Development of a preconcentration method for indomethacin in natural waters using dispersive liquid–liquid microextraction based on solidification of floating organic drop technique
Nesrin Topaç, Cennet Karadaş and Derya Kara

ABSTRACT
A new dispersive liquid–liquid microextraction method based on the solidification of a floating organic drop was developed for the preconcentration of indomethacin in natural waters followed by ultraviolet-visible (UV-Vis) spectrophotometric detection. 1-undecanol and ethanol were used as the extraction solvent and the disperser solvent, respectively. An investigation of the main experimental parameters that may affect the extraction efficiency, such as sample pH, volume of extraction and disperser solvents, sodium chloride concentration and centrifugation time was undertaken. The effect of interfering ions on the recovery of indomethacin was also examined. Under optimal conditions without any preconcentration, the limit of detection was 17.9 μg/L calculated from LOD = 3 Sb/m and was also calculated as 74.9 μg/L from the regression values of the calibration line using 3.19 Se/m. The proposed preconcentration method was successfully applied to determination of indomethacin in spiked tap water and river water samples. The recovery values for spikes added to water samples were between 94.5 and 103.0%.

Key words | dispersive liquid–liquid microextraction, indomethacin, solidification of floating organic drop, ultraviolet-Vis spectrophotometry, water

INTRODUCTION
Recently, a number of reports have demonstrated the occurrence of pharmaceuticals and their metabolites in natural waters (Debska et al. 2005; Vulliet & Cren-Olive 2011; Gros et al. 2012; Gaffney et al. 2015). After ingestion, many drugs are excreted by the human and/or animal body to the environment, causing contamination in the surface water, groundwater and even drinking water. Very often, they are only slightly transformed or even unchanged (Debska et al. 2005).

Indomethacin is used extensively because of its excellent pharmaceutical properties. It is a non-steroidal, anti-inflammatory agent with antipyretic and analgesic properties. It is an indole derivative having the systematic name 1-(p-chlorobenzoyl)-5-methoxy-2-methyl-1H-indole-3-acetic acid (Ali et al. 2015). It is used to relieve the symptoms of ankylosing spondylitis, osteoarthritis, rheumatoid arthritis and gout (Ali 1999). The common adverse effects are gastro-intestinal ulceration and bleeding, headache, depression, drowsiness, tinnitus, confusion, light-headedness, insomnia, dizziness, convulsions, coma, hypertension and blood disorders (Martindale & Reynolds 1989). Because of the importance of indomethacin and its widespread use, several research studies have developed simple and reliable analytical methods for its determination.

Several analytical techniques, including ultraviolet-visible (UV-Vis) spectrophotometry (Amoli Diva et al. 2015), micellar electrokinetic chromatography (MEKC) (Lin et al. 2006), gas chromatography (GC) (Krishna et al. 1995),...
volatilisation (Julia Arcos et al. 1998; Radi 1998; Ali 1999; El-Hefnawy et al. 2005; Babaei et al. 2012; Arvand & Gholizadeh 2013), chemiluminescence (Nie et al. 2005), capillary electrophoresis (CE) (Mardones et al. 2001; Macia et al. 2005; Makino et al. 2005), high performance liquid chromatography (HPLC) (Sato et al. 1997; Grippa et al. 2000; Al Za’abi et al. 2006; Babic et al. 2006), liquid chromatography–mass spectrometry (LC-MS) (Wang et al. 2013) and liquid chromatography–tandem mass spectrometry (LC-MS/MS) (Hoshina et al. 2011; Li et al. 2014) have been used for the determination of indomethacin in water samples and biological fluids.

