Talanta 129 (2014) 392–397

Contents lists available at ScienceDirect

Talanta

journal homepage: www.elsevier.com/locate/talanta

Optimization of the in-needle extraction device for the direct flow of the liquid sample through the sorbent layer

Monika Pietrzyńska*, Adam Voelkel

Poznań University of Technology, Institute of Chemical Technology and Engineering, pl. M. Skłodowskiej-Curie 2, 60-965 Poznań, Poland

ARTICLE INFO

Article history:
Received 3 March 2014
Received in revised form
29 May 2014
Accepted 11 June 2014
Available online 19 June 2014

Keywords:
In-needle extraction
Needle trap device
Liquid samples
Permeability in needle
Poly(styrene–divinylbenzene)
Silica sorbents

ABSTRACT

In-needle extraction was applied for preparation of aqueous samples. This technique was used for direct isolation of analytes from liquid samples which was achieved by forcing the flow of the sample through the sorbent layer: silica or polymer (styrene/divinylbenzene). Specially designed needle was packed with three different sorbents on which the analytes (phenol, p-benzoquinone, 4-chlorophenol, thymol and caffeine) were retained. Acceptable sampling conditions for direct analysis of liquid sample were selected. Experimental data collected from the series of liquid samples analysis made with use of in-needle device showed that the effectiveness of the system depends on various parameters such as breakthrough volume and the sorption capacity, effect of sampling flow rate, solvent effect on elution step, required volume of solvent for elution step. The optimal sampling flow rate was in range of 0.5–2 mL/min, the minimum volume of solvent was at 400 μL level.

1. Introduction

Sample preparation is an important analytical step. However, many conventional sample preparation methods are relatively complicated, time-consuming procedures and require large volume of organic solvents. In-needle extraction was developed as a novel sample preparation technique for chromatographic determination of trace organic compounds in aqueous and gaseous samples. Compared to conventional sorbent traps, in-needle extraction process requires much lower volumes of solvent, well below 1 mL, e.g.: 25 μL [1]. The total cost of in-needle extraction device is much lower than that of solid phase extraction (SPE) or solid phase microextraction (SPME) systems.

The needle trap device (NTD) extraction (or in-needle extraction) is described in literature very thoroughly [2–37] but it is most often applied for preparation of gaseous samples [2–4,6–10,23]. Isolation of analytes from water samples was combined with head-space (HS) or purge and trap (P&T) techniques where the analytes were trapped by transferring the vapor phase through the sorbent layer [5,11,15,24,37]. In-needle technique was relatively seldom used directly for analytes separated from liquid samples. Certainly, this limited application is associated with a high flow resistance produced by a sorbent layer.

Saito et al. [28,31] prepared the extraction device with a bundle of the polymer-coated filaments (Zylon and Technora) as the sorbent material packed into a needle. The extraction was made by pumping the aqueous sample solution into the needle extraction device. The sample flow rate during the extraction was optimized and it was found that the flow rate should be about 16 μL/min, which is equivalent to 1 mL/h.

In our previous work [38] we proposed the direct use of the in-needle technique for the preparation of liquid samples by direct passing water samples through the needle filled with sorbent material. The effectiveness of the NTD system was studied based on experimental data and chemometric evaluation (Table 1).

The range for geometrical characteristics of the sorbent has been determined, where the extraction system works properly. To estimate suitability of a given extraction system, a new parameter P_{IN} expressing the geometry of the system was proposed. The usefulness of the range of P_{IN} parameter was confirmed experimentally. This tool might be used in designing and preparation of a number of in-needle devices having similar ability to direct liquid sample preparation.

The quantitative criteria for selection of parameters of the NTD system were derived by Kaczmarek et al. [39]. The conditions were formulated for the force exerted on syringe, the volume of tested solution, for the time of test and contact time of solution with the sorbent. The last two conditions allowed to establish limits for combinations of fundamental geometrical and macroscopic structural characteristics of the system.

In 2013 macroporous poly(styrene–divinylbenzene) (PS-DVB) monoliths were prepared by in situ polymerization in stainless steel needles [40]. The new monolithic in-needle extraction (MINE) devices were used in the preparation of a series of test water samples for

---

* Corresponding author. Tel.: +48 616653745; fax: +48 616653649.
E-mail address: monikapietrzynska@gmail.com (M. Pietrzyńska).

