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Quantitative analysis of ibuprofen in pharmaceuticals and human control serum using kinetic spectrophotometry

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Abstract: The aim of this work was to develop a new kinetic spectrophotometric method for the determination of ibuprofen in pharmaceutical formulations. Ibuprofen was determined in an acidic ethanolic medium by monitoring the rate of appearance of 1-nitroso-2-naphthol, resulting from the displacement by ibuprofen of Co(III) from the tris(1-nitroso-2-naptholato)cobalt(III) complex. The optimum operating conditions regarding reagent concentrations and temperature were established. The tangent method was adopted for constructing the calibration curve, which was found to be linear over the concentration range 0.21–1.44 and 1.44–2.06 μg ml^{-1}. The optimized conditions yielded a theoretical detection limit of 0.03 μg ml^{-1} based on the 3.3 S_0 criterion. The interference effects of the usual excipients of powdery drugs, foreign ions and amino acids on the reaction rate were studied in order to assess the selectivity of the method. The developed procedure was successfully applied for the rapid determination of ibuprofen in commercial pharmaceutical formulations and human control serum. The unique features of this procedure are that the determination can be performed at room temperature and the analysis time is short. The newly developed method is simple, inexpensive and efficient for use in the analysis of a large number of samples.

Keywords: ibuprofen; kinetic spectrophotometry; validation; pharmaceutical preparation.

INTRODUCTION

Ibuprofen [*RS*-2-(4-isobutylphenyl)propionic acid] (IB) is a non-steroidal anti-inflammatory medication used especially for the relief of the symptoms of arthritis, primary dysmenorrhoea and fever, and as an analgesic, especially where there is an inflammatory component. Ibuprofen was developed by the research arm of the Boots Group. Its side effects are gastrointestinal hemorrhage and ulce-

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ration. Various methods have been used for the determination of ibuprofen in pharmaceutical and biological samples. Until now, chromatographic methods (HPLC, GC, HPTLC, TLC),[1–9] electrophoretic methods,[10–13] spectrophotometric methods[14,15] and titrimetric methods with visual and potentiometric indications[16–18] are the major technique for the determination of ibuprofen.

The aim of this work was the development and validation of a simple, rapid and selective kinetic method for the analysis of ibuprofen in commercial pharmaceutical formulations and human control serum.

EXPERIMENTAL

Apparatus

The reaction rate was monitored spectrophotometrically. The absorbance of the solution was measured at a wavelength of 375 nm, which corresponded to the absorption of 1-nitroso--2-naphthol. The readings were performed on a Perkin-Elmer Lambda 15 UV/Vis spectrophotometer, connected to a thermo-circulating bath.

An Agilent Technologies Model 1200 instrument fitted with a C_{18} (Zorbax 5μm, 250 mm×4.6 mm) analytical column was used for the HPLC analysis.

A Julabo MP-5A model thermostatic bath was used to maintain the reaction temperature at 22.00±0.02 °C.

The pH measurements were made using a Hanna Instruments pH meter.

The solutions were thermostated at 22.00 ± 0.02 °C before the beginning of the reaction.

Reagents

A stock solution (1.0×10^{-3} mol l^{-1}) of ibuprofen was prepared daily in ethanol from pharmaceutical 99.59 % certified products, kindly provided by the Pharmaceutical Laboratory Galenika, a.d., Belgrade, Serbia.

An acetic acid solution (HOAc, 10 mol l^{-1}) was prepared from glacial HOAc (Merck).

A 1-nitroso-2-naphthol solution (1.0×10^{-3} mol l^{-1}) (Merck) was prepared by dissolving a known amount in ethanol.

A potassium bromate solution (0.1 mol l^{-1}) was prepared by dissolving a known amount in water.

A stock cobalt(II) solution (1.7×10^{-3} mol l^{-1}) was prepared by dissolving $CoCl_2\cdot6H_2O$ (Merck) in water. A working solution (1.7×10^{-5} mol l^{-1}) was obtained by diluting the stock cobalt solution with water.

The ionic strength was kept constant at 0.10 by adding an appropriate amount of NaCl solution (1.0 mol l^{-1}).

Analytical grade chemicals and deionized water (MicroMed high purity water system, TKA Wasseraufbereitungssysteme GmbH) were used for the preparation of all solutions.

