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DETERMINATION OF IBUPROFEN IN COMBINED DOSAGE FORMS AND CREAM BY DIRECT UV SPECTROPHOTOMETRY AFTER SOLID-PHASE EXTRACTION

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Abstract: Solid-phase extraction method followed by direct UV spectrophotometry at 264 nm was developed and applied for the selective ibuprofen determination in two-component formulation of ibuprofen and pseudoephedrine-HCl, combined powder which contains ibuprofen in the form of salt with L-arginine and 10% ibuprofen cream. Procedures for ibuprofen determination in complex pharmaceutical preparations by direct UV spectrophotometry lack selectivity because of interferences of other active substances and fat components. A limited number of spectrophotometric methods applicable to these samples are based on derivative (first and second-order) UV spectroscopy. Common HPLC procedures are more selective but more expensive and for creams also require some type of extraction because the large amount of oily excipients would clog up the column. The proposed solid-phase extraction method proved to be suitable for analysis of ibuprofen in combined tablets, powders and creams by direct UV spectrophotometry. Also the method provides an effective clean-up of the cream and allows ibuprofen determination by HPLC analysis. For the extraction three different commercial sorbents were tested: anion exchange Oasis® MAX, hydrophilic-lipophilic balanced Oasis® HLB and reverse-phase Chromabond® C18ec. The optimization of the SPE method was first done on standard ibuprofen solutions and then the suitability of the method was checked on solutions of commercial pharmaceutical samples. The method yields good results for all three types of commercial preparations on the anion-exchange Oasis® MAX cartridges, with recoveries of 90-100.2%. The interferences in UV analysis were not registered and good precision (RSD < 6%) was obtained. The present method has been verified as accurate as the reference HPLC with the great advantage of less expensive instrumentation. For this reason, the method would be suitable for a routine and rapid drug quality control.

Keywords: ibuprofen, solid-phase extraction, UV determination, combined dosage forms, cream

Ibuprofen (non-steroidal anti-inflammatory drug) is present on the market in a number of products in which it is either the only active substance or in combination with other active ingredients or excipients. In addition to classical anti-inflammatory drugs which contain only ibuprofen and excipients, two-component formulations in which ibuprofen is combined with pseudoephedrine or where ibuprofen is in the form of salt, most commonly L-arginine salt, have often been prescribed in the past few years. Two-component formulation of ibuprofen and pseudoephedrine-HCl is effective in cold and flu symptoms and is used as an anti-inflammatory and nasal decongestant for upper respiratory infections. The L-arginine salt of ibuprofen (ibuprofen arginate) is a highly soluble salt formed by combining racemic ibuprofen with the amino acid L-arginine. L-arginine, a naturally occurring essential amino acid, renders ibuprofen more soluble in water and facilitates its rapid absorption across gastric and enteric mucosa, which delivers the well-known analgesic properties of conventional ibuprofen in a faster, more effective way (1). On the market there is also topical semi-solid product of ibuprofen in the form of cream, which minimizes the gastrointestinal side-effects of oral ibuprofen and provides relatively consistent drug levels at the application site for prolonged periods (2).

In all of these complex formulations other active ingredients or excipients may interfere with

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ibuprofen determination. Tablets and powders contain significant amount of various excipients and fillers. Many of them are polar compounds and show absorption in the UV range. Further, pseudoephedrine and ibuprofen have overlapping UV spectra in aqueous and alcoholic solutions and cannot be determined by direct UV spectrophotometry. In cream, the active substance is dispersed in complex emulsion containing hydrophobic and hydrophilic compounds, emulsifying agents and preservatives. Sodium and potassium salts of fatty acids, cationic surfactants and non-ionic surfactants are commonly used as excipients in creams (3). These excipients do not have strong chromophores but they have to be removed, because they can significantly contaminate chromatographic column in HPLC analysis, whereas in UV spectrophotometry they disable ibuprofen determination because the obtained solution is an emulsion.