http://dx.doi.org/10.1016/j.talanta.2014.06.026
0039-9140/

Table 1
Needle extraction devices

Lp.	Name	Material	I.D. [mm]	*L* [mm]	Application	Phase	Flow rate [mL/min]	Year	Ref.
Needle extraction device filled partially or fully with sorbent material									
1	NTD	Tenax	N/A	N/A	VOC	Gas	N/A	1978	[2]
2	In-needle trap	Glass wool	0.39	5	Diesel exhaust	Gas	1	2001	[8]
3	NTD	Tenax	0.5	N/A	BT in tobacco smoke	Gas	N/A	2003	[9]
4	NTD	PDMS\DVB\Carboxen	0.39	3\2\2	BTEX	Gas	5 or 10	2005	[10]
5	INCAT	Porapak Q Alumina	1.1 or 0.9	50 or 7	BTEX from liquid	HS	N/A	2006	[5]
6	NTD	Carbopack X	1.1 or 0.9	50	BTEX from liquid	HS	N/A	2008	[11]
7	NTD	DVB	0.643	10	BTEX	Gas	1.9	2008	[12]
8	NTD	DVB	0.39	5 or 10	BTEX	Gas	1.9	2008	[13]
9	NTD	Carboxen 1000	0.39	37 or 48	BTEX	Gas	0.012-0.016	2008	[14]
10	NTD	DVB (synthesized by polimerization)	0.5	N/A	Formic and acetic acids from aqueous	HS	7.8	2008	[15]
11	NTD	DVB	0.32	10	BTEX	Gas	100	2008	[16]
12	NTD	TenaX\Carbopack\Carboxen 1000	0.41	10\10\10	Breath analysis	Gas	60	2009	[17]
13	NTD	DVB	22 g	N/A	Mosquito coil smoke	Gas	N/A	2009	[18]
14	In-needle	Copolymer MAA or EGDMA	N/A	N/A	Acetone	Gas	8.33	2009	[19]
15	NTD	DVB	0.41	N/A	Tobacco smoke	Gas	N/A	2010	[20]
16	Needle trap	Carbopack X	0.6	51	BTEX	Gas	N/A	2010	[21]
17	NTD	Carbon nanotube–sol–gel	N/A	N/A	PAHs from aquatic media	N/A	N/A	2011	[22]
18	Needle microextraction trap	Carbopack X	0.39	10	VOC	Gas	15	2011	[23]
		TenaX	0.39	10	VOC	Gas	15		
19	Needle extraction	DVB (synthesized by polimerization)	0.5	N/A	Acetic acid and formic acid from liquid	HS	N/A	2012	[24]
20	Needle trap micro-extraction	DVB\Carbopack X\Carboxen 1000 PDMS\Carbopack X\Carboxen 1000 DVB I/Carboxen 1000 PDMS I/Carboxen 1000 Copolymer MAA i EGDMA	0.39	10\10\10 10\10\10 10\10 10\10 20	VOC	Gas	60	2012	[25]
Needle extraction device filled with adsorption capillary									
21	INCAT	GC column DB5	0.2 i 0.4	N/A	VOC	Gas	N/A	1997	[3]
22	INCAT	Colloidal graphite	0.25	N/A	BTEX	Gas	N/A	1999	[4]
23	INCAT	Tenax TA 35 mg	1.8	N/A	BTEX	Gas	N/A	2009	[6]
24	INCAT	Tenax TA 35 mg	1.8	N/A	BTEX	Gas	N/A	2010	[7]
Needle extraction device filled with polimerem polymer-coated filaments									
25	Needle extraction device	Polymer-coated filaments	0.3	30	Liquid	Liquid	16 μL/min	2007	[28]
26	Packed needle extraction device	Polymer-coated filaments	0.5	85	Bisfenol A	Liquid	16 μL/min	2009	[31]
Needle extraction device covered with a sorptive layer – commercially available									
27	SPDE	PDMS i PDMS/AC	0.5	56	BTEX	HS	3	2007	[36]
28	SPDE	PDMS/AC	0.8	70	BTEX n-aldehydes	HS	6	2008	[37]
Needle extraction device filled with monolithic material									
29	MINE	Styrene/DVB	2.7	50	Phenols from liquid	Liquid	0.1–4	2013	[40]

chromatographic analysis. The extraction of phenolic compounds from water samples was carried out by pumping liquid samples through the MINE device. Obtained results indicate a high efficiency of in-needle extraction systems based on monolithic materials.

1.1. The aim of work

The aim of this study was to investigate the optimal conditions of the extraction process (sorption and desorption) using the in-needle technique. Sorbent materials, placed in the in-needle will be examined in several ways with using a series of test compounds. One of the important parameters will be the breakthrough volume, which determines the maximum volume of water sample which can be passed through the sorbent. Constant mass of analytes will be sorbed from various sample volumes. It leads to the determination of maximum sample volume, that can be pumped through a needle filled with sorbent material. The sorption capacity, indicating the maximum mass of analyte that can be extracted from water samples, have to be also determined. The influence of process parameters on the recovery will be investigated: effect of sampling flow rate, solvent effect on elution step, required volume of solvent for elution step.

