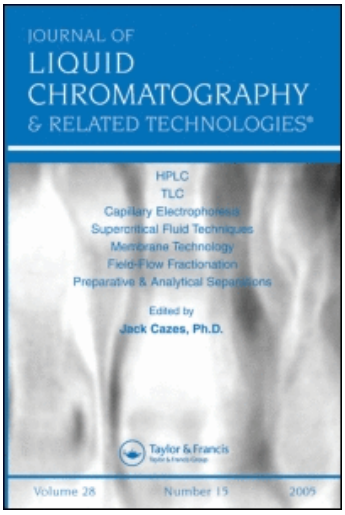

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□ *NP-TLC and RP-TLC techniques with densitometry have been established for the identification and the quantification of ibuprofen in selected pharmaceutical preparations, namely: Nurofen, Ibuprom, and Ibum. Analyses were performed on silica gel 60F_{254} plates using n-hexane-ethyl acetate-acetic acid, 15:5:0.7, v/v (NP-TLC) and on RP18F_{254s} plates using methanol-water, 9:1, v/v (RP-TLC). UV densitometry was performed at 200 and 224 nm for NP-TLC and RP-TLC analysis, respectively. NP-TLC and RP-TLC techniques with the densitometry and the spectrodensitometry applied to the investigation and the determination of ibuprofen in pharmaceutical preparations are selective, precise, and accurate. The techniques also realize the criterion of the linearity in the required range of ibuprofen concentrations.*

Keywords densitometry, NP-TLC, pharmaceutical analysis, quantitative analysis, RP-TLC, spectrodensitometry

INTRODUCTION

Currently, the most important field of application of thin layer chromatography is in the pharmaceutical field. The number of publications in the field of pharmacy have been steadily increasing.[1,2]

Many phenol derivatives have definite pharmacological and biological properties. Ibuprofen is a non-steroidal anti-inflammatory drug. It is used for the relief of symptoms of arthritis, primary dysmenorrhea, fever, and as an analgesic, especially where there is an inflammatory component. Ibuprofen may be useful in the treatment of severe orthostatic hypotension.[3,4] In some studies, ibuprofen showed superior results when compared to a placebo in the prophylaxis of Alzheimer's disease, when given in low doses over a long

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time.[5] Ibuprofen has also been associated with a lower risk of Parkinson's disease, and may delay or prevent Parkinson's disease.[6]

Phenolic drugs, including ibuprofen, can be investigated by thin layer chromatography.[7–10] Starek et al. described the application of NP-TLC on silica gel using chloroform-acetone-toluene (12:5:2, v/v) and chloroform-ethyl acetate (1:1, v/v) as mobile phases for quantitative determination of 2-arylpropionate derivates in pharmaceutical preparation.[7]

The aim of this study was the comparison of the application of NP-TLC and RP-TLC with densitometry for quantitative determination of ibuprofen in selected pharmaceutical preparations.

EXPERIMENTAL

Apparatus

Densitometer: Camag (Muttenz, Switzerland) TLC Scanner 3 with witCats 1.4.2 software.

Computer: Geforce 8600 GT 512MB/128BIT, RAM 2GB; Hewlett-Packard DeskJet 930 printer (Microsoft Office 2003 Premium, Statistica 7.0).

IKA Ultra-Turrax® Tube Drive Workstation with BMT-20-S Tube for grinding with glass balls.

NP-TLC plates: 10×20 cm aluminium plates precoated with 0.20 mm layers of silica gel 60 F_{254} (E. Merck, # 1.05554, lot: HX767953).

RP-TLC plates: 10×20 cm aluminium plates precoated with RP18 F_{254s} layers (E. Merck, # 1.05559, lot: OB687316).

The 5 µL Camag micropipettes (Muttenz, Switzerland) were used to apply the solutions to the plates.

Chromatographic chamber: twin-trough chamber (Camag, Muttenz, Switzerland).

Chemicals

Ibuprofen meets USP testing specification: Cat. No I7905 (Sigma – Aldrich; lot: 063K1117) and was used as a standard. All chemicals and reagents used for TLC were analytical grade and were purchased from POCh, Gliwice, Poland.

Pharmaceutical Preparations

Pharmaceutical preparations including ibuprofen, namely: Nurofen/200 mg in coated tablets (Reckitt Benckiser Healthcare, lot: 11 R), Ibuprom/200 mg in a tablet (US Pharmacia International Inc., Poland;

lot: 1163681), and Ibum/200 mg in elastic capsule (PPF Hasco-Lek S.A., Poland; lot: 031107) were investigated.