Different methods for simultaneous determination of ibuprofen and pseudoephedrine in combined dosage forms are developed. High-performance liquid chromatography is one of the most popular and sensitive method which can separate ibuprofen and other active substances in tablets (4), granules (5), soft capsules (6), creams (7) and syrup preparation (8). For the HPLC determination in creams protective precolumn and washing after 10 injections were used. Capillary zone electrophoresis was also proposed for the active constituents determination in ibuprofen tablets (9).

For the analysis of multicomponent ibuprofen preparations many UV spectropfotometric methods have been proposed. Because of near absorption maximums of ibuprofen (264 nm and 272 nm) and pseudoephedrine (240-260 nm) these methods are based on first or second derivative spectrophotometric assay (10, 11), ratio spectra derivative spectrophotometry and chemometric techniques (12, 13) or formation of color copper complexes with different absorption wavelengths (14). Only one paper deals with the method of direct and derivative UV spectrophotometric analysis of ibuprofen in pharmaceutical cream after solid-phase extraction (15).

Solid phase extraction is widely used tools for sample cleanup, but in the analysis of drugs from pharmaceuticals is rarely used. In comparison with classical liquid-liquid extraction it has many advantages, the most important is a much higher selectivity, the use of smaller quantities of toxic organic solvents and the shorter time of performance. High selectivity and specificity of SPE methods is achieved by a wide range of the sorbents for polar, hydrophobic and ionic interactions, unlike liquid-liquid extraction which is limited to equilibrium distribution of the substance between two liquid phases. In contrast to the large number of papers relating to the extraction and determination of ibuprofen from biological samples, there are a limited number of literature references concerning its extraction from combined pharmaceutical preparations or creams.

The aim of this work was to develop a method for determination of ibuprofen without interferences in complex pharmaceutical matrices such as creams and combined dosage forms. The method involves sample pretreatment by solid-phase extraction (SPE) and analytical determination by UV spectrophotometry at 264 nm. The optimal conditions for the extraction as well as the recovery have been tested for three different types of sorbents/cartridges: Oasis® HLB (Waters), Chromabond® C18ec (Macherey-Nagel) and Oasis® MAX (Waters). The described method has been applied to the determination of ibuprofen in commercial pharmaceutical preparations.

EXPERIMENTAL

Apparatus

The spectrophotometric analyses were performed on Evolution 60 spectrophotometer (Thermo-Fisher Scientific USA). Spectra were measured with a 10 mm quartz cell. Solid-phase extraction was done on Visiprep SPE Vakuum Manifold 12-port model, Supelco 57030-U, Sigma-Aldrich Chemie. pH was measured by using Hanna Instruments pH meter. HPLC analysis was performed on Agilent 1200 Series apparatus (Agilent Technologies Inc., Santa Clara, CA, USA) equipped with the diode array and multiple wavelength detector.

Materials and reagents

Pharmaceutical certified product of ibuprofen was of analytical grade (99.6%) and provided by the Pharmaceutical Laboratory Galenika, a.d., Belgrade, Serbia. Stock solution of ibuprofen, concentration of 0.5 mg/mL was prepared in methanol and stored at 4^{o}C.

SPE was performed on Oasis® MAX (1 cc, Waters Corporation, Milford, Mass., USA), Oasis® HLB (1 cc, Waters Corporation, Milford, Mass., USA) and Chromabond® C18ec (1 mL/100 mg, Macherey-Nagel, GmbH, Düren, Germany).

Methanol 99.9% Reag. Ph. Eur.-Reag. USP for analysis was from Carlo Erba Italy. All other reagents used were of analytical grade.

Commercial pharmaceutical preparations of ibuprofen were purchased as follows: film tablets under the trade name "Defrinol forte" by Galenika-Serbia, powder under the trade name "Spedifen Zambon" by Bonifar-Serbia and cream under the trade name "Brufen 10%" by Galenika-Serbia.