Indomethacin like other many pharmaceuticals enters surface waters from wastewater treatment plants (Jiménez et al. 2017). Its concentrations can vary from 20 to 100 ng/L in wastewater treatment plants although concentrations of about 1 µg/L have also been reported (Radjenovic et al. 2009; Sui et al. 2009), about 10–20 ng/L in depurated effluents (Zhou et al. 2009) and between 0.1 and 100 ng/L in river water (Kim et al. 2009; Yamamoto et al. 2009; Zhou et al. 2009; Lewandowski et al. 2011). Therefore, the required sensitivity of the analytical techniques used for quantification of indomethacin must be sufficiently low so as to determine 0.1 ng/L. Due to the low concentrations of indomethacin existing in natural waters, a preconcentration step during the sample preparation plays an important role in the determination of pharmaceutical chemicals in various samples. Traditional extraction methods, such as liquid–liquid extraction (LLE) and solid phase extraction (SPE), are time-consuming and often need a large volume of sample and toxic organic solvents. These are hazardous to both human health and to the environment (Jouibari et al. 2014). Various analytical methods such as air-assisted liquid–liquid microextraction (AALLME) (Farajzadeh et al. 2016), dispersive liquid–liquid microextraction (DLLME) (Tu et al. 2015; Chen et al. 2016), single-drop microextraction (SDME) (Vazquez et al. 2016), dispersive nanomaterial-ultrasound assisted-microextraction (DNUM) (Pebdani et al. 2016), microextraction by packed sorbent (MEPS) (Iadaresta et al. 2015), solid-phase microextraction (SPME) (Yu et al. 2012; Peltenburga et al. 2015), polymer monolith microextraction (PMME) (Lyu et al. 2015), ionic liquid-dispersive liquid–liquid microextraction combined with micro-solid phase extraction (IL-DLLME-μ-SPE) (Ge & Lee 2013), dispersive liquid–liquid microextraction-solidification of floating organic drop (DLLME-SFO) (Sanagi et al. 2013) and continuous hollow fibre liquid–phase microextraction (CHF-LPME) (Es’haghi 2009) have been used for the determination of various drugs.

The DLLME-SFO method is based on the principle of DLLME and solidified floating organic drop microextraction (SFODME). In this extraction procedure, a mixture of extraction solvent having low density, low toxicity and a melting point near room temperature (e.g., 1-undecanol) and a disperser solvent is injected into an aqueous sample forming a cloudy solution. The analytes in the aqueous solution pass into the extraction solvent. After centrifugation, the droplet of extraction solvent floating on the surface of the aqueous phase/disperser solvent mixture is then rapidly solidified in an ice bath so that it may easily be collected. The collected extractant melts immediately at room temperature and can then be used for subsequent selected instrumental analysis (Wu et al. 2011; Li et al. 2015). This method is very straightforward. The mass transfer between the sample and the extractant droplet is as fast as DLLME because of the large contact surface, and the technique has a shorter extraction time than liquid–liquid microextraction based on the solidification of floating organic droplet (LLME–SFO).

In this work, a new DLLME-SFO method was developed for the preconcentration of indomethacin prior to UV-Vis spectrophotometric determination. After optimization of the experimental conditions, the proposed method was then applied to the determination of indomethacin in spiked tap water and river water samples.

**EXPERIMENTAL**

**Apparatus**

Absorbance measurements were made using a PG instruments Ltd. T80 Series UV-Vis Double Beam Spectrophotometer (Leicestershire, UK) with 1.0 cm quartz cells. All pH measurements were performed using a Hanna Instruments model 221 (Cluj-Napoca, Romania) digital pH-meter with a combined glass electrode. A Heidolph shaker model Vibramax 110 (Germany) was used for the DLLME-SFO extraction experiments. A Hettich centrifuge model Rotafix 32 A (Germany)
was used to separate the organic droplets from the cloudy aqueous solution.

**Reagents and solutions**

All the reagents used were of analytical grade, and water, purified by a reverse osmosis system, was used to prepare all the solutions. Acetic acid and ammonia from Riedel-de Haen (Sigma-Aldrich, St. Louis, MO, USA), indomethacin from Sigma (Sigma-Aldrich) and sodium dihydrogen phosphate, phosphoric acid, disodium hydrogen phosphate, sodium acetate, ammonium chloride, ethanol, methanol and 1-undecanol obtained from Sigma-Aldrich were used during the experiments. All laboratory glassware was cleaned by storing it in 10% (v/v) nitric acid overnight and then rinsing with deionized water before use. The stock standard solution of 5,000 mg/L of indomethacin was prepared in methanol and stored at 4°C. The working standard solution of 50 mg/L was prepared daily from the stock solution by dilution using 0.001 M, pH 7.0 phosphate buffer solution. This standard solution was prepared fresh every day in order to avoid any degradation. Buffer solutions, each of a concentration of 0.2 M, were used to adjust the pH of the solutions. The buffers tested were: sodium dihydrogen phosphate/phosphoric acid (at pH 2–3), sodium acetate/acetic acid (at pH 4–5), sodium dihydrogen phosphate/disodium hydrogen phosphate (at pH 6–8) and ammonium chloride/ammonia (at pH 9).

