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Journal of Pharmaceutical and Biomedical Analysis
25 (2001) 679–683

JOURNAL OF
PHARMACEUTICAL
AND BIOMEDICAL
ANALYSIS

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Short communication

Spectrofluorometric determination of ibuprofen in pharmaceutical formulations

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Received 16 December 1999; received in revised form 20 October 2000; accepted 24 October 2000

Abstract

The spectrofluorometric determination of ibuprofen in pharmaceutical tablets, creams and syrup is described. It involves excitation at 263 nm and emission at 288 nm. The linear range is 2–73 mg L^{-1}. Other drugs or excipients present in the different formulations do not interfere, except in the case of chlorzoxazone containing tablets. Due to its strong absorbance in the spectral range the chlorzoxazone does interfere, so that in this case the proposed method can't be applied. © 2001 Elsevier Science B.V. All rights reserved.

Keywords: Spectrofluorometry; Determination of ibuprofen; Ibuprofen

1. Introduction

Ibuprofen is a substituted arylpropionic acid, which exists predominantly in the ionized, anionic form at physiological pH [1].

Ibuprofen has been determined, specially, by gas liquid or high performance liquid chromatography [2–33]. In order to design simple methods for quality control in pharmaceutical preparations [34–36], a spectrofluorometric method for the quantitation of ibuprofen in tablets, creams and syrups is reported. This method is rapid, selective and sensitive. To the best of our knowledge, this is the first attempt to determine ibuprofen in pharmaceutical formulations by spectrofluorimetry.

2. Experimental

2.1. Apparatus

All fluorescence measurements were done on a Shimadzu RF-5301 PC spectrofluorometer equipped with a 150 W Xenon lamp, using 1.00 cm quartz cells. Experimental parameters were slit width 3 nm, $\lambda_{exc} = 263 \pm 2$ nm; $\lambda_{em} = 288 \pm 1$ nm.

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PII: S0731-7085(00)00584-7

Absorbance measurements were done on a Beckman DU 640 spectrophotometer using 1.00 cm quartz cells (Section 3).

HPLC procedure was carried out using (a) column RP-18 Lichrocart 125-4, particle diameter 5 μm/Lichrosp, (b) mobile phase acetonitrile (pump A)–phosphoric acid (pump B), pH 2.50 in the rate (A:B) = (55:45), (c) flow of 2 ml/min, (d) detection wavelength: 230 nm, (e) room temperature, and (f) time retention registered approximately 2.73 min (Section 3).

2.2. Reagents

Ibuprofen: Marsing & Co. Ltd. A/S. Denmark Batch Lot No. 0840898, purity assay 99.9% (normal limits 98.5–101.8%).

A stock solution of ibuprofen 400 mg/l, was prepared by dissolving ibuprofen (Marsing & Co.) in NH_3 Merck 0.2 M. The standard solutions were prepared by conveniently diluting the stock solution with NH_3 Merck 0.2 M.

2.2.1. Pharmaceutical preparations

Tablets, creams and syrups were obtained from the following laboratories: Searle, Sintyal, Monsanto Argentina SAIC (Ibupirac, Ibupiretas, Ibupirac syrup, Ibupirac fem, Ibupirac flex, Ibupirac migra, Ibupirac cream), Parke Davis (Ponstin syrup) and processed as described below.

2.3. Calibration curve

Solutions for the calibration curve were prepared by suitable dilution of the stock solution with NH_3 0.2 M in a volumetric flask. The concentration range was 2–73 mg/l. The fluorescence intensity was measured at $\lambda_{em} = 288$ nm, irradiating at $\lambda_{exc} = 263$ nm. The equation for the calibration curve is $I = A + BC$, where I is the fluorescence intensity (in arbitrary units), and C is the concentration of ibuprofen in mg/l. After least-squares linear fit of the fluorescence emission data, we obtained $A = 7.9$ (4); $B = 5.97$ (9); $R^2 = 0.999$ with $n = 33$ (three replicates of 11 points). The detection limit was 2 mg/l calculated as either $3S_{bl}A/B$ or as $\{k[S_{bl}^2 + S_A^2 + S_B^2(A/B)]^{1/2}\}/B$ where $k = 3$ and S_{bl} is the standard deviation of a set of 10 replicates corresponding to the analytical blank sample [37].

2.4. Procedure for unknown aqueous samples and pharmaceutical samples

Aqueous samples were prepared by diluting the stock solution with NH_3 0.2 M. Commercial tablets were processed as follows: an amount of triturated tablets containing 20 mg of ibuprofen was weighed, dissolved with NH_3 0.2 M into a 50 ml volumetric flask, sonicated for 20 min and filtered. Final dilutions with NH_3 0.2 M were carried out in order to obtain concentrations of 20, 40 and 60 mg/l within the linear calibration range. The election of these concentration values was not arbitrary. On the contrary, it was based on the fact that the central part of the calibration curve (50%, 100% and 150% of the target central value 40 mg/l), was selected.

For creams or syrups, a suitable amount containing 20 mg of ibuprofen was placed into a 50 ml volumetric flask and diluted with NH_3 0.2 M, in order to obtain concentrations of 20, 40 and 60 mg/l within the linear calibration range.