Procedure for dosage forms preparation

The developed SPE method was applied to the analysis of ibuprofen in commercially available pharmaceuticals in three dosage forms: tablets, powder and cream. Each formulation was differently prepared. The obtained sample solutions were applied to the selected SPE cartridges.

Tablets

According to the label, "Defrinol forte" contains 200 mg of ibuprofen and 30 mg of pseudoephedrine HCl per tablet. A total of ten tablets were weighed and then the protective film was removed with deionized water. After drying, the tablets were pulverized and homogenized. After fine powdering, accurately weighed three portions which contained 25 mg of ibuprofen each, were dissolved in 30 mL of methanol and stirred on magnetic stirrer for 30 min. After extraction with methanol, the obtained solutions were quantitatively transferred to a 50 mL volumetric flasks and diluted to volume with methanol. The concentration of these solutions of samples should be 0.5 mg/mL. Further, the obtained solutions were filtered through MN 619 de. ∅ 125 mm (Macherey–Nagel, Germany) filter paper.

Powder

According to the manufacturer's label the powder contains 200 mg of ibuprofen in the form of salt with L-arginine per 3.0 g of preparation. For the analysis, mass of 3 packages of "Spedifen Zambon" was measured. A mass of powder which contained 25 mg of ibuprofen was measured in triplicate and dissolved in the volumetric flasks with 50 mL of deionized water. The concentration of these sample solution should be 0.5 mg/mL.

Cream

The commercial product of "Brufen 10%" contains 100 mg of ibuprofen per 1 g of cream. The mass of cream which contained 25 mg of ibuprofen was measured in triplicate, dissolved in 30 mL of methanol and stirred for 30 min using a magnetic stirrer. The supernatants were transferred into 50 mL volumetric flasks and diluted to volume with methanol. The concentration of these sample solution should be 0.5 mg/mL. The obtained solutions were filtered through MN 619 de. ∅ 125 mm (Macherey-Nagel, Germany) filter paper.

Solutions for SPE

Working solutions of ibuprofen standard were prepared from the stock ibuprofen solution (0.5 mg/mL). Working solutions of pharmaceutical samples were prepared from the solutions obtained as described in Procedure for dosage forms preparation.

Different methods of preparation of standard and sample solution for HLB, MAX and C18ec sorbents are based on acid-base properties and polarity of active substance and provide more effective separation of ibuprofen from interfering compounds. For HLB and C18 cartridges 1 mL of ibuprofen solution was mixed with 1.5 mL of 2% CH_3COOH to obtain final solution which has pH 3.0. For MAX cartridge, 1 mL of ibuprofen solution was mixed with 1 mL 2% NH_4OH and 0.5 mL of methanol or deionized water. The obtained solution had pH 10.0.

UV spectrophotometric analysis

After the SPE step obtained eluates were analyzed by direct UV spectrophotometry. The amount of ibuprofen was determined by using calibration curve at 264 nm. For this purpose calibration graph was constructed. From the stock standard ibuprofen solution (0.5 mg/mL) working standard solutions in the range of 0.1-0.5 mg/mL were prepared by appropriate dilution with methanol.

The analysis of all samples was repeated 5 times.

HPLC analysis

The results of ibuprofen determination by UV analysis after SPE were compared with reference HPLC method for the tablet and cream dosage forms according to British Pharmacopoeia (16). RP-chromatography was done on Zorbax Extende C18 column (4.6 × 150 mm, 3.5 μm) at 30°C with an isocratic mobile phase at a flow rate of 1.5 mL/min. The mobile phase composition was water : methanol : ortophosphoric acid (247 : 750 : 3, v/v/v). Ibuprofen was detected by absorbance at 264 nm. After validation, the method was applied for the drug sample solution prepared as described in Procedure for dosage forms preparation.