Procedure

General Procedure. In order to obtain good mechanical and thermal stability, the instruments were run for 10 min before the first measurement. The reaction was performed in a reaction-mixture vessel with four compartments. A solution of 1-nitroso-2-naphthol was placed in one compartment, ibuprofen and acetic acid in the second, $KBrO_3$ in the third, and cobalt(II), electrolyte for ionic strength control and ethanol (total volume 10 ml) in the fourth compartment. The vessel was thermostated at 22.00±0.02 °C and the reaction was initiated by mixing. The reaction solution was put into a cell and the absorbance at 375 nm was measured spectrophotometrically every 30 s over a period of 5−6 min after mixing against the reagent blank prepared similarly.

Procedure for tablets and cream. A total of 20 tablets of each of the two studied pharmaceutical preparations (Ibuprofen, Panfarma, Belgrade, Serbia and Brufen®, Galenika a.d., Belgrade, Serbia) containing IB were weighed and finely powdered using a pestle and mortar. An accurately weighed quantity of the resulting powder, equivalent to 400.0 mg (weight of one tablet) of IB was dissolved in 25.00 ml of ethanol. Then it was centrifuged at 1800 rpm for 10 min and filtered through a 0.45 μm membrane filter (Millipore) directly into a 100.00 ml standard volumetric flask. The residue was washed three times with 15.00 ml of ethanol for complete recovery of the drug. The washings were added to the volumetric flask which was then filled to the mark with the same solvent. 2.50 ml of this solution was made up to 100.00 ml with ethanol to obtain a solution the expected IB concentration of which was 100.0 μg ml^{-1}. For kinetic determination, aliquots of this solution were transferred into vessels. For HPLC determination, aliquots of ibuprofen solution were transferred to a 10.00 ml volumetric flask and evaporated to dryness in a water bath. The residue was reconstituted with mobile phase and 20 μl was transferred into a glass vial for automatic injection into the HPLC system.

In the case of cream (Brufen®, Galenika a.d., Belgrade, Serbia), 4.000 g, which corresponded to 400.0 mg of ibuprofen, was weighed and mixed with 25.00 ml of ethanol. The mixture was stirred intensively for 30 min, centrifuged at 1800 rpm for 10 min and filtered through a 0.45 μm membrane filter (Millipore) directly in a 100.00 ml volumetric flask. The further preparation was the same as in the case of the tablets.

In all cases, it was assumed that the actual content of the tablet and cream corresponded to that reported by the manufacturing laboratories.

Serum sample preparation. Human lyophilized control serum (Lyotrol N, bioMérieux® sa, France) was used. The serum sample was spiked at two concentrations levels. The concentration of IB was chosen to match its normal therapeutic concentration in human serum.[19] To 0.50 ml of serum, the appropriate amount of the stock solution of ibuprofen (10 mg ml^{-1}) and 15 ml of ethanol was added and, after brief vortex mixing, it was centrifuged for 5 min at 3000 rpm to deposit the protein precipitate. The separated supernatant was collected in a 25.00 ml standard volumetric flask and filled up to the mark with the same solvent. The serum sample contained 100.0 μg ml^{-1} ibuprofen. Aliquots of this solution were transferred into vessels. For the kinetic determination, $Fe^{3+}$was masked by adding an appropriate amount of F^- (1.0×10^{-4} g ml^{-1}). For the HPLC determination, aliquots of the ibuprofen solution were transferred to a 10.00 ml volumetric flask and evaporated to dryness in a water bath. The residue was reconstituted with mobile phase and 20 μl was transferred into a glass vial for automatic injection into the HPLC system.

Comparative method. The employed procedures for the comparative methods (HPLC and alkalimetric (NaOH) titration with visual indication (phenolphthalein as the indicator)) are described in the British Pharmacopoeia[17] and US Pharmacopoeia.[18] Ibuprofen was detected and quantified on a 250 mm×4.6 mm Zorbax C_{18} (5 μm) analytical column operating at room temperature. The mobile phase, a mixture of phosphoric acid–acetonitrile–water, 0.5:340:600 v/v, was allowed to equilibrate and diluted to 1000 volumes with water. The eluate was monitored at 214 nm. Injection of the samples (20 μl) was performed using an autosampler. The flow rate of the mobile phase was 2.0 ml min^{-1}.