**Optimization of the experimental variables**

In order to obtain a compromise between extraction efficiency and time management, different experimental parameters that affect the performance of DLLME-SFO, such as the effects of sample pH, 1-undecanol and ethanol volumes, NaCl concentration and extraction and centrifugation times were investigated and optimized. The optimization of the analytical parameters was performed using a 5 mL standard solution containing 5.0 mg/L of indomethacin. The collected organic drop was diluted to 5 mL with ethanol before analysis without any preconcentration. A univariate optimization procedure was undertaken, i.e., varying one parameter at a time, keeping the others constant.

**DLLME-solidification of floating organic drop procedure**

An aliquot of NaCl solution (0.25 mL of 2 M) and 1 mL of pH 4.0 sodium acetate buffer solution were added to 5 mL of sample containing indomethacin in a polyethylene centrifuge tube. Then, 0.25 mL of ethanol (disperser solvent) and 80 μL of 1-undecanol (extraction solvent) were added to this sample solution. The mixture was shaken at 2,000 rpm for 7.5 min using a Vibramax 110 shaker. A turbid solution consisting of fine droplets of extraction solvent dispersed in the sample solution was formed. This solution was then centrifuged for 5 min at 4,000 rpm. After this process, fine droplets of 1-undecanol coalesced and the organic solvent collected at the upper surface of the sample solution. The conical test tube was put into an ice bath and the 1-undecanol droplet containing the analyte was solidified after 20 min and adhered to the inner surface of the tube. The aqueous phase was easily decanted and the remaining solid solvent melted immediately. The organic phase was then diluted to 2.5 mL with ethanol. The absorbance of the solution was measured at 209 nm using a 1 cm quartz cell against a reagent blank solution that was prepared without adding any indomethacin. When preparing calibration graphs, the standards were put through the same preparation procedure as the samples.

**Sample preparation**

A tap water sample obtained from Balıkesir University and a river water sample obtained from Küçük Bostancı River were analysed using the proposed method. The river water samples were filtered using cellulose membrane filters (0.45 μm pore size) and were stored in pre-cleaned polyethylene bottles at 4°C. The proposed method given above was applied to these samples. Before the proposed method described above was applied, the pH of 5 mL aliquots of the water samples was adjusted to 4.0 using sodium acetate buffer solution.

**RESULTS AND DISCUSSION**

**Optimization of the experimental variables**

The analytical parameters that affect the performance of DLLME-SFO for the preconcentration of indomethacin,
such as sample pH, 1-undecanol and ethanol volumes, NaCl concentration, extraction and centrifugation times and sample volume were investigated and optimized.

**Effect of sample pH**

Since the pH of sample solution determines the ionic state of analytes, it is a very important factor for the extraction of acidic or basic analytes (Suh et al. 2015). The structure of indomethacin is given in Figure 1. This shows that indomethacin is an acidic drug (pKa 4.5). It is stable in neutral or slightly acidic media and dissociates in strong alkali media (Ali et al. 2015). It is also soluble in ethanol, ether, acetone, castor oil and is practically insoluble in water (O’Neil 2013) whereas 1 g of indomethacin can be dissolved in about 30 mL of chloroform (Osol 1980). To increase the affinity of the analyte for the extraction into the extraction solvent, the pH of the sample solution should be adjusted to a specific pH at which the analyte is in its neutral form (Suh et al. 2015). The effect of sample pH on the extraction efficiency was investigated over the pH range of 2.0–9.0, with results being shown in Figure 2. The highest analytical signal was obtained at pH 4.0. At higher pH values, the analytical signals sharply decreased. Therefore, pH 4.0 was selected for all subsequent experiments.

**Effect of extraction solvent volume**

To examine the effect of extraction solvent volume on the extraction efficiency in DLLME-SFO method, different volumes of 1-undecanol (40, 60, 80, 100 and 125 μL) were studied. Ethanol (0.5 mL) was added to each solution. According to the results given in Figure 3, the analytical signals increased up to 80 μL of 1-undecanol and then decreased. The highest analytical signal was obtained using 80 μL of 1-undecanol and, therefore, this volume of 1-undecanol was used as extraction solvent in subsequent experiments.

**Effect of disperser solvent volume**

The volume of disperser solvent is very important because it directly affects extraction solvent solubility in the aqueous phase and therefore influences the efficiency of the method (Celik et al. 2015). The effect of the volume of ethanol on the extraction efficiency was studied over the range 0.1–1.0 mL. The results are given in Figure 4. The results showed that the analytical signals increased up to 0.25 mL of ethanol and then decreased. Therefore, 0.25 mL of ethanol was selected as the optimum volume of the disperser solvent.