RESULTS AND DISCUSSION

Considering that ibuprofen has two absorption maxima (264 and 272 nm) it was important to determine the sensitivity of the UV method at these two

wavelengths. For this purpose, separate calibration curves at 264 and 272 nm were constructed by a least squares fit. Linear regression analysis was performed for calibration curves at two wavelengths.The limit of detection and limit of quantitation were calculated as kSD/b, where $k = 3$ for LOD and 10 for LOQ. SD is the standard deviation of the intercept, and b is the slope of the calibration line. Limit of quantitation was 0.028 mg/mL for both wavelengths but the slope of the line is better for calibation graph obtained at 264 nm, and therefore, this wavelength was selected for further ibuprofen determination.

Optimization of SPE method

SPE method optimization has been done with the standard methanol ibuprofen solution concentration of 0.5 mg/mL. A number of variables were tested during the optimization procedure: the nature of the sorbent, the influence of a washing step, the pH values of the sample solutions, the pH values of solvents mixtures for washing and eluting, as well as the volume of the solvents and mixture of solvents for conditioning the cartridges. Optimization was achieved through several steps: first, the recovery of ibuprofen from the standard solution was tested on three types of cartridges (HLB, C18ec and MAX) with the pH values being changed in the interval from pH 3.0 to pH 10.0. These sorbents have different retention mechanism. MAX cartridge has been optimized to achieve high selectivity and sensitivity for extracting acidic compounds with anion-exchange groups. This is mixed-mode polymeric sorbent and powerful anion-exchanger which contains ionized quaternary amino groups located on the surface of the divinylbenzene-N-vinylpyrrolidone copolymer. HLB cartridge (hydrophilic-lipophilic balance) finds its application in the reverse-phase SPE systems. This cartridge can retain both polar and non-polar molecules due to the presence of lipophilic divinylbenzene and hydrophilic N-vinylpyrrolidone groups. C18ec cartridge contains endcapped octadecyl phase and shows interaction with very nonpolar, hydrophobic organic compounds.

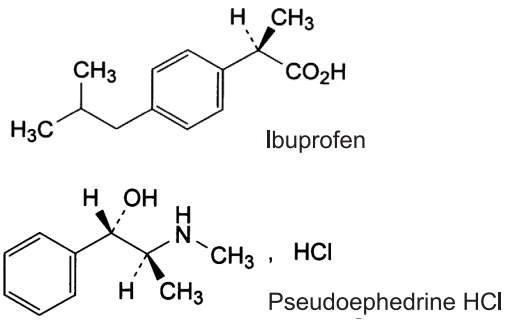

Figure 1. Chemical structures of ibuprofen and pseudoephedrine-HCl

Critical parameters in SPE methodology were active substances solubility and pH selection. Ibuprofen is a weak acid which is water insoluble but shows good solubility in methanol (17). Pseudoephedrine, on the other hand, is a base and is both water and alcohol soluble. Chemical structures of these drugs are shown in Figure 1. Ionization of ibuprofen depends on the pH values of the solution. It is negatively charged above pH 6.4 and in neutral form at pH less than 2.4. The equation (1) was applied in order to calculate the percentage of both ionized and non-ionized forms in different pH:

$$\% \text{ ionization} = \frac{10^{pH - pKa}}{1 + 10^{pH - pKa}} \qquad (1)$$

Pseudoephedrine is a weak base with pKa 9.8 and it is cationic in acidic and neutral solutions. L-arginine has guanidine group and it is a strong organic base with pKa 12.48. Guanidine functional group is positively charged even at alkaline conditions. In order to investigate the retention of ibuprofen on hydrophilic-lipophilic sorbent (HLB), octadecyl-modified silica (C18) and strong anion exchanger (MAX), pH of the ibuprofen solutions was varied in the range from 3.0 to 10.0.