RESULTS AND DISCUSSIONS

Mechanism of the reaction

According to Kolthoff and Jacobsen,[20] divalent cobalt coordinates with two ligands (1-nitroso-2-naphthol, R(NO)OH), liberating two hydrogen ions for each cobalt ion present:

$$Co^{2+} + 2R(NO)OH \rightarrow Co[R(NO)O]_2 + 2H^+$$

Analyses of the cobalt(II) complex indicated six-coordination, in fact, the cobalt(II) complex corresponded to $Co[R(NO)O]_2 \cdot 2H_2O$. In the present work cobalt(II) was oxidized with $KBrO_3$, whereby tris(1-nitroso-2-naptholato)cobalt(III), $Co[R(NO)O]_3$, was formed.[21] The complex absorbs at 410 nm, while 1-nitroso--2-naphthol absorbs at 370 nm. In acidic medium, the 370 nm band shifts to 375 nm.[22] In the presence of ibuprofen, the absorption band at 410 nm[22] disappeared and appeared at 375 nm (Fig. 1), ibuprofen displacing cobalt(III) from the com-

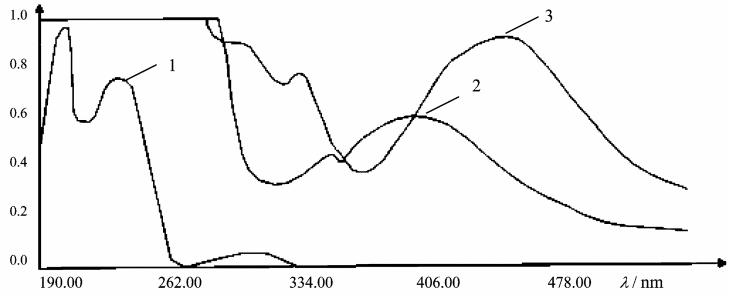

Fig.1. Absorption spectra of: 1) ibuprofen (1.0×10^{-5} mol l^{-1}), 2) 1-nitroso-2-naphthol (1.0×10^{-5} mol l^{-1}) and 3) tris(1-nitroso-2-naphtholato)cobalt(III) complex in ethanolic acetic acid.

plex with 1-nitroso-2-naphthol. The cobalt(III) forms a complex with ibuprofen. Physical studies of cobalt(III) ibuprofenate ($[Co_2(Ibup)_4]^{2+}$), (Ibup = ibuprofenato ion)) showed that in this complex four carboxylate groups are bridging two cobalt atoms (similar to other cobalt(III) carboxylates).[23,24] Ibuprofen was determined by monitoring the rate of appearance of 1-nitroso-2-naphthol in ethanolic acidic medium (Fig. 2):

$$2Co[R(NO)O]_3 + 4IB + 2H^+ \rightarrow [Co_2(Ibup)_4]^{2+} + 6R(NO)OH$$

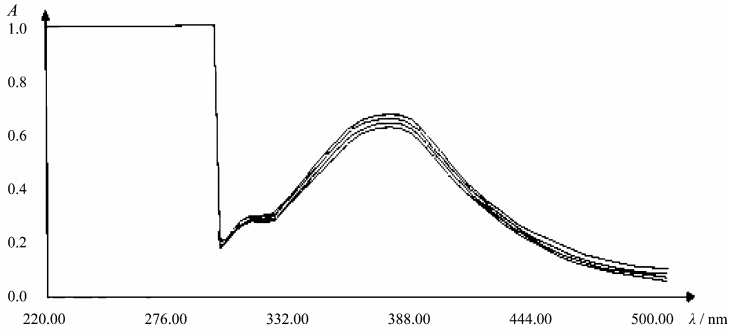

Fig. 2. Repetitative scans of the appearance of 1-nitroso-2-naphthol in ethanolic acetic acid recorded in 2 min intervals in presence of 1.0×10^{-5} mol l^{-1} IB; $c_{R(NO)OH} = 1.0\times10^{-5}$ mol l^{-1}, $c_{CH_3COOH} = 1.0$ mol l^{-1}, $c_{KBrO_3} = 1.0\times10^{-3}$ mol l^{-1}, $c_{Co^{2+}} = 1.7\times10^{-6}$ mol l^{-1}; $t = 22.00\pm0.02$ °C.

Kinetic studies

The tangent method was used for processing of the kinetic data. The rate of the reaction was obtained by measuring the slope of the linear part of the kinetic curves of the absorbance-time plot (slope = dA/dt).

In order to determine the lowest possible determinable concentration of ibuprofen, the working conditions required optimization. Therefore, the dependence of the rate of reactions on the concentration of each of the reactants was determined.

The effect of the concentration of acetic acid (Fig. 3) was studied in the range 1.0−6.0 mol l^{-1}. It can be seen that the reaction rate increased with increasing concentration of acetic acid up to 4.5 mol l^{-1}; beyond this concentration, the rate of the reaction remained constant. For further work a concentration of 5.0 mol l^{-1} was used.

