hydrochloride and the iron(III) ion was determined by Job's method of equimolar solutions. The concentration of aqueous allprenolol hydrochloride and iron(III) chloride solutions was 2 × 10^{-2} mol l^{-1}. The plot reached a maximum value at a mole fraction, X_{max}, of 0.33 which indicates the formation of the allprenolol hydrochloride–iron(II) complex (2:1) (Fig. 2).

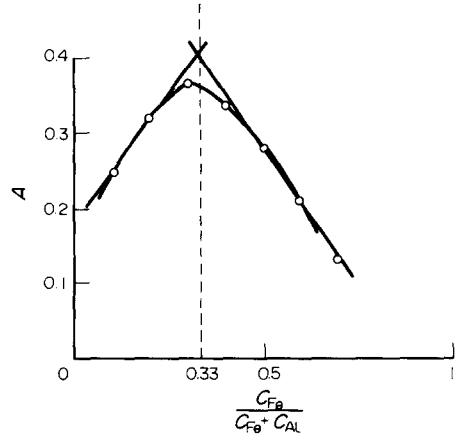

Figure 2
Job's curve of equimolar solutions: λ_{max} = 477 nm; pH 1.30 ± 0.02; μ = 1; [allprenolol hydrochloride] and [iron(III) chloride] = 2 × 10^{-2} mol l^{-1}.

Conditional stability constant of the complex

The conditional stability constant of the complex was calculated according to Sommer's method by using a Job's plot of equimolar solutions. The results are presented in Table 1. By Job's method of non-equimolar solutions, curves for a five-fold and ten-fold excess of reagent were obtained (Fig. 3). The conditional stability constant was then calculated in the following way:

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

where p = 5 or p = 10, divided by the total volume of solution used in each case (12 ml).

Table 1
Conditional stability constant for the allprenolol hydrochloride–iron(III) complex: pH = 1.30; μ = 1; T = 25 ± 0.5°C

Sommer's method*				
log $\bar{K}'$	logK'_{min}	log K'_{max}	SD	RSD (%)
4.747	4.55	4.56	0.010	2.59

Job's method of non-equimolar solutions†		
p	X_{max}	log K'
5	0.333	4.55
10	0.208	4.56

*SD = standard deviation, RSD = relative standard deviation, n = 10.
†n = 12.

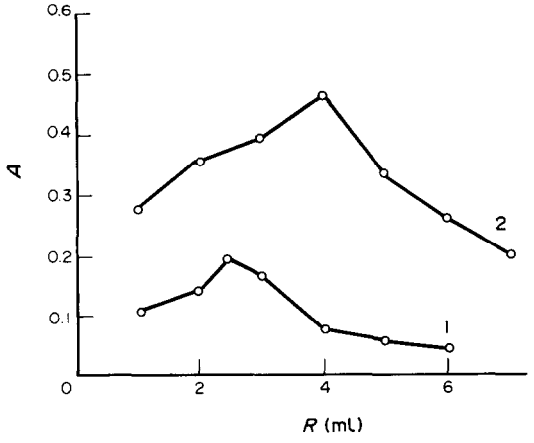

Figure 3
Job's curves of non-equimolar solutions: [allprenolol hydrochloride] = 2 × 10^{-2} mol l^{-1}; p = 5 (curve 1) X_{max} = 0.33, p = 10 (curve 2); pH 1.30 ± 0.02; μ = 1; R = iron(III) chloride, X_{max} = 0.208.

The values of log K' are presented in Table 1. The values for log K' from both methods are in good agreement.

Quantification and linearity of the method

A linear relationship between absorbance and allprenolol hydrochloride concentration was established. Beer's law was verified over the concentration range 0.6–2.4 mmol l^{-1}. The regression equation was y = 0.00034 + 0.0082x, with a correlation coefficient (r) of 0.9980 (n = 7) indicating good linearity. The detection limit was 0.6 mmol l^{-1} of allprenolol hydrochloride. The standard deviations (SD) varied from 0.01019 to 1.250 as shown in Table 2. Low values of relative standard deviation (RSD) and relative error ($S_{\bar{x}}$) indicate that the allprenolol hydrochloride–iron(III) complex can be used for the quantitative analysis of allprenolol in pharmaceutical dosage form.

Application to dosage form

The applicability of the method was examined by analysing "Aptin" tablets. The RSD of the spectrophotometric method when applied to "Aptin" tablets was 2.52%. A high recovery value of 98% and a SD value of 1.250 confirm the stability of the proposed method for the routine analysis of pharmaceutical dosage form (Table 2).

In conclusion, it may be considered that the proposed method, using iron(III) chloride as an analytical reagent, can be suitable for the accurate and sensitive analysis of allprenolol hydrochloride both in bulk drug and dosage forms.

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Table 2
Results of the spectrophotometric determination of allprenolol hydrochloride in the bulk drug and "Aptin" tablets (50 mg)

	Taken (mg ml^{-1})	Found (mg ml^{-1}) X_{min}, X_{max}, $\bar{X}$	SD	$S_{\bar{x}}$	RSD (%)	R (%)
Allprenolol hydrochloride (bulk drug)	0.400	0.37523, 0.40657, 0.39090	0.01019	0.00385	2.59	97.7
Allprenolol hydrochloride ("Aptin" tablets)	0.400	0.3787, 0.4069, 0.3928	1.250	0.47245	2.52	98.2

Conditions: λ_{max} = 477 nm; pH 1.30 ± 0.02; n = 7.

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