The first step in SPE methodology is characterization of sample and selection of appropriate preparation procedure. This step depends on physical form of dosage forms and physico-chemical properties of active substance. Characterization of the samples was done in terms of molecular weight, functional groups, polarity, acid-base properties, pKa values and solubility of analyte and other substances in the sample matrix. Dissolving a sample of "Defrinol" tablets in methanol results in extraction of both ibuprofen and pseudoephedrine, therefore, methanol extraction is not enough for separating these two active ingredients. UV spectrophotometric determination of ibuprofen in the obtained extract is inaccurate because these two substances absorb at very similar wavelengths (264 nm for ibuprofen and 257 nm for pseudoephedrine) (18). The additional extraction and separation of ibuprofen from pseudoephedrine from the tablet solution is necessary. According to the product declaration, 'Spedifen' contains 200 mg of ibuprofen in salt form with L-arginine. Since ibuprofen is in the form of salt, good water solubility is to be expected. L-arginine, on the

other hand, is water soluble but not alcohol soluble, so adjusting the pH values of the solution and choosing appropriate washing and eluting solvents mixtures, can result in good extraction of ibuprofen and its separation from L-arginine. According to the product declaration, 1 gram of the 'Brufen' cream contains 100 mg of ibuprofen in molecular form and a number of hydrophobic and hydrophilic excipients. Dissolving the cream samples in methanol results in formation of emulsion which cannot be accurately analyzed by UV spectrophotometry. For the quantitatively extraction of ibuprofen from the methanol emulsion, appropriate sorbent and solvent selection is very important.

On the basis of the physico-chemical properties of sorbents, as well as the polarity and solubility of ibuprofen, pseudoephedrine and L-arginine, it was assumed that ibuprofen will be retained on the HLB and C18ec cartridges if the solution has pH 3, while good extraction of ibuprofen on the MAX cartridge is achieved in basic solution with the pH 10. Two percent solutions of weak acid and base were used for pH regulation according to Marlatt et al. (19). As a washing solution for HLB and C18ec sorbents a 2% solution of acetic acid was used, while MAX sorbent was washed up by 2% solution of ammonium hydroxide. We assumed that the washing of sorbents was necessary for accurate recovery values because of our results showed that recovery was slightly higher than expected when the washing step wasn't done.

SPE protocols

Before use, the SPE columns were conditioned and equilibrated with 2 mL of methanol and 3 mL of deionized water. Solutions of ibuprofen, which were passed through HLB and C18 columns are adjusted by 2% acetic acid to pH 3.0. For extraction on MAX cartridges pH of the ibuprofen solution is set to 10.0 with 2% ammonium hydroxide. The sample solutions were passed through the conditioned cartridges at the flow rate no greater than 1 mL/min. After sample loading, the sorbents were washed with 1 mL of 2% CH_3COOH (HLB and C18ec) and 1 mL of 2% NH_4OH (MAX). Ibuprofen was eluted from HLB and C18 cartridges with 3 × 1 mL of methanol, while elution from MAX sorbent was performed with 3 × 1 mL of a mixture methanol : 2% CH_3COOH (2 : 1,v/v).

Table 1. The accuracy and precision of the SPE method.

Cartridge	Taken (mg/mL)	Found (mg/mL) $\bar{x}$ ± SD	Recovery (%)	RSD (%)
HLB	0.500	0.450 ± 0.0042	90.0	0.93
C18ec	0.500	0.534 ± 0.0035	106.8	0.66
MAX	0.500	0.492 ± 0.0024	98.4	0.49

$\bar{x}$ - mean value of 3 repeated measurements. SD - standard deviation of the mean

Table 2. Ibuprofen determination in commercial pharmaceutical preparations by UV spectrophotometry after SPE.