**Salting-out effect of NaCl**

The salting-out effect can also be a very important phenomenon in LLE since the extraction efficiency may significantly
improve by the addition of salt to the aqueous sample. Different volumes (0–1.25 mL) of 2 M NaCl and 1 mL of pH 4.0 sodium acetate buffer solution were added to the polyethylene centrifuge tubes, then their final volumes were completed to 5 mL, to investigate this effect on the extraction efficiency. Therefore, different concentrations of NaCl (0.0–0.5 M) were obtained in the final solutions. As seen in Figure 5, absorbance signals increased up to 0.1 M NaCl and then decreased. Therefore, 0.1 M NaCl was used for all subsequent experiments.

Effect of extraction time

Extraction time has an important role in this extraction method to obtain quantitative extraction of the analyte. Not only can it improve the trueness and bias of the method, but it can also help to maintain equilibrium between the aqueous sample and the organic solvent. The effect of extraction time on the extraction yield of indomethacin was studied over the range of 2–15 min. Absorbance signals increased significantly from 2 min to 5 min and then rose at a slower rate up to an extraction time of 7.5 min and then remained nearly constant until an extraction time of 15 min. Therefore, an extraction time of 7.5 min was selected for further experiments.

Effect of centrifugation time

Centrifugation is a necessary step to obtain two distinguishable phases in the extraction tubes. The effect of centrifugation time upon on the extraction performance of indomethacin was studied over the range of 2–15 min at 4,000 rpm. The highest absorbance signal was obtained at 5 min of centrifugation. Therefore, a centrifugation time of 5 min was selected for further experiments.

Sample volume effect

The sample volume is a very important experimental parameter that affects the preconcentration factor. For this purpose, different volumes (5–40 mL) of aqueous solution, each containing 25 μg indomethacin, were extracted under optimum conditions (sample pH 4.0, 80 μL of 1-undecanol, 0.25 mL of ethanol, 0.1 M NaCl, extraction time of 7.5 min, centrifugation time of 5 min). The results obtained are given in Table 1. Quantitative recoveries (101.1 and 100.9%) were obtained for 5 and 10 mL sample volumes, respectively. Preconcentration factors of 2 and 4 were obtained for 5 and 10 mL of sample solution by diluting the organic droplet to 2.5 mL with ethanol. It was noted that full recovery was not achieved for sample volumes greater than 10 mL.

<table>
<thead>
<tr>
<th>Sample volume (mL)</th>
<th>Found indomethacin (μg)a</th>
<th>Recovery (%)</th>
<th>Preconcentration factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>25.27 ± 0.42</td>
<td>101.1</td>
<td>2</td>
</tr>
<tr>
<td>10</td>
<td>25.23 ± 0.39</td>
<td>100.9</td>
<td>4</td>
</tr>
<tr>
<td>20</td>
<td>21.31 ± 1.85</td>
<td>85.2</td>
<td>8</td>
</tr>
<tr>
<td>30</td>
<td>18.32 ± 3.91</td>
<td>73.3</td>
<td>12</td>
</tr>
<tr>
<td>40</td>
<td>14.94 ± 5.83</td>
<td>59.8</td>
<td>16</td>
</tr>
</tbody>
</table>

aMean ± standard deviation based on three replicate determinations.
Higher preconcentration factors could be obtained by diluting the extractant drop carrying the analytes to lower volumes using smaller spectrophotometry cells in the analysis. For example, if dilution to 1 mL was used, a preconcentration factor of 10 would be achieved for a sample volume of 10 mL. In this case, detection limits at the μg/L level would have been achieved, which would be very impressive for UV-Vis detection.

**Effect of interfering species**

It is necessary to demonstrate the selectivity of the developed microextraction method for the determination of indomethacin. Therefore, the effects of some cations and anions and humic acid that are common elements in water samples were investigated. Different amounts of the interfering species were added to the test solutions containing 3.0 or 5.0 mg/L indomethacin and then the recommended extraction procedure was applied. The results are given in Table 2 and demonstrate that 100 mg/L PO4³⁻, CO3²⁻, Ca²⁺, Mg²⁺, Co²⁺, Mn²⁺, Ni²⁺, Cu²⁺, and Cd²⁺ and 25 mg/L Cr³⁺ and Fe³⁺, 10 mg/L humic acid, 1 mg/L NO₃⁻ did not affect the extraction and determination of indomethacin significantly. The interference from nitrate can easily be eliminated by passing the water sample through an anion exchange resin. This would retain the nitrate and separate it from the analyte prior to applying the proposed method.