Preparation Sample of *Nurofen* and *Ibuprom* Tablets

Nurofen and *Ibuprom* tablets were separately ground for 5 min with speed equal to 6000 rpm using IKA Ultra-Turrax® Tube Drive Workstation with BMT-20-S tube for grinding with glass balls. The obtained powders of *Nurofen* and *Ibuprom* tablets (20 mg active substance weighing the powder to an accuracy of 0.1 mg) were shaken with methanol (10 mL) for 5 min with speed equal to 6000 rpm using IKA Ultra-Turrax® Tube Drive Workstation. After shaking, the solutions were filtered through a medium density filter (Filtrak 389, Niederschlag, Germany).

Preparation Sample of *Ibum* in Elastic Tablets

Elastic tablets of the pharmaceutical preparation *Ibum* were dissolved in methanol using measuring flask (25 mL). From this solution was next prepared the solution of the concentration of active substance (ibuprofen) equal to 1.60 mg mL^{-1}.

Preparation of Standard Solution of Ibuprofen

Standard solutions of ibuprofen were prepared by dissolving ibuprofen in methanol.

Thin Layer Chromatography

The plates were prewashed with methanol and dried for 24 h at room temperature. Before use the plates used in NP-TLC were activated at 120°C for 30 min.

The solutions of *Nurofen, Ibuprom*, and *Ibum* samples (5 μL and 2 μL) were spotted manually on the chromatographic plates.

Mixtures of n-hexane-ethyl acetate-acetic acid (15:5:0.7, v/v) and methanol-water (9:1, v/v) were used as the mobile phases in NP-TLC and RP-TLC, respectively. Of the mobile phases, 50 mL was used in all cases. After saturation of the chamber with the mobile phase vapor for 15 min, the plates were developed vertically at room temperature (20 ± 1°C) to a distance of 7.5 cm. The plates were then dried for 20 h at room temperature (20 ± 1°C) in a fume cupboard.

Spectrodensitometric Analysis

A spectrum scan was recorded using a Camag Scanner TLC 3 operated in absorbance mode and controlled by WinCATS 1.4.2 software. The radiation source was a deuterium lamp emitting a continuous UV spectrum between 190 and 450. Starting wavelength was 200 nm and ending wavelength was 450 nm. The slit dimensions were 8.00×0.40 mm, Macro; the optimized optical system was resolution; the scanning speed was 20 nm s^{-1}; the data resolution was 1 nm $step^{-1}$; the measurement type was remission; and the measurement mode was absorption; the optical filter was second order.

Densitometric Analysis

Densitometric scanning was then performed at the respective absorption maximum of ibuprofen (at 200 nm for NPTLC analysis on silica gel, and at 224 for RP-TLC analysis on RP18 plates). The radiation source was a deuterium lamp emitting a continuous spectrum between 190 and 450 nm. The slit dimensions were 8.00×0.40 mm, Macro; the optimized optical system was light; the scanning speed was 20 mm s^{-1}; the data resolution was 100 μm $step^{-1}$; the measurement type was remission; and the measurement mode was absorption; the optical filter was second order. Each track was scanned three times and baseline correction (lowest slope) was used.

Validation of the Method

Linearity of Detector Response

The linearity of the TLC method was evaluated by analysis of eleven standard solutions of ibuprofen of concentrations 0.12, 0.20, 0.30, 0.40, 0.50, 1.00, 1.50, 2.00, 2.50, 3.00, and 4.00 mg mL^{-1}. The solutions (5 μL) were applied to the same plate. The plates were developed using the above mentioned mobile phases (in thin layer chromatography section) and densitometrically analyzed.

Recovery

The recovery was computed as a ratio of constituent concentration determined in the model product to its weighed amount.

Precision

The precision of the method was determined as the degree of consistency between eight peak areas recorded for individual ibuprofen. For this purpose, 5 μL of solution 2.00 mg mL^{-1} was applied onto the plates. The precision was evaluated as the standard deviation and relative standard deviation.

Specificity

The specificity of the method was ascertained by comparing the R_F values and the spectrum of ibuprofen standard with the spectra obtained from the sample from an ibuprofen extract, at three different positions on the bands, i.e., peak start (S), peak apex (M), and peak end (E).