Dosage form	Cartridge	Found IB from the dosage form (mg/mL) $\bar{x}$ ± SD	Declared content (mg/mL)	Recovery (%)	RSD (%)
Tablets IB + PE	HLB	0.444 ± 0.017	0.500	88.8	3.83
	C18ec	0.438 ± 0.005		87.6	1.14
	MAX	0.465 ± 0.007		93.0	1.51
Powder IB-arginate	HLB	0.816 ± 0.005	0.500	163.2	0.62
	C18ec	0.414 ± 0.020		82.8	4.83
	MAX	0.454 ± 0.025		90.8	5.51
Cream IB + lipophilic compounds	HLB	0.906 ± 0.017	0.500	181.2	1.88
	C18ec	0.573 ± 0.005		114.6	0.87
	MAX	0.501 ± 0.006		100.2	1.20

IB - ibuprofen, PE - pseudoephedrine, - mean value of 5 repeated determinations, SD - standard deviation

Table 3. Ibuprofen determination in commercial pharmaceutical preparations by reference HPLC method.

Dosage form	Found content (mg/mL) $\bar{x} \pm$ SD	Declared content (mg/mL)	Recovery (%)	RSD (%)
Tablets (IB + PE)	0.476 ± 0.006	0.500	95.2	1.26
Powder (IB-arginate)	0.475 ± 0.011	0.500	95.0	2.31
Cream (IB + lipophilic compounds)	0.497 ± 0.008	0.500	99.4	1.61

IB - ibuprofen, PE - pseudoephedrine, - mean value of 5 repeated determinations, SD - standard deviation.

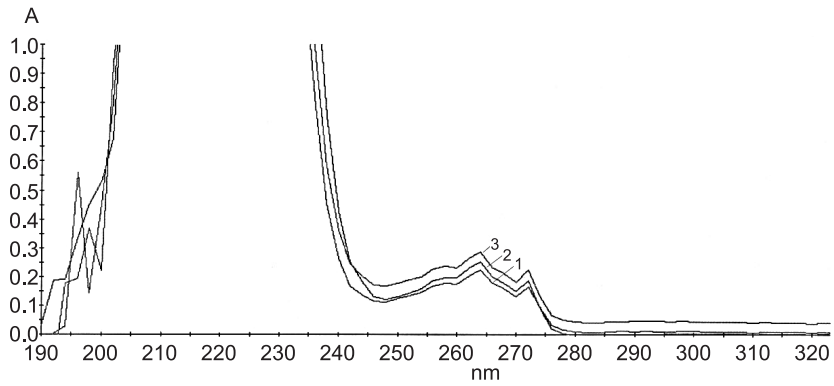

Figure 2. Absorbance spectra of ibuprofen standard solutions concentration of 0.5 mg/mL after extraction: 1) HLB, 2) MAX, 3) C18

Validation of the SPE method

SPE protocols were first evaluated on ibuprofen standard solution. Validation of developed SPE method was done by means of selectivity, accuracy and intraday precision. Recovery was calculated by comparison of absorbance at 264 nm of extracted and non-extracted standard solution. All the samples were analyzed in triplicate (Table 1).

All three types of cartridges gave satisfactory recovery values for the ibuprofen standard solution. The best recovery values, however, were obtained on the MAX cartridge. Good extraction of ibuprofen on the HLB and C18ec was achieved by adjusting the pH values of the sample to 3.0. This resulted in full transformation of ibuprofen into a molecular form, which had stronger interaction with hydrophobic sorbent groups. Washing with a 2% water solution of acetic acid will remove traces of water soluble impurities that are potentially still at the sorbent. Quite the opposite, good extraction on the MAX cartridge is achieved by total transformation of ibuprofen into ionic form at pH 10. The presence of methanol in the solution of the sample decreases solubility of ionized ibuprofen and favors its interaction with ionized groups of the sorbent. Efficient elution from this ion-exchanger is achieved by acidic water-methanol mixture which transformed ibuprofen into molecular form and facilitated its removal from the sorbent and dissolution in methanol.

