Investigation of the pindolol–Fe(III) complex and its use in the spectrophotometric determination of pindolol in bulk drug and tablets*

D. PEĆANAC,† D. RADULOVIĆ, Lj. ŽIVANOVIĆ and S. AGATONOVIĆ-KUŠTRIN

Institute of Pharmaceutical Chemistry, Faculty of Pharmacy, University of Belgrade, Vojvode Stepe 450, Belgrade, Yugoslavia

Abstract: It was found that pindolol reacts with Fe(III) chloride producing a green water soluble complex (1:1, v/v) with maximum absorbance at 635 nm. By applying the methods of Sommer and Job [Sommer *et al.*, *Folia, tomus XI, Chemia* 7, 25, 1970] the conditional stability constant of the complex at pH = 1.70 ± 0.02 was found to be log $K' = 4.95$ and the molar absorptivity of the complex to be 206 l mol^{-1} cm^{-1}. Beer's law was obeyed up to a concentration of 220 μmol l^{-1} of pindolol. The recoveries were 98–101% ($n = 7$) and the detection limit was 5 μg ml^{-1}. The described method was sufficiently simple, selective and sensitive to be suitable for the rapid and accurate determination of pindolol in tablets.

Keywords: *Pindolol; Fe(III) chloride; spectrophotometry; complexometry.*

Introduction

Pindolol, 4-[2-hydroxy-3-(isopropylamino)-propoxy]indole, is a β-adrenergic blocker in clinical use. A few reports have been published on reactions in which a coloured ion pair is formed, which is subsequently extracted by a suitable solvent and determined by spectrophotometry [1–7]. Thin layer chromatography–spectrophotometry [8] and gas chromatography [9–13] have been used for the analysis of β blockers in biological fluids. TLC, GC [14] and liquid chromatography [15–19] methods have also been described for pindolol. The aim of the present work was to study the reaction between pindolol and Fe(III) ions as a basis for its determination in pharmaceutical preparations. This work is a continuation of the authors' systematic studies on the behaviour of the complexes of β-adrenergic blockers with Fe(III) ions [20–22].

Experimental

Reagents

Pindolol (Visken®), Fe(III) chloride, hydrochloric acid and distilled water were used. All chemicals were of analytical grade (Merck, Darmstadt, Germany).

Solutions

A standard solution of pindolol containing 2×10^{-3} M in 0.1 M HCl was used. The reagent solution was 0.5 M Fe(III) chloride in 0.1 M HCl.

Apparatus

A spectrophotometer (Specord M-40, Carl Zeiss–Jena, Germany) provided with 10 mm quartz cells was used. Measurements of pH were carried out on a pH-meter ("Iskra" MA-5705, Iskra, Kranj, Yugoslavia); values were determined with a standard calomel-glass electrode system.

Procedure

Pindolol standard solution (2 ml) was placed in a 10 ml volumetric flask and 1 ml of Fe(III) chloride solution was added. The solution was diluted to volume with water and mixed. The absorbance was measured after 10 min between 400 and 800 nm against a reagent blank. All measurements were made at room temperature (25 ± 0.5°C). This procedure was applied for measuring the absorption spectrum and for the determination of pindolol in bulk drug and tablets. The absorbance maximum at 635 nm was employed. A series of six standard solutions containing from 20 to 220 μmol l^{-1} of pindolol in 0.1 M HCl was used to check

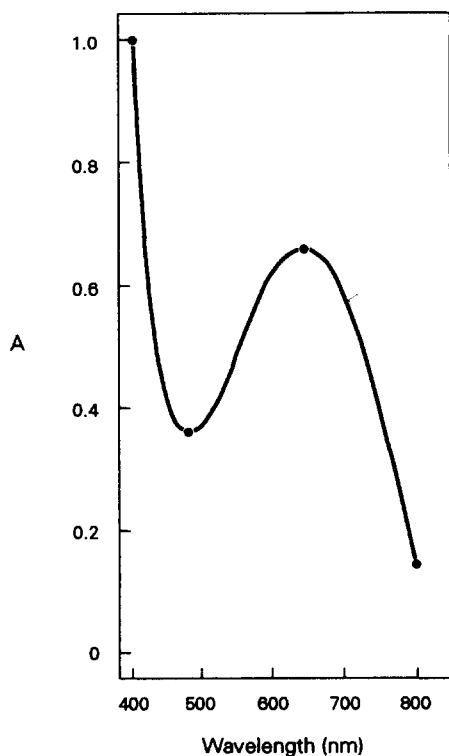adherence to Beer's law. For each solution three measurements were made at 635 nm against a reagent blank.

