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Ciprofloxacin determination by visible light spectrophotometry using iron(III)nitrate

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Abstract

A simple, rapid, efficient and inexpensive method was developed for the determination of ciprofloxacin in tablets and in solutions for infusion by visible light spectrophotometry using 1% iron(III)nitrate in 1% nitric acid. The complex formed by the iron(III)nitrate solutions and the sample and standard ciprofloxacin solutions gave origin to a compound of yellow-orange colour with maximum absorption at 435 nm, which was stable for 60 min. The Lambert-Beer law was obeyed in the concentration range of 20–100 μg/ml. The spectrophotometric method proposed for the evaluation of ciprofloxacin as a raw material and in tablets and solution for infusion is a good alternative method to that recommended by USP XXIII.

Keywords: Visible light spectrophotometry; Ciprofloxacin determination; Ciprofloxacin; Quinolone analysis

Ciprofloxacin is a broad-spectrum 6-fluoroquinolone with marked activity on most Gram-positive and Gram-negative microorganisms, including strains resistant to aminoglycosides and cephalosporine (Campoli-Richards et al., 1988; Paulsen, 1988). Ciprofloxacin has been studied in terms of therapeutic activity. However, few reports about its physicochemical analysis are available in the literature. High performance liquid chromatography is the official method recommended for the quantitative determination of ciprofloxacin both as a raw material and in tablets, solutions for infusion and eye drops (United States Pharmacopeia XXIII, 1994). For the measurements in tablet formulations, the literature has reported analytical methods such as visible light spectrophotometry (Mathur et al., 1990; Rao et al., 1990; Bhowal and Das, 1991), differential pulse polarography (O'Dea et al., 1990) and spectrofluorometry (Lal et al., 1990), only for the analysis of the tablet formulations. The objective of the present study was to propose a rapid, sensitive, easy to perform and reproducible method to quantify the ciprofloxacin in the tablets formulations as well as in the solution for infusion, using 1% iron(III)nitrate in 1% nitric acid.

Reagents and apparatus: all reagents were of analytical grade. Cyprofloxacin hydrochloride

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Table 1
Ciprofloxacin determination in tablets and solution for infusion

Method	Tablets		Solution for infusion	
	% level (mean ± SEM)[a]	CV (%)[b]	% level (mean ± SEM)	CV (%)
Official modified (HPLC)	99.98 ± 0.23	0.56	99.60 ± 0.20	0.50
Iron(III)nitrate	99.45 ± 0.13	0.31	99.91 ± 0.17	0.42
UV spectrophotometry	99.90 ± 0.79	1.94	99.30 ± 0.53	1.31
Microbiological	99.96 ± 0.86	1.91	99.93 ± 0.47	1.04
Volumetry in non-aqueous medium	99.94 ± 0.59	1.33	—	—

[a]Mean ± S.E.M. of six determinations.
[b]Percent coefficient of variation of the assay.

monohydrate standard and the tablets were provided by Bayer do Brasil S.A. and a commercially purchased solution for infusion containing 250 and 200 mg% of ciprofloxacin, respectively, in the form of hydrochloride monohydrate. The colour reagent used was a 1% iron(III)nitrate solution (w/v) in 1% nitric acid (v/v). The solution was kept at room temperature and protected from light. The apparatus used was a UV/VIS Varian spectrophotometer, series 634.

The standardisation of the method was performed starting from a standard solution containing 1.0 mg/ml ciprofloxacin. The colour reagent (0.5 ml) was added to aliquots of this solution and diluted to 50 ml with water to obtain solutions of 20, 40, 60, 80 and 100 μg/ml. Readings were taken at 435 nm. The results obtained were used to calculate the equation for the line using linear regression by the least squares method and the data were evaluated by analysis of variance (Snedecor, 1956; Guedes and Guedes, 1988).

To determine the stability of the complex formed in the reaction, readings of each point on the standard curve were taken at 15-, 30- and 60-min intervals.

Determination of cyprofloxacin in the samples: the equivalent of 25 mg ciprofloxacin standard was dissolved in 50 ml of water. The colour reagent (0.5 ml) was added to 5.0 ml of this solution and diluted to 50 ml with water, obtaining a concentration of 50 μg/ml.