Application to the pharmaceutical preparations

Recovery results for ibuprofen determination in pharmaceutical samples with various sorbents are given in Table 2. The recovery values were calculated as the ratio of found and declared ibuprofen content.

After the solid-phase extraction, UV spectra of standards and pharmaceutical samples were recorded in order to verify correct profile of ibuprofen from extracted samples. Figure 2 represents the spectra of working standard solutions after extraction, in which the presence of characteristic absorption maximum of ibuprofen is clearly visible.

Tablets

The results of ibuprofen determination from the tablets with pseudoephedrine are shown in Table 2. The recovery values were slightly lower

on the C18ec and HLB which indicates incomplete retention or elution from these sorbents. A good extraction of ibuprofen and its separation from pseudoephedrine with acceptable RSD value was achieved on the MAX cartridge. By comparing UV spectra and absorbance of ibuprofen from the samples and those of standard after SPE (Figs. 3 and 2), it was proved that ibuprofen was well retained on the MAX sorbent and was not eluted in the washing step. The absorption maximums correspond to those for the standard passed through the cartridges.

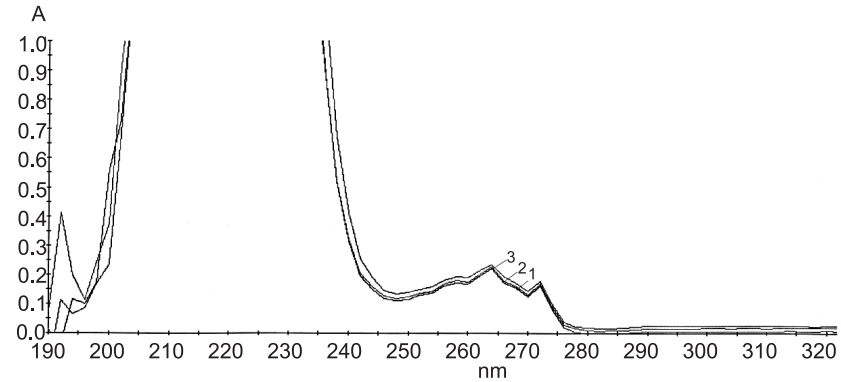

Figure 3. Absorbance spectra of ibuprofen from tablet dosage form (0.5 mg/mL) after extraction: 1) C18, 2) HLB, 3) MAX

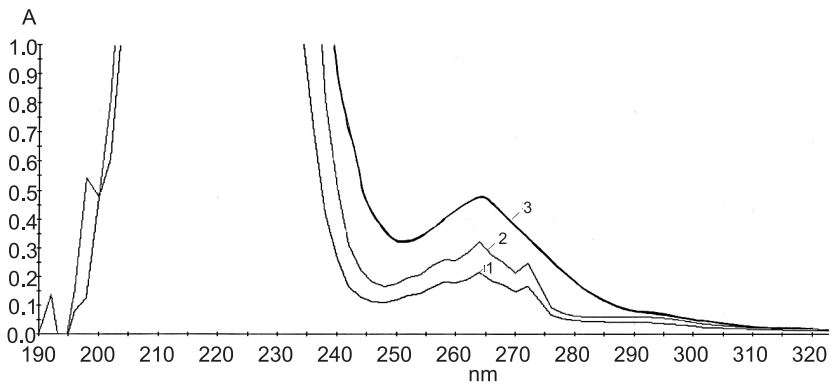

Figure 4. Absorbance spectra of ibuprofen from powder dosage form (0.5 mg/mL) after extraction: 1) C18, 2) MAX, 3) HLB