Results and Discussion

Pindolol reacts with Fe(III) chloride at pH 1.70 ± 0.02 producing a green water soluble complex. Absorption spectra were recorded over the wavelength range 480–800 nm to establish the λ_{max} position (635 nm) (Fig. 1). Fe(III) chloride was added in excess. Investigation showed that the maximum absorbance was obtained with a molar ratio of 4:1 for Fe(III)–pindolol. A pH of 1.70 ± 0.02 was chosen as the working pH. Since the shape of the absorption curve and the position of the absorption maximum did not vary with pH, it was assumed that only one type of complex is produced at pH 1.70. The composition of the pindolol–Fe(III) complex was determined by applying Job's method of equimolar solutions, the molar ratio method and the Bent–French method. By using Job's method, the curve obtained displayed a maximum at a molar fraction of X_{max} = 0.5 indicating the formation of a 1:1 complex. The measurements were

carried out at pH 1.70 ± 0.02 at 635 nm (Fig. 2).

In other experiments carried out the curve obtained with the molar ratio method showed a break point at a pindolol–Fe(III) molar ratio of 1:1, which was in agreement with the result obtained by Job's method (Fig. 3). The Bent–French method was used to determine the number of pindolol ligands in the complex. The absorbance of the complex was measured at a constant excess of Fe(III) ions and with various concentrations of pindolol. The slope (q = 0.99) indicates the participation of one pindolol ion in the formation of the complex, confirming the results of the previous methods.
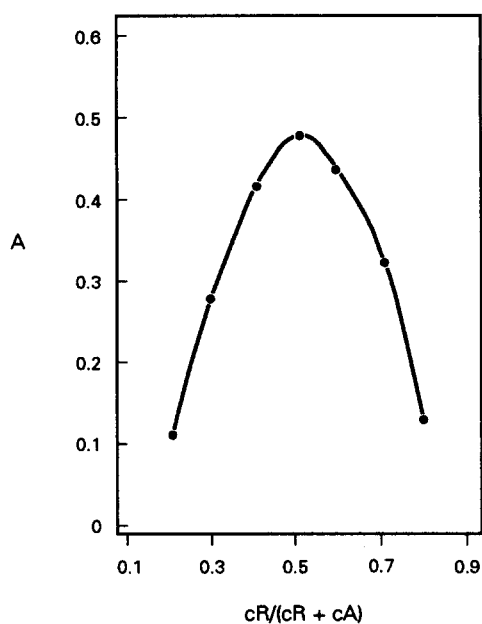
Figure 2
Job's curve of equimolar solutions at 635 nm ([pindolol] = [Fe(III)] = 5 × 10^{-3} M; pH = 1.70 ± 0.02).
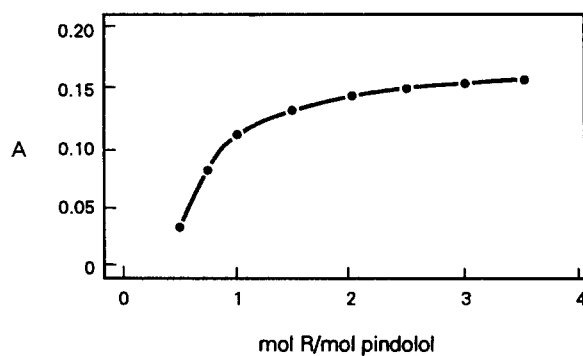
Figure 3
Molar ratio method ([pindolol] = 2 × 10^{-3} M at 635 nm; pH = 1.70 ± 0.02).

Figure 1
Absorption spectrum of pindolol–Fe(III) complex ([pindolol] = 24 × 10^{-5} M; pH = 1.70 ± 0.02).
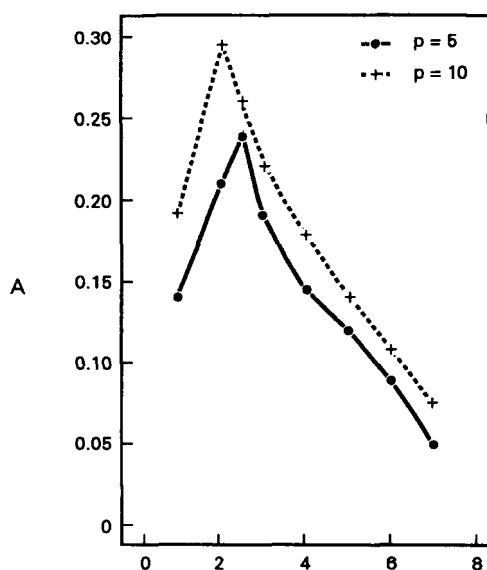
Table 1
Conditional stability constant of the pindolol–Fe(III) complex calculated according to Sommer's method

log K'	log K_{min}	log K_{max}	Sd	RSD
4.95	4.71	5.19	0.24	4.85

Conditions: pH = 1.70 ± 0.02; t = 25 ± 0.5°C; n = 3.

The conditional stability constant of the complex was calculated according to the method of Sommer et al. [23] by using Job's curve of equimolar solutions. The values for log k' obtained by this method are presented in Table 1.

By using Job's method of non-equimolar solutions, the curves obtained for a five-fold (p = 5) and a 10-fold excess (p = 10) of reagent (Fig. 4) 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:

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

where p = 5 or 10, and $c_{pindolol}$ = 1 × 10^{-3}. The values of log K' are presented in Table 2.