2. Experimental

2.1. Chemicals

Methanol p.a., ethanol p.a., hexane p.a. and dichloromethane were obtained from POCh (Gliwice, Poland). Phenol (98%), p-benzoquinone (98%), 4-chlorophenol (99%) thymol (99.5%) and caffeine (ReagentPlus®) were obtained from Sigma Aldrich (Steinheim, Germany). Water was purified by membrane technique using RO5max system for water deionization (Bichmitte).

2.2. Materials

Stainless steel needles with diameter I.D. 2.7 mm (Danlab, Poland), gas-tight syringe with 10 mL volume (Danlab, Poland),

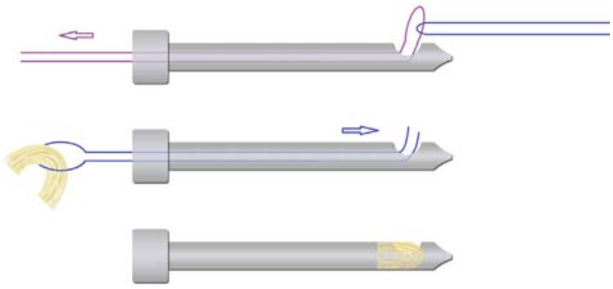

Fig. 1. Introduction of the first supporting layer into needle.

C18 sorbent – 100 μm grain size, 60 Å pore diameter, 0.65 cm^3/g pore volume (Grace, supplied by “Allchrom-Anaserwis”, Poland), C18 sorbent – 40 μm grain size, 60 Å pore diameter, 0.18 cm^3/g pore volume (J.T. Baker, supplied by WITKO, Poland), styrene–divinylbenzene copolymer (SDB) 80 μm grain size (J.T. Baker, Holland, supplied by Witko, Poland).

2.3. Needle preparation

The filling needle process consisted of three stages. First stage (Fig. 1) concerned the introduction of the first supporting layer into needle. Then, needle was filled with sorbent material (polymer or silica) with the dry pack method. The last stage concerned the introduction of the second supporting layer (also serving as a filter).

The supporting layer was used to prevent losing sorbent material. The influence of supporting layer did not present significant effect to the liquid flow, which was confirmed experimentally in our previous work [38].

2.4. Permeability of in-needle device determination

P_{IN} value indicates properly working extraction system and may be described as geometric characteristic of the needle device, since it is a combination of three significant geometrical factors, diameter of the needle (dN), sorbent's length (L) and the average diameter of sorbent's grains (dS)

$$P_{IN} = \frac{dS^2 dN^2}{L} \tag{1}$$

The needle filling should assure satisfactory flow rate with good recovery within an acceptable time. P_{IN} value higher than 1.5×10^{-12} or lower than 0.1×10^{-12} indicates insufficiently working extraction system [38].

2.5. In-needle extraction

The extraction was carried out by pumping the aqueous sample through the in-needle extraction device and then by elution of analytes.

The model water solutions contained five different compounds: p-benzoquinone; phenol; 4-chlorophenol; thymol and caffeine. All parameters of the experiment were chosen in such a way that do not affect each other, e.g. to determine the sorption capacity – the sample volume and the sample flow rate was chosen to not affect the obtained results.

To determine sorption capacity, water solutions containing each test analyte (in excess) were pumped through the in-needle device.

To select an appropriate solvent, water solutions containing 0.3 mg of each test analyte were pumped through the in-needle device.

To determine the breakthrough volume, water solutions containing 10 μg of each test analyte were pumped through the monolithic in-needle extraction device. Volume of the samples varied from 1 to 100 mL.

To determine the effect of sampling flow rate, water solutions containing 0.1 mg of each test analyte were pumped through the monolithic in-needle extraction device at different flow rate (0.1–6 mL/min); sample volume was 5 mL.

The volume of solvent required to elute analytes from the monolith was measured. The desorption process was carried out five times by 200 μL of solvent (total volume 1 mL).

To eliminate the uncertainty caused by the use of human hand as a source of driving module – pressure drop, the pump was applied. Membrane pump (KNF Neuberger) and syringe infusion pump AP22 (Ascor, Polska) have been applied to achieve the same flow conditions and drop pressure. It ensures the comparability of the results.

2.6. GC analyses

GC analyses were carried out by using a HP 5890II gas chromatograph with FID detector (supplied by Hewlett Packard-Poland, Warsaw, Poland) and with capillary column RTX-5 (Restek, supplied by AnaSerwis, Baranowo, Poland). Helium was used as a carrier gas at a flow-rate of 2.5 mL/min and a head pressure of 90 kPa. The column temperature was held at 100 °C for 1 min, then ramped at 10 °C/min to 150 °C where it was held for 4 min. Injection volume: 1 μL.