However, taking into account a linear calibration range as broad as from 2 to 73 mg/l and the high dose of ibuprofen in formulations (120–400 mg per tablet) any dilution can be obtained within the linear calibration range.

2.5. Chromatographic procedure

In order to carry out the HPLC procedure, all pharmaceutical formulations were treated before they were injected. Tablets and syrups were pre-treated as USP XXIV (United State Pharmacopoeia XXIV; [38]). Cream was pre-treated as BP 98 (British Pharmacopoeia 98; [39]). Then, 20 μl of solution of each pre-treated pharmaceutical formulation, containing ibuprofen at a level of 400 mg/l, was injected on a column RP-18 Lichrocart 125-4, particle diameter 5 μm/Lichrosp, using mobile phase acetonitrile (pump A)–phosphoric acid (pump B), pH 2.50 in the rate (A:B) = (55:45), at a flow of 2 ml/min, detecting the signal at $\lambda = 230$ nm, working at room temperature. The time retention registered was approximately 2.73 min (Section 3).

3. Results and discussion

Ibuprofen is soluble in water only in an alkaline medium (NH_3 or NaOH). In ammonia solutions, ibuprofen emits fluorescence at 288 ± 1 nm when it is excited at 263 ± 2 nm (Fig. 1). The information about the maximum concentration at which fluorescence linearity may be expected (i.e., absorbance < 0.05) was obtained from the electronic absorption spectra (Section 2) [38]. This limit was estimated up to approximately 70 mg/l. According to these data, the dynamic linear range was 2–72 mg/l. The results obtained applying the linearity tests were: $R^2 = 0.9999$; $F = 14.542$ (calculated for 1,33 degrees of freedom and $P < 0.01$), compared with a tabulated F of 7.49. Further, the T calculated for 31 degrees of freedom was 5.14, as compared with a tabulated T of 2.04 ($P < 0.01$).

As mentioned above, the detection limit was calculated as suggested by Winefordner and Long [37], taking into account the statistics involved in the difference between a given response and the blank signal and the uncertainty introduce by the presence of errors in both the slope and intercept of the calibration line [39].

Unknown aqueous samples of ibuprofen were studied applying the above procedure (Section 2) and the results are shown in Table 1. The method was then applied to different pharmaceutical preparations (tablets, syrups and creams). The results are summarised in Table 2. They are excellent, despite the following facts: (a) The isolated aromatic ring of ibuprofen shows moderate native fluorescence, but it is sufficient to serve as the basis for the determination of this drug in these formulations since its dose is high (120–400 mg per tablet). (b) In some cases (Table 2), ibuprofen is associated with other drugs and different excipients. The interference of these active ingredients was studied in particular.

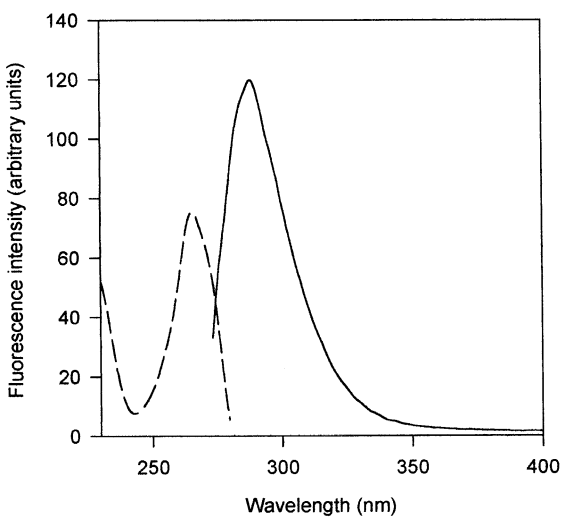

Fig. 1. Fluorescence spectra of ibuprofen (18 mg/l) in NH_3 0.2 M: (—), emission spectrum ($\lambda_{exc} = 263$ nm); (– – –), excitation spectrum ($\lambda_{em} = 288$ nm).

Table 1
Determination of ibuprofen in aqueous samples

Taken (mg/l)	Found [a] (mg/l)	Recovery (%)	RSD (%)
11.65	11.20	96	1.2
19.80	20.33	102	0.3
27.72	27.72	100	0.6
35.64	34.98	98	1.2
43.56	44.10	101	0.5
51.48	50.16	97	0.2
59.40	57.60	97	1.0
67.32	63.90	95	1.7

[a] Average of three determinations.

Standards of Homoatropine methyl bromide and Ergotamine were prepared according to their levels per tablet and excited at 263 nm. Emission spectra of them were obtained and no significant fluorescence emission was registered at the selected spectral range. We assume that the lack of interference of Homatropine and Ergotamine is based on the fact that their concentrations are by two orders of magnitude, lower in the formulations, than that of ibuprofen (Table 2). In the case of caffeine, no interference was found either in spite of the fact that it is present in one formulation at a high level of 100 mg per tablet. Emission spectrum of standard of caffeine was also obtained and no fluorescence was registered at the working wavelength.