The effect of the concentration of 1-nitroso-2-naphthol on the rate of reaction (Fig. 4) was studied in the range 0.5×10^{-5}–1.1×10^{-5} mol l^{-1}. It can be seen that the reaction rate increased with increasing 1-nitroso-2-naphthol concentration. A concentration of 1.0×10^{-5} mol l^{-1} was chosen as the optimum concentration.

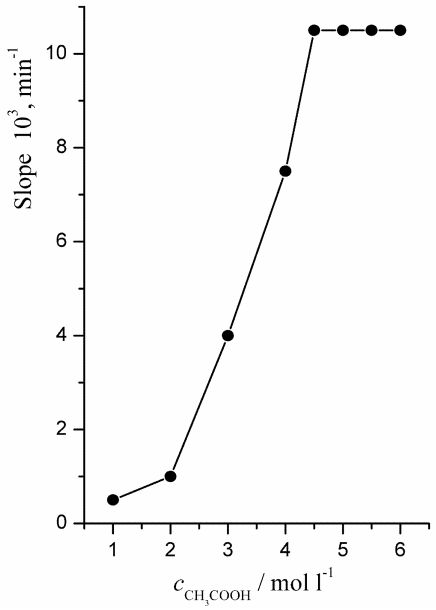

Fig. 3. Dependence of the reaction rate on the acetic acid concentration. Initial concentrations: $c_{R(NO)OH} = 1.0\times10^{-5}$ mol l^{-1}, $c_{KBrO_3} = 1.0\times10^{-3}$ mol l^{-1}, $c_{Co^{2+}} = 1.7\times10^{-6}$ mol l^{-1}; $c_{IB} = 1.0\times10^{-5}$ mol l^{-1}; t = 22.00±0.02 °C.

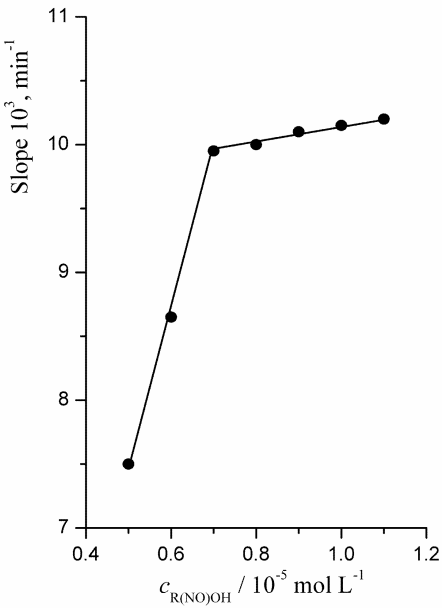

Fig. 4. Dependence of the reaction rate on the 1-nitroso-2-naphthol concentration. Initial concentrations: $c_{CH_3COOH} = 5.0$ mol l^{-1}, $c_{KBrO_3} = 2.0\times10^{-3}$ mol l^{-1}, $c_{Co^{2+}} = 1.7\times10^{-6}$ mol l^{-1}, $c_{IB} = 1.0\times10^{-5}$ mol l^{-1}; t = 22.00±0.02 °C.

The effect of the concentration of $KBrO_3$ (Fig. 5) was studied in the interval of 1.0×10^{-3}–3.0×10^{-3} mol l^{-1}. The reaction rate increased with increasing $KBrO_3$ concentration. For further work, a concentration of 2.5×10^{-3} mol l^{-1} was used.

The correlation between the slope and the Co(II) concentration is given in Fig. 6. The influence of the concentration of Co(II) on the rate of reaction was examined in the range 0.17–4.24×10^{-6} mol l^{-1}. A concentration of 3.4×10^{-5} mol l^{-1} in the final solution was used throughout the experiments.