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

[Pindolol]	p	X_{max}	log K'
1 × 10^{-3}	5	0.208	4.57
1 × 10^{-3}	10	0.167	4.03

Conditions: pH = 1.70 ± 0.02; t = 25 ± 0.5°C.

Quantification and linearity of the method

The absorbance of the complex was found to be directly related to the concentration over the range 20–220 μmol l^{-1}. The regression equation was y = −0.0062 + 0.0257x with a correlation coefficient of 0.9998 (n = 6). The molar absorptivity was found to be 206 l mol^{-1} cm^{-1}, and the lower limit of sensitivity was found to be 5 μg ml^{-1}. The recovery was checked at two different concentrations of bulk drug.

The relative standard deviations (n = 7) varied from 0.56 to 1.65%. The repeatability of the method was examined by analysing Visken® tablets. A summary of results is presented in Table 3. The recoveries varied from 98 to 101% whilst the relative standard deviations varied from 0.80 to 1.58% (n = 7). The results confirm the suitability of the proposed method for routine and control analyses of bulk drug and Visken® tablets.

Figure 4
Job's curve of non-equimolar solutions at 635 nm ([pindolol] = 1 × 10^{-3}; for p = 5 and 10, pH = 1.70 ± 0.02).

Table 3
Results of the spectrophotometric determination of pindolol in bulk drug and Visken® tablets

Sample (n = 7)	Concentration of solution (μg ml^{-1})	Found (μg ml^{-1})	Sd (μg)	RSD (%)	Sx	Recovery (%)
Pindolol bulk drug	19.86	19.86	0.112	0.56	0.0423	100
	29.86	29.86	0.490	1.65	0.1854	100
Visken® tablets	19.86	19.39	0.155	0.80	0.0587	98
(15 mg)	29.86	30.19	0.477	1.58	0.1801	101

References

[1] S. Pinzauti, E. La Porta, M. Casini and C. Betti, *Pharm. Acta. Helv.* **57**, 334–337 (1982).

[2] G. Anderman, M.O. Buhler and M. Erhart, *J. Pharm. Sci.* **69**, 215–217 (1980).

[3] F. Matsui and W.N. French, *J. Pharm. Sci.* **60**, 287–291 (1971).

[4] D. Radulović, M. Jovanović and R. Milošević, *Acta Pharm. Yugoslav.* **34**, 169–175 (1984).

[5] M. Jovanović, D. Radulović and Lj. Živanović, *Acta Polon. Pharm.* **XLIV**, 322–326 (1987).

[6] D. Radulović, M.S. Jovanović and Lj. Živanović, *Pharmazie* **41**, 434–435 (1986).

[7] M.S. Jovanović, D.M. Radulović and S.M. Vladimirov, *J. Serb. Chem. Soc.* **53**, 631–635 (1988).

[8] M. Schaefer and E. Mutschler, *J. Chromatogr.* **164**, *Biomed. Appl.* **6**, 247–252 (1979).

[9] P.H. Degen and W. Ries, *J. Chromatogr.* **121**, 72–75 (1976).

[10] D. De Bruney *et al.*, *J. Pharm. Sci.* **68**, 511–512 (1979).

[11] M.R. Bonoro, T.W. Guentert *et al.*, *Clin. Chim. Acta* **91**, 277–284 (1979).

[12] S.H. Wan, R.T. Maronde and S.B. Matin, *J. Pharm. Sci.* **67**, 1340–1342 (1978).

[13] M. Ervik, K. Kylberg-Hanssen and P.O. Lagerstrom, *J. Chromatogr. Biomed. Appl.* **182**, 341–347 (1980).

[14] V. Caplar, Z. Mikotic-Minun, H. Hofman *et al.*, *Acta Pharm. Yugoslav.* **33**, 71–85 (1983).

[15] S. Tsui *et al.*, *J. Chromatogr.* **181**, *Biomed. Appl.* **7**, 135–140 (1980).

[16] H. Winkler, W. Ried and B. Lemmer, *J. Chromatogr. Biomed. Appl.* **228**, 223–234 (1982).

[17] C. Verghese, A. McLeod and D. Shand, *J. Chromatogr.* **275**, 367–375 (1983).

[18] K.U. Buhring and A. Garbe, *J. Chromatogr.* **382**, 215–224 (1986).

[19] P.C. White, *Analyst* **113**, 1625–1629 (1988).

[20] Lj. Živanović, D. Radulović and M. Jovanović, *Pharm. Acta Helv.* **12**, 350–352 (1988).

[21] D. Radulović, D. Pećanac, Lj. Živanović and S. Agatonović-Kuštrin, *Il Farmaco* **45**(4), 447–453 (1990).

[22] D. Radulović, D. Pećanac, Lj. Živanović and S. Agatonović-Kuštrin, *J. Pharm. Biomed. Anal.* **8**, 739–742 (1990).

[23] L. Sommer, V. Kuban and J. Havel, *Folia, tomus XI, Chemia* **7**, 25 (1970).