Since the detector used in this work is UV-Vis, which is not a selective and specific detector, the presence of other similar organic compounds could potentially lead to a positive interference if they are extracted simultaneously. However, the proposed extraction/preconcentration method has been proven to work, but a chromatographic technique, e.g., HPLC, may be required to separate concomitant drugs/drug metabolites prior to UV-Vis detection.

**Analytical performance of the proposed method**

Under the optimized conditions, a calibration curve for indomethacin was constructed using the proposed method by putting standard solutions through the same preparation procedure as the samples. Therefore, calibration standard solutions of indomethacin at the concentration range of 1–4 mg/L in 5 mL of sample solutions were prepared. The equation of the calibration graph was A = 0.1876 C + 0.0004 (with a correlation coefficient 0.9998). In this equation, A is absorbance and C is the concentration of indomethacin in the solution (mg/L). The limit of detection, defined as LOD = 3 Sb/m and where Sb is the standard deviation of 20 replicate blank signals and m is the slope of the calibration curve, was 17.9 μg/L without any preconcentration. The limit

<table>
<thead>
<tr>
<th>Interfering species</th>
<th>Added as</th>
<th>Amount added interfering species (mg/L)</th>
<th>Amount added indomethacin (mg/L)</th>
<th>Recovery of indomethacin (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Humic acid</td>
<td>Humic acid</td>
<td>10</td>
<td>3</td>
<td>107.9 ± 5.3</td>
</tr>
<tr>
<td>PO4³⁻</td>
<td>Na₃PO₄</td>
<td>100</td>
<td>3</td>
<td>103.3 ± 2.3</td>
</tr>
<tr>
<td>CO3²⁻</td>
<td>Na₂CO₃</td>
<td>100</td>
<td>3</td>
<td>103.2 ± 2.0</td>
</tr>
<tr>
<td>Ca²⁺</td>
<td>CaCl₂</td>
<td>100</td>
<td>5</td>
<td>100.7 ± 0.4</td>
</tr>
<tr>
<td>Mg²⁺</td>
<td>MgCl₂</td>
<td>100</td>
<td>5</td>
<td>99.1 ± 4.7</td>
</tr>
<tr>
<td>Co²⁺</td>
<td>CoCl₂, 6H₂O</td>
<td>100</td>
<td>5</td>
<td>101.9 ± 5.4</td>
</tr>
<tr>
<td>Mn²⁺</td>
<td>MnCl₂, 2H₂O</td>
<td>100</td>
<td>5</td>
<td>101.6 ± 2.5</td>
</tr>
<tr>
<td>Ni²⁺</td>
<td>NiCl₂, 6H₂O</td>
<td>100</td>
<td>5</td>
<td>110.3 ± 1.5</td>
</tr>
<tr>
<td>Cu²⁺</td>
<td>Cu(CO₂CH₃)₂, 2H₂O</td>
<td>100</td>
<td>5</td>
<td>95.9 ± 3.2</td>
</tr>
<tr>
<td>Cd²⁺</td>
<td>CdCl₂, H₂O</td>
<td>100</td>
<td>5</td>
<td>96.7 ± 4.9</td>
</tr>
<tr>
<td>Fe³⁺</td>
<td>FeCl₃, 6H₂O</td>
<td>25</td>
<td>5</td>
<td>105.8 ± 0.9</td>
</tr>
<tr>
<td>Cr³⁺</td>
<td>CrCl₃, 6H₂O</td>
<td>25</td>
<td>5</td>
<td>105.5 ± 5.5</td>
</tr>
<tr>
<td>NO₃⁻</td>
<td>KNO₃</td>
<td>1</td>
<td>5</td>
<td>107.6 ± 5.7</td>
</tr>
</tbody>
</table>
of detection was also calculated as $74.9 \, \mu g/L$ from the regression values of the calibration line using $3.19 \, Se/m$ without any preconcentration. These values can be improved between two- and ten-fold depending on preconcentration factor. Pooled repeatability of standard deviations over 5 days for three runs on each day from a subset of data collected in $5 \, mg \, L^{-1}/C0$ standard solution was calculated to be $0.016 \, mg \, L^{-1}/C0$.