Five tablets were placed in 400 ml of water. The mixture was shaken for 30 min and diluted to 500 ml. The preparation was filtered. The equivalent to 2.5 mg/ml ciprofloxacin was used, 0.5 ml of the colour reagent was added and diluted to 50 ml with water, to obtain a concentration of 50 μg/ml. After 15 min, the absorbance of the solutions was determined at 435 nm using a solution containing 0.5 ml of the colour reagent and 50 ml water as the blank; 2.5 ml of the solution for infusion was used, the colour reagent (1.0 ml) was added and diluted to 100 ml with water to obtain a concentration of 50 μg/ml. The preparation was submitted to the same conditions as the tablets sample. Six determinations were carried out in triplicate for each pharmaceutical form to evaluate percent concentration in the samples.

The recovery test was carried out adding aliquots of standard ciprofloxacin solution (500 μg/ml) to the tablet solution (2.5 mg ciprofloxacin). The colour reagent (0.5 ml) was added and diluted to 50 ml with water, and 55, 60, 65 and 70 μg/ml concentrations were obtained. To test the solution for infusion, the equivalent to 5.0 mg ciprofloxacin, was used. Aliquots of standard solution and 0.5 ml colour reagent were added and diluted to 100 ml with water. The concentrations obtained were 52.5, 55, 57.5 and 60 μg/ml.

The Lambert-Beer law was obeyed at the concentration range of 20–100 μg/ml. The correlation coefficient obtained for the line was 0.9996 and the mean percent coefficient of variation for this method was 0.46. The experimental values obtained for the determination of ciprofloxacin in samples are presented in Table 1 and compared to those obtained with other methods currently used.

The results of the recovery test performed for the samples for this method are presented in Table 2. Compounds such as phenols, amides, nitriles and amines react with iron(III)nitrate (Santoro et al., 1989). This reaction is used for the identification of different drugs (Stevens, 1986) and for quantitative analyses (Surman, 1987). For this reason, in the present study we investigated the possibility of using this spectrophotometric method for the quantitative determination of ciprofloxacin. The ultraviolet spectra of the standard and samples solutions were similar, showing no interferents in these tests. The results obtained demonstrated that the proposed method could be utilized for the ciprofloxacin quantification. Reaction between the iron(III)nitrate solution and the standard and sample solutions gave origin to a compound of yellow-orange colour with maximum absorption at 435 nm. The importance of the use of iron(III)nitrate was based on the fact that, in contrast to other iron(III)salts, the concentration of this salt remains constant (Morita and Assumpcão, 1972), which makes its use more suitable for the stability of the complex formed in the quantification of the active drug. There are no literature data about the complex formed between ciprofloxacin and iron(III)nitrate; however, due to the similarity to reactions with iron(III)chloride, the probable ratio of the complex formed is 2:1. Preliminary assays with 1 and 5% iron(III)nitrate demonstrated that the absorbances obtained were similar. When 0.5, 1.0, 2.0 and 5.0 ml of the colour reagent were added, similar values were obtained. In the present study we used a 0.5-ml volume of the reagent for the assay since, according to the literature, an excess of iron(III) ions in solution may modify the colour and consequently the absorbance of the complex formed. The absorbance readings of the solution at each point on the standard curve taken at 15-, 30- and 60-min intervals did not differ significantly at the $p < 0.05$ level, demonstrating the stability of the complex formed. The mean percent levels determined by the method proposed did not differ significantly at the $p < 0.01$ level from those determined by other methods. To summarise, the results indicate that this is an acceptable alternative method for the routine quality control of this drug in the formulations studied, when compared to the modified official method and to other methods.

Table 2
Experimental values obtained in the recovery test for ciprofloxacin samples in the form of tablets and solution for infusion

Sample	Amount of standard (μg/ml)		% Recovery
	Added	Recovered	
Tablets	5.00	4.95	99.00
	10.00	9.65	96.50
	15.00	14.45	96.33
	20.00	19.57	97.85
	2.50	2.49	99.60
Infusion	5.00	4.92	98.40
	7.50	7.36	98.13
	10.00	9.75	97.50

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