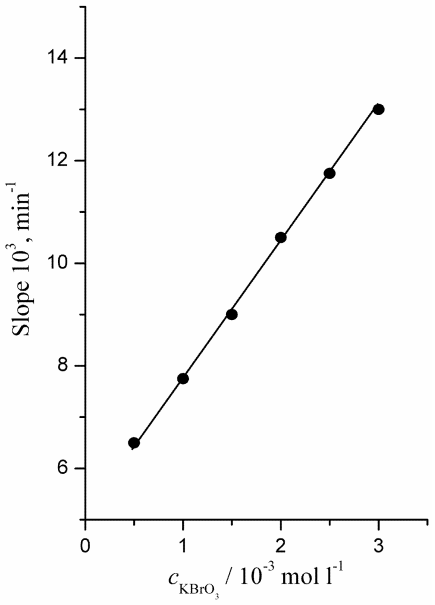

Fig. 5. Dependence of the reaction rate on the $KBrO_3$ concentration. Initial concentrations: c_{CH_3COOH} = 5.0 mol l^{-1}, $c_{R(NO)OH}$ = 1.0×10^{-5} mol l^{-1}, $c_{Co^{2+}}$ = 1.7×10^{-6} mol l^{-1}, c_{IB} = 1.0×10^{-5} mol l^{-1}; t = 22.00±0.02 °C.

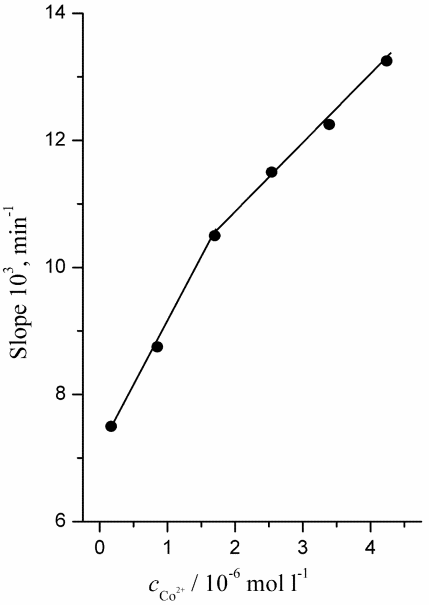

Fig. 6. Dependence of the reaction rate on the cobalt(II) concentration. Initial concentrations: c_{CH_3COOH} = 5.0 mol l^{-1}, $c_{R(NO)OH}$ = 1.0×10^{-5} mol l^{-1}, c_{KBrO_3} = 2.5×10^{-3} mol l^{-1}, c_{IB} = 1.0×10^{-5} mol l^{-1}; t = 22.00±0.02 °C.

The effect of temperature on the reaction rate was studied at 292, 295, 298, 301 and 304 K. The absorbance–time curves obtained at these temperatures indicated the temperature dependence of the reaction rate. The rate for different concentrations of ibuprofen at each temperature was calculated and utilized for plotting the calibration curve. At temperature > 298 K, the linear dynamic range of the determination decreased. The linear dynamic range, regression equation and temperatures are summarized in Table I. The best linearity was obtained at 295 K and hence this temperature was selected as the optimum temperature for the determination process.

The least squares equation ($y = bx + a$, where b and a are the slope and intercept, respectively) for the calibration graph and correlation coefficient, r^2[25]

for the determination of ibuprofen in the concentration range 0.21 to 1.44 μg ml^{-1} under the optimal reaction conditions (c_{CH_3COOH} = 5.0 mol l^{-1}, $c_{R(NO)OH}$ = = 1.0×10^{-5} mol l^{-1}, c_{KBrO_3}= 2.5×10^{-3} mol l^{-1}, $c_{Co^{2+}}$ = 3.4×10^{-6} mol l^{-1}, t = = 22.00±0.02 °C) were calculated:

$$\text{Slope}\times 10^3 = 1.647c_{IB} + 2.645 \qquad r = 0.9989$$

where slope is the slope of the linear part of the kinetic curve of the absorbance–time plot (slope = dA/dt = εl(dc/dt)) and c_{IB} is the ibuprofen concentration expressed in μg ml^{-1}.

TABLE I. Linear dynamic range, regression equation and correlation coefficient at different temperatures

T / K	Linear dynamic range, μg ml^{-1}	Regression equation	Correlation coefficient, r
292	0.41–1.44, n = 5	Slope×10^3 = 1.279c_{IB} + 1.946	0.9986
295	0.21–1.44, n = 6	Slope×10^3 = 1.647c_{IB} + 2.645	0.9989
298	0.21–1.44, n = 6	Slope×10^3 = 3.237c_{IB} + 3.031	0.9985
301	0.21–1.03, n = 4	Slope×10^3 = 2.902c_{IB} + 4.483	0.998
304	0.21–1.03, n = 4	Slope×10^3 = 6.831c_{IB} + 5.095	0.9983

The variance (S_0^2) of the calibration line was evaluated to be 2.566×10^{-4} μg ml^{-1}. The low value of the variance indicates negligible scattering of the experimental data points around the line of regression. The quantitative parameters of the analysis are given in Table II.

