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Spectrofluorometric determination of piroxicam

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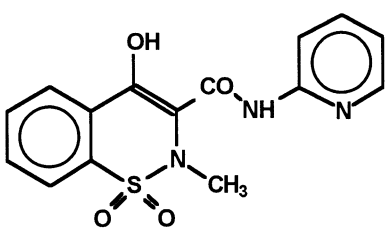
Abstract

The spectrofluorometric determination of piroxicam [4-hydroxy-2-methyl-*N*-(2-pyridyl)-2II-1,2-benzothiazine-3-carboxamide-1,1-dioxide] in pharmaceutical tablets is described. It involves excitation at 330 nm of an acid solution (HNO_3 0.5 M) of the drug, and measurement of the fluorescence intensity at 440 nm. The linear range is 0.01–1.25 μg ml^{-1}. © 1998 Elsevier Science B.V. All rights reserved.

Keywords: Spectrofluorometry; Determination of piroxicam

1. Introduction

Piroxicam [4-hydroxy-2-methyl-*N*-(2-pyridyl)-2H-1,2-benzothiazine-3-carboxamide-1,1-dioxide] is the prototype of a new class of nonsteroidal anti-inflammatory drugs ($NSAID_s$) that has been named 'oxicams' [1,2]. It is an enolic acid with a pKa of 6.3 in dioxane-water (1:2) [1,2].



Piroxicam

Piroxicam produces a rapid and effective response in the treatment of many diseases such as rheumatoid arthritis, osteoarthritis, ankylosing spondylitis, gout juvenile rheumatoid arthritis, musculoskeletal disorders, postpartum pain and sport injuries [2]. The most important side effect that has been reported is gastrointestinal effect (ulcer, bleeding ulcers, etc). Other side effects such as headache, dizziness, aplastic anemia, skin rushes, palpitations, edema, tinnitus are less important and infrequent [2,3].

Scientific literature reports several analytical methods for the determination of piroxicam in plasma, serum, buffers solutions and pharmaceutical preparations [4], such as polarographic [5] and voltametric techniques [6], UV and visible spectrophotometry [7,8], flow injection spectrophotometry [9], high performance liquid chromatography [10–18], coulometry [19], capillary zone electrophoresis and micellar electrokinetic

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capillary chromatography [20] and nuclear magnetic resonance spectrometry [21]. There seems to be no reports on the application of spectrofluorimetry to the determination of this important pharmaceutical. However, it is well known that the main advantages of the latter method are its simplicity, high sensitivity and specificity.

The present report suggests that piroxicam can be rapidly and efficiently determined in pharmaceutical preparations (capsules) by a spectrofluorometric method.

2. Experimental

2.1. Apparatus

All fluorescence measurements were done on a SHIMADZU RF-5301 PC spectrofluorophotometer equipped with a 150 W Xenon lamp. Usual experimental parameters were: slit width; 5.0 nm, $\lambda_{exc} = 330$ nm; $\lambda_{em} = 440 \pm 10$ nm.

Absorbance measurements were done on a Beckman DU 640 spectrophotometer using 1.00 cm quartz cells.

2.2. Reagents

A stock solution of piroxicam (10 μg ml^{-1}) was prepared by dissolving 10.0 mg of piroxicam in 10 ml of NaOH 0.5 N. Then, 10 ml of HNO_3 1 N were added and the resulting mixture was placed into a 1000.0 ml volumetric flask and diluted with HNO_3 0.5 N. A standard solution of piroxicam (5 μg ml^{-1}) was prepared by conveniently diluting the stock solution with HNO_3 0.5 N. The stock solution was prepared once a day and stored in the refrigerator before measuring the fluorescence.

2.3. Calibration curve

Solutions for the calibration curve were prepared by convenient dilutions of the standard solution with HNO_3 0.5 N in order to obtain concentrations in the range 0–5 μg ml^{-1}. Fluorescence intensity was measured immediately at 440 ± 10 nm ($\lambda_{exc} = 330$ nm). In this case the equation is: $I = A + BC$, where I is the fluorescence intensity (in arbitrary units), $A = 1.0(1)$, $B = 16.3(2)$, C = concentration of piroxicam (in the range 0.01–1.25 μg ml^{-1}), $r = 0.998$, $n = 49$. Relative standard deviations (R.S.D.) were: 1.2% for $C = 0.300$ μg ml^{-1} ($n = 15$) and 1.8% for $C = 0.750$ μg ml^{-1} ($n = 15$). The detection limit (D.L., calculated as $2\sigma/B$), was 0.012 μg ml^{-1} (σ = S.D. of A).

2.4. Procedure for pharmaceutical samples (capsules)

Samples of 10.0 mg of triturated capsules were weighed on an analytical balance; 10 ml of NaOH 0.5 N were added, and the mixture was shaken vigorously for at least 10 min. Then, 10 ml of HNO_3 0.5 N were added and the resulting solution was placed into a 100.0 ml volumetric flask and diluted with HNO_3 0.5 N. The mixture was filtered and conveniently diluted with HNO_3 0.5 N. The corresponding dilutions were prepared and the fluorescence intensity was measured 2 h later (it was found that the intensity increased with time until it reached a maximum).