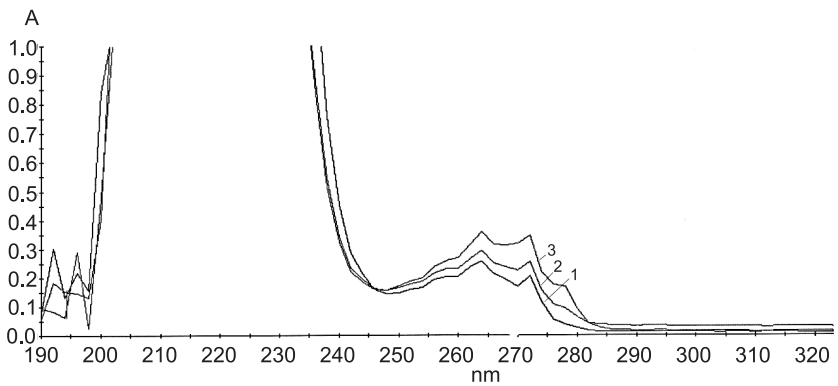

Figure 5. Absorbance spectra of ibuprofen from cream solution (0.5 mg/mL) after extraction: 1) MAX, 2) C18, 3) HLB

Powder

Extraction of ibuprofen from 'Spedifen' on the HLB cartridges results in very high recovery values, which points to some of the excipients strongly remaining on the sorbent. The remaining excipient is soluble in eluent and absorbs in the same UV region as ibuprofen which significantly increases the absorbance at 264 nm (Fig. 4.). The best recovery values were obtained on the anion-exchanger MAX cartridge (Table 2).

Cream

Separation of ibuprofen from the surfactants and fatty components present in a cream by SPE can be very difficult. Due to its structure, the HLB cartridge can retain many moderately polar, hydrophilic-lipophilic substances which are present in creams and which can interfere with ibuprofen determination. The HLB sorbent gave very high recovery values (Table 2), so this type of cartridge is not appropriate for extracting ibuprofen from a cream. The C18ec sorbent also resulted in higher recovery values, which indicates retention and interferences some lipophilic compounds from pharmaceutical cream. The best extraction yield was obtained on the MAX cartridge (100.2%). In Figure 5, a change in the spectra can be noticed between the absorption maximum at 264 nm and 272 nm. The shape of the absorption bands is particularly modified for the HLB cartridge, which confirms the interference and explains extremely high recovery values. On the other hand, the absorption band for the MAX sorbent is the same form as for the standard solution.

The content of ibuprofen in commercial "Defrinol" tablets, "Spedifen" powder and "Brufen" cream was also determined by the reference HPLC method (16) (Table 3). The accuracy and precision of determination for each commercial drug formulation were compared between two analytical methods with F-test and *t*-test at 95% confidence level. The results obtained from the proposed UV/SPE method on Oasis MAX anion-exchange cartridge is in close agreement with the results obtained by the reference HPLC method. Statistical analysis using Student's *t*-test for accuracy and F-test for precision gave no significant difference between the proposed method on anion-exchange cartridge and HPLC method at the 95% confidence level. The calculated t-values for tablets, powder and cream were 2.68, 1.72 and 0.89, respectively, and did not exceed the tabulated value t = 2.8.

CONCLUSION

Procedures for ibuprofen determination in complex pharmaceutical preparations involving direct UV spectrophotometry without any extraction treatment lack selectivity because of interferences of other active substances and fat components in creams. Common HPLC procedures are more selective but more expensive and for creams require extraction because the large amount of oily excipients would clog up the column. A limited number of spectrophotometric methods applicable to the determination of ibuprofen in these samples are based on derivative (first and second-order) UV spectroscopy. The proposed solid-phase extraction method proved to be suitable for analysis of ibuprofen in combined tablets, powders and creams by direct UV spectrophotometry. The method yields good results for the extraction of ibuprofen from all three types of commercial preparations on the anion-exchange Oasis® MAX cartridge, with recoveries of 90-100.2%. The presented method has been verified as accurate as the reference HPLC and UV derivative spectrophotometry methods with the great advantage of less expensive instrumentation. The method would be suitable for a routine and rapid drug quality control. Also the method provides an effective clean-up of the cream and allows ibuprofen determination by HPLC analysis.

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