TABLE II. Quantitative parameters of the analysis

Calibration range, μg ml^{-1}	0.21–1.44, n = 6
Regression equation	Slope×10^3 = 1.647c_{IB} + 2.645
Slope±SD	(1.647±0.015)×10^{-3}
Intercept±SD	(2.645±0.014)×10^{-3}
Correlation coefficient, r	0.9989
Variance, S_0^2	2.566×10^{-4}
Detection limit, μg ml^{-1}	0.03
Quantification limit, μg ml^{-1}	0.1

The following kinetic equation for the reaction was deduced based on the obtained graphic correlations.

$$\text{Rate} = kc_{R(NO)OH}c_{KBrO_3}c_{Co^{2+}}c_{IB}$$

where k is a constant proportional to the rate constant of the reaction.

The equation is valid for the following concentrations: CH_3COOH, 4.5−6.0 mol l^{-1}; R(NO)OH, 0.7×10^{-5}–1.1×10^{-5} mol l^{-1}; $KBrO_3$, 1.0×10^{-3}–3.0×10^{-3} mol l^{-1}; Co(II), 1.7×10^{-6}–4.24×10^{-6} mol l^{-1} and IB, 0.21−1.44 μg ml^{-1}.

The activation energy for the reaction was calculated from linear regression of Arrhenius plot (log k *vs.* 1/T) and found to be 89.38±0.82 kJ mol^{-1}.

The limits of detection (*LOD*) and quantification (*LOQ*) were evaluated using the following equations:[26–29]

$$LOD = 3.3S_0/b$$
$$LOQ = 10S_0/b$$

where S_0 is the standard deviation of the calibration line and b is the slope. They were found to be 0.030 and 0.10 μg ml^{-1}, respectively.

The precision and accuracy of the system were studied by performing the experiment 5 times for different concentrations of ibuprofen. The results of accuracy and precision of the recommended procedure are presented in Table III.

TABLE III. Accuracy and precision of the determination of ibuprofen

Taken, μg ml^{-1}	Found[a] $x\pm SD$, μg ml^{-1}	RSD[b] / %	$100(x-\mu)/\mu$[c]
0.21	0.22±0.01	3.93	4.76
0.83	0.82±0.02	2.58	–1.2
1.44	1.45±0.02	1.14	0.69

[a]Mean and standard deviation of five determinations at the 95 % confidence level; [b]relative standard deviation; [c]accuracy of the method

Interference studies

To assess the selectivity of the method, the interference of those species accompanying IB in pharmaceutical formulations was studied. The tolerance limits (expressed as the w/w ratios) for the species studied in the determination of 1.65 μg ml^{-1} of IB are given in Table IV. As can be seen, the usual components of powdery drugs (fructose, glucose, lactose, mannitol and sorbitol), the vitamins B_1, B_6 and B_{12}, and Li^+, Na^+ and K^+ do not interfere with the method because the amounts tolerated are much higher than those usually present in pharmaceutical formulations. Binders, such as gelatin, and fillers, such as talc, are insoluble in ethanol, which was used for dissolving the pharmaceutical preparations. Silicon dioxide is also insoluble in ethanol. It should also be noted that higher tolerance levels exist for the presence of the amino acids Ala, Phe, Asp, Met, Tyr, Trp and Ser, the 2-carboxy metabolite of ibuprofen, (2-[4-(2-carboxypropyl)phenyl]propionic acid), and Mn^{2+} and Cd^{2+}. The amino acids His, Arg, Lys and Gly, as well Ca^{2+}, Zn^{2+} and Mg^{2+} interfere with the method. More severe interferences were observed for Fe^{3+} (masked with F^-) and Cu^{2+} ions. No interference was observed when up to 100-fold concentrations of nicotinic acid, citric acid, stearic acid, Si^{4+} and $C_2O_4^{2-}$ were present.