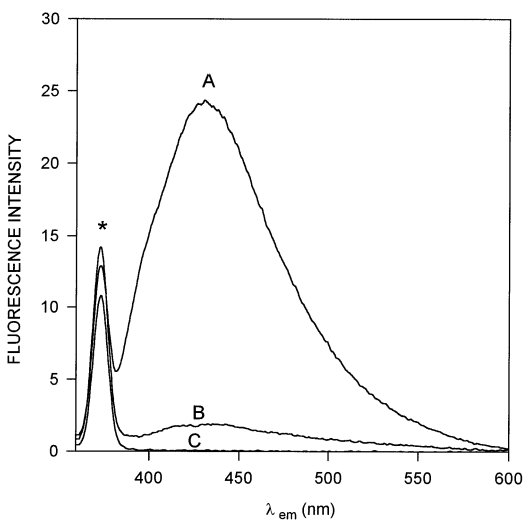

Fig. 1. (A) Fluorescence emission spectrum of piroxicam (1.5 μg ml^{-1}) in HNO_3 0.5 N (pH ≈ 0.7); (B) same as A but in alkaline medium (NaOH 0.5 N, pH ≈ 12.7); (C) emission spectrum of HNO3 0.5 N. In all cases $\lambda_{exc} = 330$ nm. The peak marked with an asterisk is the solvent Raman line.

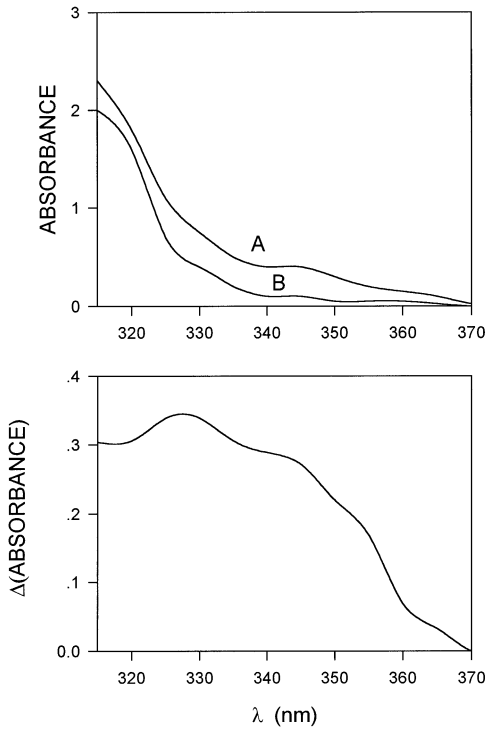

Fig. 2. Top: electronic absorption spectra of (A) a solution of piroxicam (5 μg ml^{-1}) in HNO3 0.5 N; (B) HNO3 0.5 N. Bottom: difference spectrum (A–B).

3. Results and discussion

In the present work we discuss the application of spectrofluorometry in order to determine the amount of piroxicam in pharmaceuticals samples (capsules). Although piroxicam is soluble in alkaline solutions [1], it only emits fluorescence in acid solutions (see Fig. 1). We found that a suitable procedure was to dissolve it in NaOH 0.5 N, adding excess HNO_3 0.5 N in order to measure the intensity of fluorescence or to register the fluorescence emission spectrum. A suitable excitation wavelength is 330 nm, with the corresponding emission maximum at 440 ± 10 nm.

The use of HNO_3 should in principle give better results than HCl, since an important variation in the values of intensity of fluorescence as well as a shift of the emission maximum with time were observed by using the latter acid. Concentrations of HNO_3 of 0.5 N or 1 N seem to be preferable in this case since higher concentrations could decompose the samples.

Table 1
Determination of piroxicam in pharmaceutical samples (capsules)

Piroxicam taken (μg ml^{-1})	Found (μg ml^{-1}) Rec %; R.S.D.%*
0.160	0.155 (96.9;5.2)
0.330	0.327 (99.0;2.6)
0.660	0.614 (93.1;4.2)
0.700	0.683 (97.6;3.9)
0.790	0.787 (99.6;1.0)
0.900	0.840 (93.3;2.3)
1.050	0.960 (91.0;2.1)
1.260	1.120 (89.0;8.0)

* Average of three determinations.

The absorbance of piroxicam solutions was measured by a differential method (see Fig. 2). These measurements indicate that the maximum value of the concentration of piroxicam at which linearity can be expected is roughly 0.75 μg ml^{-1} (since this latter concentration corresponds to an absorbance of approximately 0.05) [22]. However, it was found experimentally that the calibration plot is linear in the range 0.01–1.25 μg ml^{-1} (see Section 2 for details on the calibration graph).

Pharmaceutical samples (capsules of 20 mg of piroxicam) were studied with this method. The samples were prepared by the above described procedure. The concentration of piroxicam can be calculated using the calibration plot, with the corresponding results shown in Table 1. The recoveries seem to be independent on the concentration, provided the latter lies within the linear range given above.

In conclusion, it has been shown that piroxicam can be rapidly determined in pharmaceutical samples (capsules) using a spectrofluorometric method.

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