RESULTS AND DISCUSSION

On the basis of spectrodensitometric analysis it was shown that the band characterized by absorption maximum of ibuprofen are placed at $\lambda_{max} =$ 200 nm and $\lambda_{max} = 224$ nm for NP-TLC and RP-TLC analysis, respectively.

In the present work, the amounts of ibuprofen in samples of pharmaceutical preparations (*Nurofen, Ibuprom, Ibum*) were calculated from the area of chromatographic bands. Typical densitograms of ibuprofen (10 µg) coming from the extract of pharmaceutical preparation *Nurofen* and analyzed by NP-TLC and RP-TLC techniques are presented in Figures 1 and 2, respectively. Similar densitograms were obtained for the analysis of *Ibuprom* and *Ibum* samples. One chromatographic band was observed on all densitograms from analysis of *Nurofen, Ibuprom, Ibum* samples and ibuprofen standard investigated by NP-TLC and RP-TLC techniques.

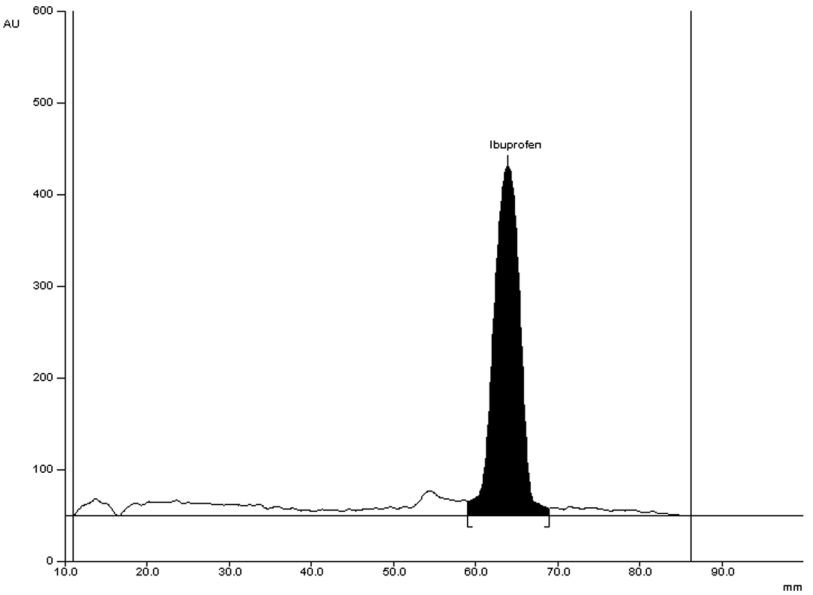

FIGURE 1 Densitogram of *Nurofen* sample with 10 µg ibuprofen declared by manufacturer analyzed by NP-TLC.

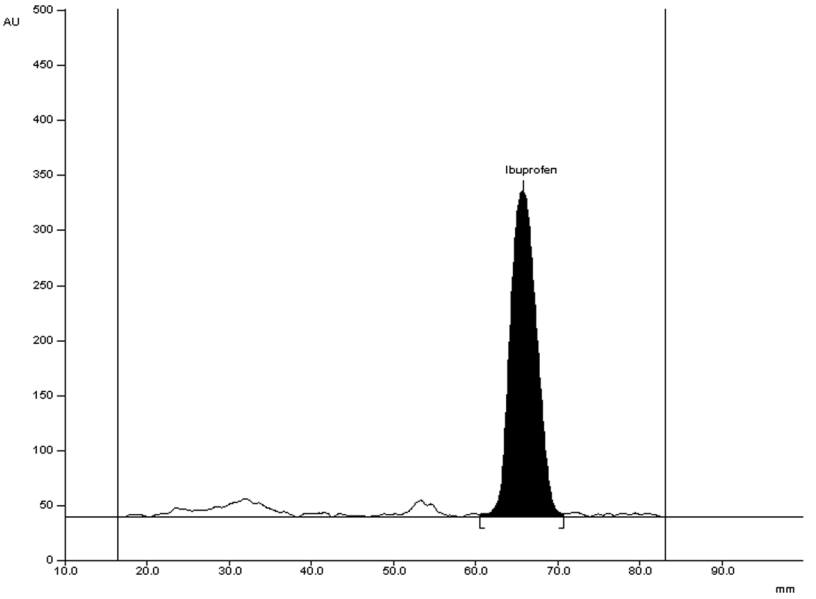

FIGURE 2 Densitogram of *Nurofen* sample with 10 μg ibuprofen declared by manufacturer analyzed by RP-TLC.