TABLE IV. Effect of foreign species on the determination of 1.65 μg ml^{-1} of ibuprofen

Foreign species	I[a] / %	Tolerance level ($c_{\text{Interferent}}/c_{\text{IB}}$)
Fructose, glucose, lactose, B_1, B_6, B_{12}, Li^+, Na^+, K^+, mannitol, sorbitol	5–10	10^3
Mn^{2+}, Cd^{2+}, Si^{4+}, F^-, $C_2O_4^{2-}$	5–10	10^2
Ala, Phe, Asp, Met, Tyr, Trp, Ser, nicotinic acid, citric acid, stearic acid	< 5	–

TABLE IV. Continued

Foreign species	I^a / %	Tolerance level ($c_{Interferent}/c_{IB}$)
His, Arg, Lys, Gly, Ca^{2+}, Zn^{2+}, Mg^{2+}, 2-[4-(2-carboxypropyl)phenyl] propionic acid	5–10	10
[b]Fe^{3+}, Cu^{2+}	Interference	1

[a]Interference coefficient, $I = (c^0_{IB} - c_{IB})/ c^0_{IB}$ (c^0_{IB} and c_{IB} are the measured concentrations of ibuprofen without and with the interfering species); [b]masked with fluoride ions

Applicability of the proposed method

The proposed method was applied for the determination of ibuprofen in three pharmaceutical formulations using the direct calibration curve. They were treated as described in the Experimental section. As can be seen in Table V, the results obtained for this method are in accordance with the official HPLC method. Also, good recovery was observed in the case of the serum sample (Table VI), indicating that the constituents of the human control serum did not interfere (Fe^{3+} were masked with F^- and the proteins were precipitated) in any way with the detection of ibuprofen. The HPLC chromatograms of the determination of ibuprofen in tablets (1.03 μg ml^{-1}) and the spiked serum (0.52 μg ml^{-1}) are given in Fig. 7. Therefore, the proposed method could be used for the determination of ibuprofen in serum samples. The results of the proposed method were statistically compared with those of the official method using a point hypothesis test.[30,31] Tables V and VI show that the calculated F and *t* values at the 95 % confidence level are less than the theoretical ones, confirming no significant differences between the performance of the proposed and the official method.

TABLE V. Determination of ibuprofen by the kinetic and the official methods (titrimetric method and HPLC)

Pharmaceutical preparation	Taken μg ml^{-1}	IB found by the proposed method[a] $x\pm SD$, μg ml^{-1}	*RSD*[a] %	Recovery[a] %	HPLC[a] $x\pm SD$ μg ml^{-1}	*F* value[b]	*t* value[b]	Titrimetric method[a] $x\pm SD$ μg ml^{-1}
Brufen®[c]	0.83	0.85±0.02	3.16	102.41	0.84±0.03	1.36	0.609	0.86±0.01
Ibuprofen[d]	1.03	1.01±0.03	2.5	98.06	1.02±0.02	1.63	0.687	1.00±0.02
Brufen®[e]	1.44	1.42±0.02	1.32	98.61	1.41±0.01	3.41	1.054	1.39±0.02

[a]Data are based on the average obtained from five determinations; [b]theoretical *F* value ($v_1 = 4$, $v_2 = 4$) and *t* value ($v = 8$) at the 95 % confidence level are 6.39 and 2.306, respectively; [c]tablets (from Galenika a.d., Belgrade, Serbia) containing ibuprofen 400 mg and excipients; [d]tablets (from Panfarma, Belgrade, Serbia) containing ibuprofen 400 mg and excipients; [e]cream (from Galenika a.d., Belgrade, Serbia) containing ibuprofen 1g/100 mg (50 g) and excipients

TABLE VI. Determination of ibuprofen in human control serum by the standard addition method

Proposed method µg ml^{-1}		*RSD*[a] %	Recovery[a] %	HPLC[a] $x\pm SD$, µg ml^{-1}	*F* value[b]	*t* value[b]	Titrimetric method[a] $x\pm SD$, µg ml^{-1}
Added	Found[a] $\bar{x} \pm SD$						
0.31	0.33±0.01	3.92	106.45	0.32±0.02	2.18	1.027	0.35±0.01
0.52	0.50 ±0.02	3.78	96.15	0.51±0.01	2.39	0.861	0.48±0.02

[a]Data are based on the average obtained from five determinations; [b]theoretical *F* value (v_1 = 4, v_2 = 4) and *t* value (v = 8) at the 95 % confidence level are 6.39 and 2.306, respectively

