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Short communication

Spectrophotometric determination of nizatidine in pharmaceutical preparations[1]

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1. Introduction

It is generally accepted that nizatidine is effective as an H_2-receptor antagonist in the treatment of gastric and duodenal ulcers. Methods for the quantitative analysis of nizatidine in biological fluids and in pharmaceutical formulations include HPLC and UV spectrophotometry [1–5].

In earlier work the authors developed a potentiometric method for determination of nizatidine in aqueous solution and in dosage forms [6]. The potentiometric titrations of nizatidine were carried out in Britton–Robinson buffer at pH 3.50. The potential change during the titration occurred when the molar ratio of nizatidine: Pd(II) was 1:1.

On the basis that potentiometric determination of nizatidine in water and dosage forms gave reliable and reproducible results [6], it was decided to use Pd(II) ion as an analytical reagent for the spectrophotometric determination of nizatidine. The present paper reports results obtained during a spectrophotometric study of the colour reaction of nizatidine with Pd(II). The optimum reaction conditions, spectral characteristics, stability constant and composition of the complex have been established. The main aim of this work, therefore, was to develop a colorimetric method for determination of nizatidine in dosage forms.

2. Experimental

2.1. Apparatus

A Pye Unicam SP-6-500 spectrophotometer with matched 10 mm quartz cells and a Radiometer PHM 62 pH meter calibrated with standard buffer solutions were used.

2.2. Reagents

Nizatidine standard substance (Eli Lilly and Company) p.a. was used as working standard.

Galitidine[R] capsules (150 and 300 mg nizatidine) and ampoules (25 mg ml^{-1}) were produced by Galenika (Belgrade). To analyse the capsules,

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the contents of ten capsules were mixed. A weighed amount of powder was dissolved in water and the filtrate was made up to 100 ml with water to give a solution of approximately 5×10^{-3} M.

All other chemicals were of analytical-grade purity (Merck). Doubly-distilled water was used.

2.3. Solutions

For analytical purposes a freshly prepared 5×10^{-3} M aqueous solution of pure nizatidine was used as the stock solution. Palladium(II) chloride standard solution (2.08×10^{-2} M) was prepared as described previously [6], and then standardized gravimetrically [7].

The ionic strength of the final solution was kept constant by addition of 2 M potassium chloride solution.

Britton–Robinson buffer solutions [8] covering the pH range 2.31–7.95 were prepared by mixing 0.04 M phosphoric acid, boric acid and acetic acid with the appropriate volume of 0.2 M sodium hydroxide and sufficient 2 M potassium chloride to bring the ionic strength to 0.2 M.

2.4. Procedure

Palladium(II) chloride standard solution (0.2 ml) and potassium chloride (2.50 ml) were placed in a 10 ml standard flask and an aliquot (0.1–0.9 ml) of 10^{-3} M nizatidine was added. The pH was adjusted by adding 5.00 ml of Britton–Robinson buffer (pH 3.50) and the solution was diluted to volume with water. The absorbance at 340 nm was measured after 5 min against a reagent blank. All measurements were made at room temperature (25 ± 0.5°C).

3. Results and discussion

The reaction between nizatidine and palladium(II) chloride was investigated over the pH range 2.35–7.95 in Britton–Robinson buffer solutions. Absorption curves (Fig. 1) show that the absorbance of the complex increases from pH 2.35 to pH 4.32, and then decreases. The position of the absorption maximum of the complex shifted slightly with pH, from 325 nm (pH 2.35) to 318 nm (pH 7.95).

A Britton–Robinson buffer (pH 3.50) was used to provide the working pH. The complex gave an absorption peak at 325 nm. Because nizatidine had a significant absorbance at the wavelength of maximum absorbance of the complex, and showed negligible absorbance at 340 nm, all measurements were performed at 340 nm against a reagent blank, palladium(II) chloride. Investigation of the effect of reagent concentration showed that a two-fold molar ratio of palladium(II) to analyte is necessary for maximum complex formation. It was found that increasing the ionic strength increases the absorbance of the complex and an ionic strength of 0.50 M was used to provide the working conditions. Under these conditions the colour takes 5 min for full development, and the absorbance remained unchanged for up to 24 h.