Validation data for the presented methods are summarized in Table 1. The statistical data shown in Table 1 indicate that linear relationships exists between area of peaks [AU] and concentration of ibuprofen standard [μg per spot]. The plot was linear in the range 2.50 to 12.50 μg per spot for NP-TLC and RP-TLC analysis.

– *For Analysis on Silica Gel 60 F_{254} Plates (NP-TLC)*

$$\begin{aligned} &S = 1195.8(\pm 46.7)x + 2961.4(\pm 387.3) \\ &n = 5;\ r = 0.998;\ s = 369.3;\ F = 655;\ p < 0.0005; \end{aligned} \tag{1}$$

– for analysis on RP18 F_{254s} plates (RP-TLC)

$$\begin{aligned} &S = 1140.0(\pm 73.4)x + 2939.3(\pm 608.7) \\ &n = 5;\ r = 0.994;\ s = 580.4;\ F = 241;\ p < 0.001. \end{aligned} \tag{2}$$

where: S is the area of densitometric band; x is the amount of spotted ibuprofen standard [μg]; r is the correlation coefficient; s is the standard errors of the estimate, F is the values of the Fisher test; and p is the significance level.

The graphs of residuals against the concentration of ibuprofen were also plotted. It was observed that the residuals were distributed both above and below the zero residuals line. The limits of detection (LOD) and limit

TABLE 1 Method-Validation Data for the Quantitative Determination of Ibuprofen by NP-TLC and RP-TLC with Densitometry[a]

Method Characteristic	Results	
	NP-TLC	RP-TLC
Wavelength, nm	200 nm	224 nm
R_F	0.61	0,67
Linearity range [μg spot^{-1}]	2.50 ÷ 12.50	2.50 ÷ 12.50
Correlation coefficient (r)	0.998	0.994
Limit of detection (LOD) [μg spot^{-1}]	0.60	1.00
Limit of quantitation (LOQ) [μg spot^{-1}]	12.50	12.50
Precision of spotted ibuprofen, n = 9	$\bar{x}$ = 148000,2[AU]	$\bar{x}$ = 14364,1 [AU]
	SD = 157.0	SD = 138.9
	RSD = 1.06%	RSD = 0.97%
	$\mu = \bar{x} \pm 118{,}4$	$\mu = \bar{x} \pm 104.7$
Precision of densitometer work, n = 8	$\bar{x}$ = 14800.0[AU]	$\bar{x}$ = 14363,8 [AU]
	SD = 138.9	SD = 118,6
	RSD = 0.94%	RSD = 0.82%
	$\mu = \bar{x} \pm 113.2$	$\mu = \bar{x} \pm 96.7$
Recovery, %	$\bar{x}$ = 98.16%	$\bar{x}$ = 96.06%
	SD = 1.21	SD = 1.45
	RSD = 1.28%	RSD = 1.81%

[a]SD – standard deviation.
RSD – relative standard deviation.

of quantitation (LOQ), were 0.60 and 12.50 μg per spot as well as 1.00 and 12.50 μg per spot for NP-TLC and RP-TLC analysis, respectively (Table 1).

The precisions of spotted ibuprofen standard (10 μg), which was spotted nine times on chromatographic plates are very good; relative standard deviation (RSD) values are equal 1.06% and 0.97% for NP-TLC and RP-TLC analysis, respectively. Also investigated was the proper functioning of the TLC densitometer in the range of the area measurement of densitometric band. Therefore, the plates precoated with silica gel 60 F_{254} and RP-18 F_{254s} with ibuprofen spotted (10 μg) were scanned eight times. Relative standard deviation (RSD) values for ibuprofen standard (10 μg), which was spotted once and scanned eight times, equals 0.94% and 0.82% for NP-TLC and RP-TLC analysis, respectively.

The recovery of the NP-TLC and RP-TLC techniques, as determined by using the model product, was very high and was equal to 98.16% and 96.06%, respectively.