A comparison of the characteristic data obtained using the method developed with other methods reported in the literature for the determination of indomethacin is summarized in Table 3. This clearly shows that the detection limit for the proposed method is better than or comparable to those obtained using other methods (Sato et al. 1997; Ali 1999; Mardones et al. 2001; Nagaraja et al. 2003; Lin et al. 2006; Michail & Moneeb 2011; Riano et al. 2012; Amoli Diva et al. 2015).

Table 3 | Comparison of the proposed method with other methods for the determination of indomethacin

<table>
<thead>
<tr>
<th>Method</th>
<th>Technique</th>
<th>Sample type</th>
<th>Detection limit (LOD) ($\mu g/L$)</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>ELISA</td>
<td>ELISA reader</td>
<td>Tap water, drinking water, river water and surface water</td>
<td>0.01$^c$</td>
<td>Huo et al. (2007)</td>
</tr>
<tr>
<td>CSV</td>
<td>DPSV</td>
<td>Urine and plasma</td>
<td>3.8, 190</td>
<td>Ali (1999)</td>
</tr>
<tr>
<td>SPE</td>
<td>MEKC-UV</td>
<td>Plasma</td>
<td>100$^c$</td>
<td>Lin et al. (2006)</td>
</tr>
<tr>
<td>SPE</td>
<td>On-line CE</td>
<td>Urine and serum</td>
<td>12$^d$</td>
<td>Mardones et al. (2001)</td>
</tr>
<tr>
<td>SPE</td>
<td>HPLC-UV</td>
<td>Plasma</td>
<td>50$^c$</td>
<td>Sato et al. (1997)</td>
</tr>
<tr>
<td>SM-LLME</td>
<td>HPLC-UV</td>
<td>Urine</td>
<td>12.216$^c$</td>
<td>Riano et al. (2012)</td>
</tr>
<tr>
<td>MHSPE</td>
<td>UV-Vis</td>
<td>Plasma and urine</td>
<td>8.6$^d$</td>
<td>Amoli Diva et al. (2015)</td>
</tr>
<tr>
<td>Diazotized p-phenylenediamine dihydrochloridere agent</td>
<td>UV-Vis</td>
<td>Capsules</td>
<td>160$^d$</td>
<td>Nagaraja et al. (2003)</td>
</tr>
<tr>
<td>SPE</td>
<td>HPLC-DAD</td>
<td>Urine</td>
<td>10$^c$</td>
<td>Michail &amp; Moneeb (2011)</td>
</tr>
<tr>
<td>DLLME-SFO</td>
<td>UV-Vis</td>
<td>Tap water and river water</td>
<td>17.9$^d$, 74.9$^c$ (without any preconcentration)</td>
<td>This work</td>
</tr>
</tbody>
</table>


$^c$Limits of detection were calculated based on $S/N = 3$ (signal-to-noise ratio = 3).

$^d$Limits of detection were calculated based on $3 \, Sb/m$.

$^e$Limits of detection were calculated based on $3 \, Se/m$.

Application of the method to natural samples

The applicability of the proposed method was evaluated by analysing tap water and river water samples for indomethacin. The accuracy of the proposed method was checked by spiking the samples with $2.0 \, mg/L$ of indomethacin. The results of these spike/recovery experiments are given in Table 4. Good recoveries (94.5–103.0%) were obtained for the analyte in these samples, demonstrating the applicability and accuracy of the DLLME-SFO method.

CONCLUSIONS

In the present work, a new DLLME-SFO method was developed for the determination of indomethacin in tap water...
and river water samples. The proposed method is reliable, efficient, inexpensive and simple. In addition, due to the low consumption of organic solvents, it is environmentally friendly. If the method were to be adopted for detection using other analytical techniques, such as HPLC or LC-MS, the separation of indomethacin from other organic compounds in biological samples would also be possible. In addition, since dilution would not be necessary, significantly improved LOD would be achieved. Techniques such as LC-MS not only separate different species but may also improve the LOD substantially. The matrix separation properties of the proposed method would be transferrable to other instrumental analytical techniques.

ACKNOWLEDGEMENTS

The authors are grateful for the financial support obtained from the Unit of the Scientific Research Projects of Balikesir University (Project No. 2015/198).

REFERENCES


Grippa, E., Santini, L., Castellano, G., Gatto, M. T., Leone, M. G. & Saso, L. 2000 Simultaneous determination of


Nagaraja, P., Vasantha, R. A. & Yathiranjan, H. S. 2003 Sensitive spectrophotometric method for the determination of


First received 6 October 2017; accepted in revised form 27 December 2017. Available online 23 January 2018