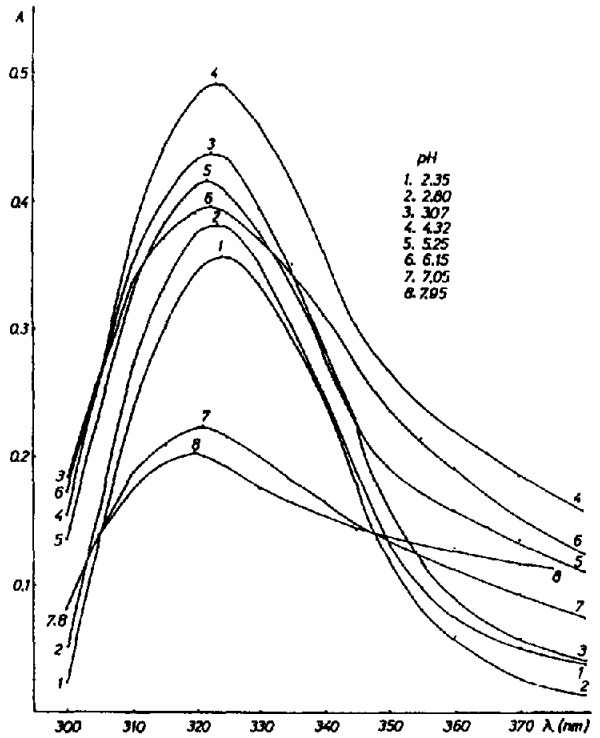

Fig. 1. The effect of pH on complex formation between nizatidine and Pd(II). [Nizatidine] = 4×10^{-5} M, [Pd(II)] = 2×10^{-4} M, $\mu = 0.5$ M.

Table 1
Conditional stability constant of the nizatidine–Pd(II) complex[a]

Sommer's method ($N = 12$)	log K' 4.513	SD 0.119	S_x 0.049	RSD (%) 2.632
Asmus's method ($n = 3$)	A_{ext} 0.19	A_k 0.148	log K 4.673	
Job' method of non-equimolar solutions ($n = 3$)				
$C_{(N)}$	P	x_{max}		log K
5×10^{-4} M	5	0.125		4.980

[a] Conditons: pH 3.50 ± 0.05; $\mu = 0.50$ M; temperature $= 25.0 \pm 0.5$°C

3.1. The composition of the complex and conditional stability constant

The composition of the complex formed was established by the continuous variation method [9,10], the molar-ratio method [11] and the Bent–French method [12]. All three methods showed that a 1:1 complex was formed.

To determine the conditional stability constant (K'), the methods of Sommer et al., [13], Asmus [14] and the Job method of non-equimolar solutions [10] were used. The mean values of log K' are presented in Table 1.

3.2. Quantification and application to dosage forms

Beer's law was verified in a Britton–Robinson buffer solution at pH 3.50 and $\lambda_{max} = 340$ nm. A linear relationship between the absorbance and the concentration of nizatidine was obtained over the range 1×10^{-5}–9×10^{-5} M. The molar absorptivity at 340 nm is 6.3×10^3 l mol^{-1} cm^{-1}. The regression equation was $y = 0.026 + 1.938x$ and the correlation coefficient (r) was 0.9998, indicating excellent linearity. The reliability of the method was checked at three different concentrations and the results are summarized in Table 2. The relative standard deviation varied from 3.28% to 1.27% for concentrations of nizatidine of 0.0829–0.2486 mg. The applicability of the method for the determination of nizatidine in dosage forms was examined by analyzing Galitidine^R capsules (150 and 300 mg) and ampoules (25 mg ml^{-1}). Table 2 shows that the results are accurate and reproducible, and that the proposed colorimetric method can be applied for the analysis of nizatidine in pharmaceutical preparations.

Table 2
Spectrophotometric determination of nizatidine with Pd(II)

Nizatidine bulk drug			RSD(%) ($n = 7$)
Amount (mg)	Found (mg)	Recovery (%)	
0.0829	0.0842	102	3.28
0.1658	0.1647	99.3	1.66
0.2486	0.2495	100	1.27
Galitidine preparations of nizatidine			RSD(%) ($n = 7$)
Nominal amount	Found	Recovery (%)	
Capsules: 300 mg	304.7 mg	102	1.69
Capsules: 150 mg	153.4 mg	102	2.77
Injections: 25 mg ml^{-1}	25.2 mg ml^{-1}	101	2.71

In conclusion, it may be considered that the proposed method, using palladium(II) chloride as an analytical reagent, is suitable for the accurate and sensitive analysis of nizatidine in pharmaceutical formulations.

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