The specificity of the methods were ascertained by comparing the R_F values of ibuprofen standard, and ibuprofen from *Nurofen, Ibuprom*, and *Ibum* samples, respectively. In each case, the R_F values of ibuprofen standard, and ibuprofen from *Nurofen, Ibuprom*, and *Ibum* samples were equal to 0.61 and 0.67 for NP-TLC and RP-TLC analysis, respectively. The identities of ibuprofen standard with ibuprofen from *Nurofen, Ibuprom*, and *Ibum* samples

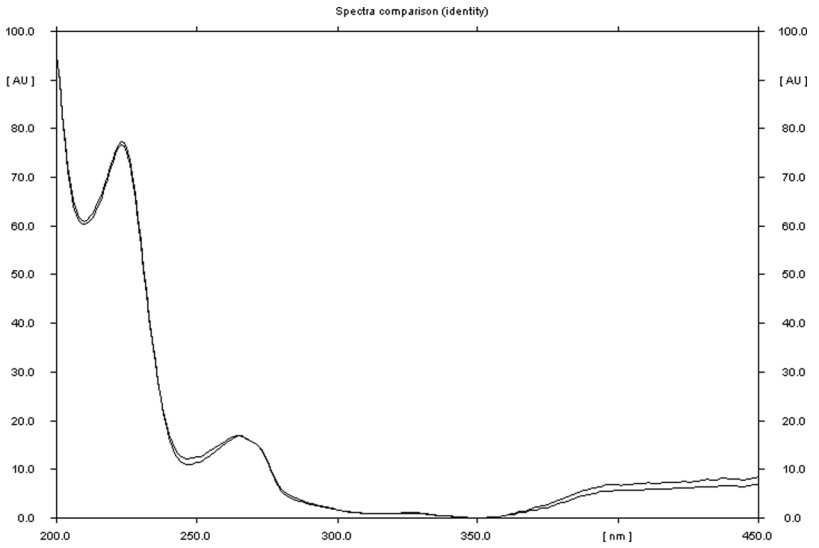

FIGURE 3 Comparison of spectrodensitogram of ibuprofen standard (10 µg) with spectrodensitogram of ibuprofen from *Nurofen* sample (10 µg ibuprofen declared by manufacturer) analyzed by NP-TLC.

were investigated on the basis of the comparison of their spectra. The comparison of spectrodenstitograms of ibuprofen standard, and ibuprofen from the *Nurofen* sample investigated by NP-TLC and RP-TLC techniques are presented in Figures 3 and 4, respectively. Similar comparisons of the

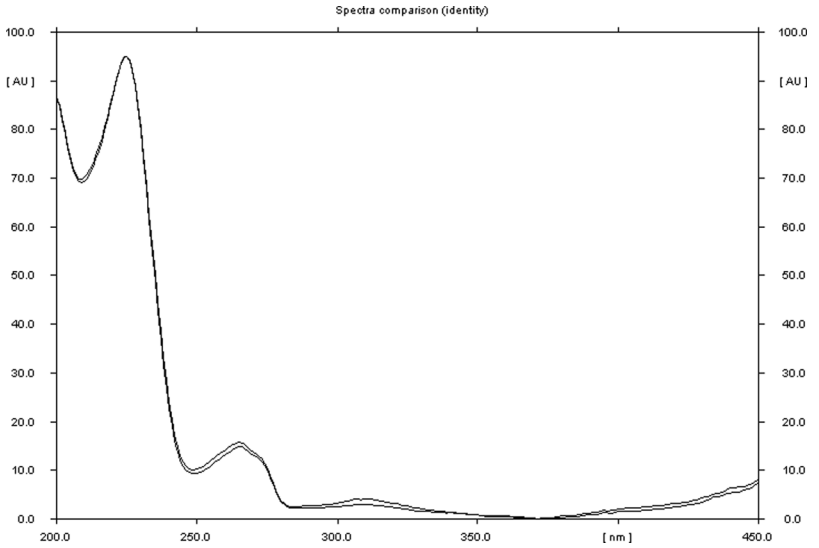

FIGURE 4 Comparison of spectrodensitogram of ibuprofen standard (10 µg) with spectrodensitogram of ibuprofen from *Nurofen* sample (10 µg ibuprofen declared by manufacturer) analyzed by RP-TLC.