Absorption spectra was also obtained and we postulate that the real reason of the lack of interference is that the cut-off wavelength of caffeine is 300 nm where the emission spectrum of ibuprofen has its maximum.

An exception in Table 2 seems to be the pharmaceutical preparation Ibuflex, which contains chlorzoxazone. The fluorescence emitted by ibuprofen in the presence of chlorzoxazone is lower than that emitted by pure ibuprofen at the same concentration. Emission spectrum of standard solution of chlorzoxazone, prepared according to its level per tablets, was obtained exciting at 263 nm and no fluorescence emission was registered in this spectral range. Absorption spectra of chlorzoxazone were also obtained and strong absorbance in the selected spectral range was found. Therefore, we accept that the reason of the interference is that the maximum absorption wavelength of chlorzoxazone is 288 nm just where the emission spectrum of ibuprofen has its maximum too.

Table 2
Determination of ibuprofen in pharmaceutical preparations

Preparation	Composition	Ibuprofen found [a] (Rec. %)
Ibupiretas (tablet)	Ibuprofen 120 mgExcipients	116 ± 1 mg (97%)
Ibupirac (tablet)	Ibuprofen 400 mgExcipients	396 ± 3 mg (99%)
Ibumigra (tablet)	Ibuprofen 400 mgCaffeine 100 mgErgotamine tartrate 4 mgExcipients	390 ± 2 mg (98%)
Ibufem (tablet)	Ibuprofen 400 mgHomoatropine methyl bromide 4 mgExcipients	408 ± 1 mg (102%)
Ibuflex (tablet)	Ibuprofen 400 mgChlorzoxazone 250 mgExcipients	344 ± 3 mg (86%)
Ibupirac (cream)	Ibuprofen lisinate 5% P/P [b]Excipients	4.98% P/P (99%)
Ibupirac (syrup)	Ibuprofen 2 g/100 mlExcipients	1.99 ± 0.05 g/100 ml (99%)
Ponstin (syrup)	Ibuprofen 2 g/100 mlExcipients	2.08 ± 0.05 g/100 ml (104%)

[a] Average of three determinations ± S.D. of each work concentration within linear range. Recoveries were calculated considering that the preparations contain the amount reported by the manufacturing laboratories. All values are given in mg per tablet, except in the case of the cream and syrup.

[b] The abreviation P/P means g of ibuprofen per 100 g of cream.

Table 3
Determination of ibuprofen in pharmaceutical formulations by HPLC

Preparation	Composition	Ibuprofen found [a] (Rec. %)
Ibupiretas (tablet)	Ibuprofen 120 mgExcipients	117 ± 1 mg (97.2%)
Ibupirac (tablet)	Ibuprofen 400 mgExcipients	401 ± 1 mg (100.2%)
Ibumigra (tablet)	Ibuprofen 400 mgCaffeine 100 mgErgotamine tartrate 4 mgExcipients	396 ± 1 mg (98.9%)
Ibufem (tablet)	Ibuprofen 400 mgHomoatropine methyl bromide 4 mgExcipients	410 ± 1 mg (102.7%)
Ibuflex (tablet)	Ibuprofen 400 mgChlorzoxazone 250 mgExcipients	398 ± 1 mg (99.4%)
Ibupirac (cream)	Ibuprofen lisinate 5% P/P [b]Excipients	4.99% P/P (99.8%)
Ibupirac (syrup)	Ibuprofen 2 g/100 mlExcipients	1.99 ± 0.03 g/100 ml (99.6%)
Ponstin (syrup)	Ibuprofen 2 g/100 mlExcipients	2.01 ± 0.06 g/100 ml (100.5%)

[a] Average of three determinations ± S.D. of each work concentration within linear range. Recoveries were calculated considering that the preparations contain the amount reported by the manufacturing laboratories. All values are given in mg per tablet, except in the case of the syrup and cream.

[b] The abbreviation P/P means g of ibuprofen per 100 g of cream.

For this reason, in the case of chlorzoxazone, such a method is not acceptable. In order to validate the method designed in the present paper, ibuprofen was quantified in all pharmaceutical formulations by HPLC (Section 2). The results are shown in Table 3. There is no significant difference between the recoveries of both methods, except in the case of Ibuflex, which contains ibuprofen and chlorzoxazone.

In conclusion, it has been shown that ibuprofen can be determined in pharmaceutical preparations using a rapid, sensitive and selective spectrofluorometric method, except in the case of the simultaneous presence of chlorzoxazone.

Acknowledgements

Financial support from the University of Rosario, Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET) and Agencia Nacional de Promoción Científica is gratefully acknowledged. We also thank Searle-Sintyal and Monsanto Argentina SIAC, for the supply of the pharmaceutical preparations and chlorzoxazone standard; Farm. Eduardo Quiroga (Colegio de Farmacéuticos de la Provincia de Buenos Aires, Laboratorio de Control de Calidad) who made the HPLC analyses; Prest Drugstore and Bacciardi Pharmacy for the supply of standard drugs, Dr. Teodoro Kauffmann and Laboratorio Lafedar de Santa Fé.

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