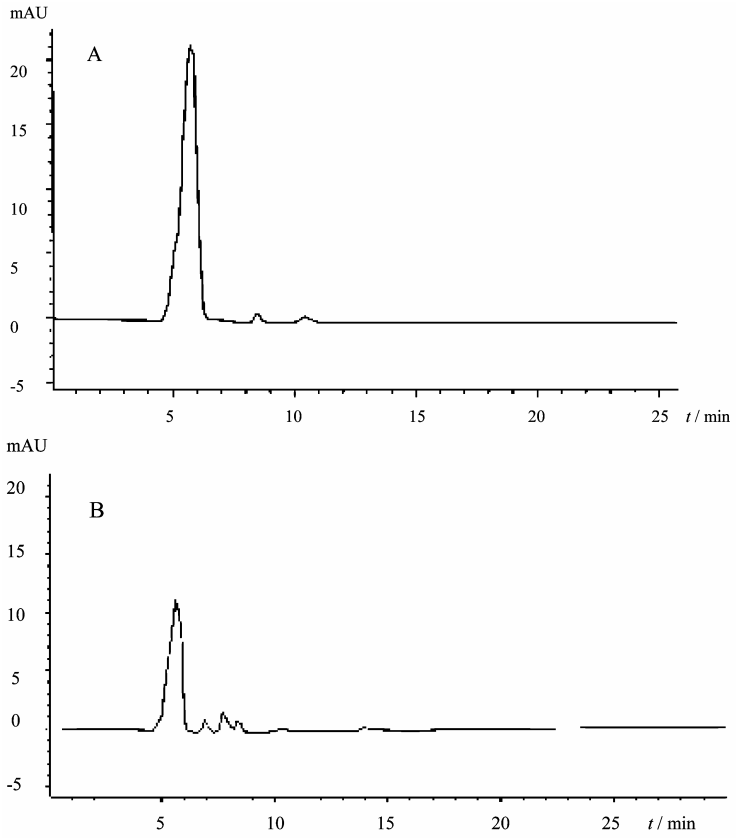

Fig. 7. HPLC chromatograms of: A) ibuprofen tablets (1.03 µg ml^{-1}) and B) serum spiked with 0.52 µg ml^{-1} ibuprofen. Column: C18 (Zorbax, 5µm, 250 mm×4.6 mm). Mobile phase: phosphoric acid–acetonitrile–water, 0.5:340:600 (v/v). Detection: spectrophotometer at 214 nm.

CONCLUSIONS

In conclusion, the proposed kinetic–spectrophotometric method for the determination of ibuprofen in pharmaceutical samples reported in this paper is simple, rapid and inexpensive and is very appropriate for routine quality control

analyses of the active drug in the laboratories of hospitals, the pharmaceutical industries and research institutions. Statistical comparison of the results with the official method showed good agreement and indicated no significant difference in accuracy and precision. The proposed method has also a wider linear dynamic range and lower detection limit in comparison with the spectrophotometric determination of ibuprofen (Table VII).

TABLE VII. Comparison of the proposed kinetic–spectrophotometric method with spectrophotometric determination of ibuprofen

Method	Linear dynamic range, *LOD*	Ref.
Spectrophotometry	100–1300 μg ml^{-1} 62 μg ml^{-1}	14
	6–60 μg ml^{-1}	32
	0.5–3.2 mg ml^{-1}	33
	10–40 μg ml^{-1}	34
	10–500 μg ml^{-1}	35
	0.21–1.44 μg ml^{-1} 1.44–2.06 μg ml^{-1} 0.03 μg ml^{-1}	This work

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И З В О Д

ОДРЕЂИВАЊЕ ИБУПРОФЕНА У ФАРМАЦЕУТСКИМ ПРЕПАРАТИМА И ХУМАНОМ КОНТРОЛНОМ СЕРУМУ КОРИШЋЕЊЕМ КИНЕТИЧКЕ СПЕКТРОФОТОМЕТРИЈЕ

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Циљ рада био је разрада нове кинетичке методе за одређивање ибупрофена у фармацеутским препаратима и хуманом контролном серуму. Ибупрофен је одређиван мерењем брзине појављивања 1-нитрозо-2-нафтола, који настаје услед његовог истискивања из трис-(1-нитрозо-2-нафтолато)кобалт(III) комплекса. Одређени су оптимални услови. Примењена је тангентна метода и добијена калибрациона крива која је линеарна у интервалу концентрације ибупрофена од 0,21–1,44 и 1,44–2,06 μg ml^{-1}. Граница детекције на основу 3,3 S_0 критеријума је 0,03 μg ml^{-1}. Испитан је утицај пуниоца, јона и аминокиселина на брзину реакције. Развијена метода је примењена за одређивање ибупрофена у фармацеутским препаратима и хуманом контролном серуму. Предност методе се огледа у томе што су одређивања врешена на собној температури и у кратком временском интервалу. Нова метода је једноставна и омогућава брзо одређивање ибупрофена у поменутим узорцима.

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