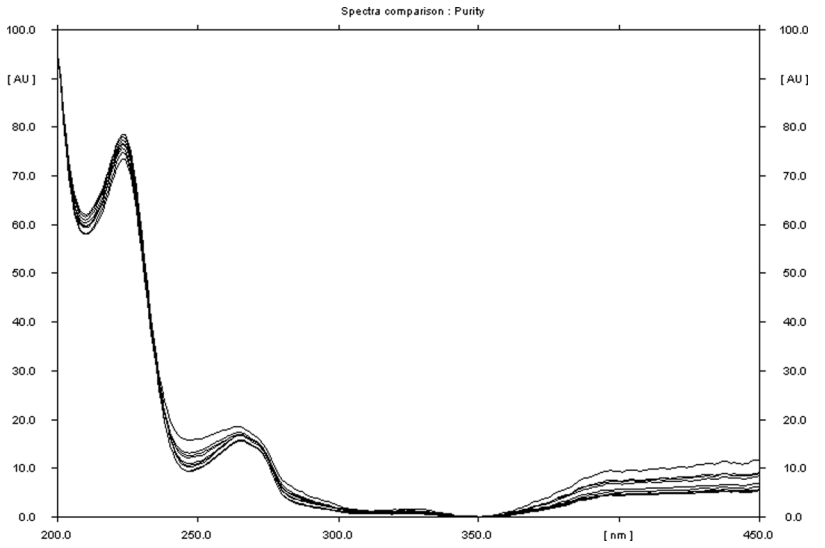

FIGURE 5 Comparison of spectrodensitogram of ibuprofen coming from *Nurofen* sample and standard solutions about different concentrations of ibuprofen investigated by NP-TLC technique.

TABLE 2 Statistical Data Concerning Results of Quantitative Determination of Ibuprofen in Extract of Coated Tablets *Nurofen* Investigated by NP-TLC and RP-TLC with Densitometry

	Analysis Performed by			
	NP-TLC Technique		RP-TLC Technique	
	Amount of Ibuprofen in Extract of Coated Tablets *Nurofen* Declared by Manufacturer			
	10 µg	**4 µg**	**10 µg**	**4 µg**
Number of analysis	6	6	6	6
Average amount of ibuprofen [µg]	9.71	3.87	9.84	4.01
Minimum amount of ibuprofen [µg]	9.53	3.77	9.64	3.94
Maximum amount of ibuprofen [µg]	10.02	4.03	10.10	4.12
Variance	0.031	0.012	0.031	0.004
Standard devitation (SD)	0.18	0.11	0.18	0.06
Relative standard deviation [%]	1.85%	2.84%	1.83%	1.52%
Confidence interval of arithmetic mean with confidence level equal 95%	$\mu = 9.71 \pm 0.18$	$\mu = 3.87 \pm 0.11$	$\mu = 9.84 \pm 0.18$	$\mu = 4.01 \pm 0.06$
Amount of ibuprofen [%] in relation to the amount of ibuprofen declared by manufacturer	97.1%	96.8%	98.4%	100.2%
Average amount of ibuprofen [%] in relation to the amount of ibuprofen declared by manufacturer	96.9%		99.3%	

spectrodensitograms were obtained for ibuprofen standard with ibuprofen from *Ibuprom* and *Ibum* samples. The purities of ibuprofen peaks from *Nurofen, Ibuprom*, and *Ibum* samples were also assessed by comparing the spectra obtained from a ibuprofen standard at the peak start, peak apex, and peak end of the spot. It was found that $r(S,M) > 0.998$, and $r(M,E) > 0.998$ for all analyses performed by NP-TLC and RP-TLC techniques. Comparison of the spectrodensitogram of ibuprofen from the *Nurofen* sample and standard solutions of different concentrations of the ibuprofen standard investigated by the NP-TLC technique are presented in Figure 5. The very good correspondence between spectrodensitograms was stated. In all cases, the absorption maximum (λ_{max}) is equal to 200 nm and 224 nm for analyses performed by NP-TLC and RP-TLC, respectively.

Statistical data concerning the results of quantitative determination of ibuprofen in the samples of pharmaceutical preparations, namely: *Nurofen, Ibuprom*, and *Ibum*, are presented in Tables 2 to 4. It was stated that ibuprofen amounts in the pharmaceutical preparation *Nurofen* determined by NP-TLC and RP-TLC are equal to 96.9% and 99.3%, respectively, in relation to the amounts of ibuprofen declared by the manufacturer. It was stated that ibuprofen amounts in pharmaceutical preparation *Ibuprom* determined by

TABLE 3 Statistical Data Concerning Results of Quantitative Determination of Ibuprofen in Extract of the Tablets *Ibuprom* Investigated by NP-TLC and RP-TLC with Densitometry

	Analysis Performed by			
	NP-TLC Technique		RP-TLC Technique	
	Amount of Ibuprofen in Extract of the Tablets *Ibuprom* Declared by Manufacturer			
	10 µg	**4 µg**	**10 µg**	**4 µg**
Number of analysis	6	6	6	6
Average amount of ibuprofen [µg]	10.18	4.25	9.69	3.96
Minimum amount of ibuprofen [µg]	9.93	4.08	9.50	3.83
Maximum amount of ibuprofen [µg]	10.41	4.38	9.95	4.13
Variance	0.036	0.016	0.025	0.016
Standard devitation (SD)	0.19	0.12	0.16	0.12
Relative standard deviation [%]	1.87%	2.82%	1.65%	3.03%
Confidence interval of arithmetic mean with confidence level equal 95%	$\mu = 10.18 \pm 0.19$	$\mu = 4.25 \pm 0.12$	$\mu = 9.69 \pm 0.16$	$\mu = 3.96 \pm 0.12$
Amount of ibuprofen [%] in relation to the amount of ibuprofen declared by manufacturer	101.8%	102.0%	96.9%	99.0%
Average amount of ibuprofen [%] in relation to the amount of ibuprofen declared by manufacturer	101.9%		98.0%	

TABLE 4 Statistical Data Concerning Results of Quantitative Determination of Ibuprofen in Extract of Elastic Tablets *Ibum* Investigated by NP-TLC and RP-TLC with Densitometry

	Analysis Performed by			
	NP-TLC Technique		RP-TLC Technique	
	Amount of Ibuprofen in Extract of Elastic Tablets *Ibum* Declared by Manufacturer			
	8 μg	**3,2 μg**	**8 μg**	**3,2 μg**
Number of analysis	6	6	6	6
Average amount of ibuprofen [μg]	8.11	3.30	8.06	3.22
Minimum amount of ibuprofen [μg]	7.89	3.19	7.96	3.08
Maximum amount of ibuprofen [μg]	8.30	3.42	8.16	3.34
Variance	0.028	0.008	0.005	0.008
Standard devitation (SD)	0.17	0.09	0.07	0.09
Relative standard deviation (RSD) [%]	2.10%	2.73%	0.87%	2.80%
Confidence interval of arithmetic mean with confidence level equal 95%	$\mu = 8.11 \pm 0.17$	$\mu = 3.30 \pm 0.09$	$\mu = 8.06 \pm 0.07$	$\mu = 3.22 \pm 0.09$
Amount of ibuprofen [%] in relation to the amount of ibuprofen declared by manufacturer	101.4%	103.1%	100.8%	100.6%
Average amount of ibuprofen [%] in relation to the amount of ibuprofen declared by manufacturer	102.2%		100.7%	

NP-TLC and RP-TLC techniques equal 101.9% and 98.0%, respectively, in relation to the amounts of ibuprofen declared by the manufacturer. It was stated that ibuprofen amounts in pharmaceutical preparation *Ibum* determined by NP-TLC and RP-TLC equal 102.2% and 100.7%, respectively, in relation to the amounts of ibuprofen declared by the manufacturer.

Ibuprofen content in investigated pharmaceutical preparations, namely: *Nurofen, Ibuprom, and Ibum,* are consistent with Polish Pharmakopoeia recommendations,[11] because ibuprofen content in the preparation should not be smaller than 95% and larger than 105% of declared value.

CONCLUSIONS

NP-TLC and RP-TLC techniques with the densitometry and the spectrodensitometry applied to the investigation and the determination of ibuprofen in pharmaceutical preparations, namely: *Nurofen, Ibuprom*, and *Ibum*, are selective, precise, and accurate. The techniques also realize the criterion of the linearity in the required range of concentrations. It was stated that the comparison of the spectrodensitogram of ibuprofen standard with the

spectrodensitogram of ibuprofen coming from pharmaceutical preparation sample (*Nurofen, Ibuprom*, and *Ibum)* can be used in the investigation of its identity. The ibuprofen content in the investigated pharmaceutical preparations, namely: *Nurofen, Ibuprom, and Ibum,* are consistent with Polish Pharmakopoeia recommendations, because the ibuprofen content in the pharmaceutical preparations is equal from 96.9% to 102.2% in relation to the content declared by the manufacturer.

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