2.7. Data evaluation

All the results obtained were analyzed statistically. Each extraction procedure was repeated five times. A Q-Dixons text was used to determine and reject statistical outliers with a critical value of 0.71 at 95% confidence [41].

3. Results and discussion

Evaluation of the usefulness of in-needle devices was based on the P_{IN} parameter. The acceptable flow resistance of the sorbent layer is crucial for the sorption and desorption processes occurring in the device. P_{IN} values calculated according to Eq. (1) are appropriately 0.23×10^{-12} for C18 (grain size 40 μm), 0.93×10^{-12} for SDB and 1.46×10^{-12} for C18 (grain size 100 μm). It means that all values are located in the suggested P_{IN} range [38].

3.1. Sorption capacity

Sorption capacity is one of the important parameters, indicating the mass of analyte that can be retained on sorbent material.

The maximum mass of analyte that can be extracted from water samples was determined (Fig. 2). The highest sorption capacity was achieved for SDB filled needle on which 28 mg of 4-chlorophenol was sorbed. The difference in sorption capacity between the polymer and the silica material was enormous. In the case of silica materials, sorption capacity did not exceed 5 mg of each analyte. The difference between the silica materials (40 μm and 100 μm) is visible but not as significant.

3.2. Breakthrough volume

Breakthrough volume, defined as the maximum volume of water sample which can be passed through the sorbent without eluting of analytes by the sample matrix. Constant mass of analytes was sorbed from various sample volumes.

The recovery level was satisfactory (> 90%) when up to 30 mL of the water sample was passed through each in-needle device filled with SDB material (Fig. 3a). However, in the case of silica materials, breakthrough volume may cause significant problems

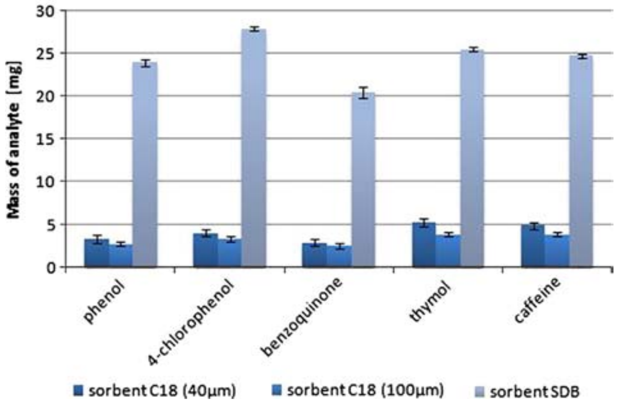

Fig. 2. Sorption capacity; sample flow rate was 1 mL/min.

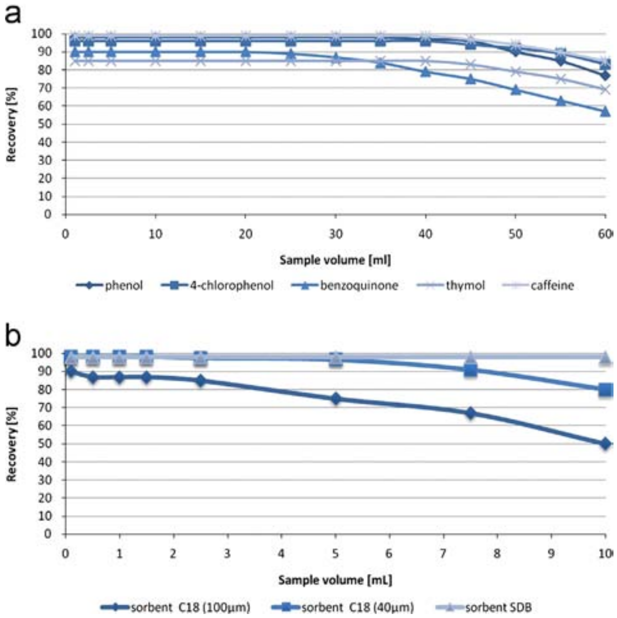

Fig. 3. Breakthrough volume of sorbent materials located in the needle was determined for (a) needle filled with SDB (various analytes) and (b) three different sorbents with phenol as analyte; sample flow rate was 1 mL/min and volume of the solvent (ethanol) was 1 mL.

for whole sample preparation step. Only 5 mL of liquid sample can be introduced to needle filled with 40 μm silica material (Fig. 3b).

3.3. The effect of sampling flow rate

The contact time of sample with the sorbent material is crucial for the sorption level in examined systems (Fig. 4). To achieve high sorption (and consequently the extraction level), the flow rate should not be higher than 2 mL/min. The same high recovery was achieved at a flow rate between 0.2 mL/min and 2.0 mL/min in the case of polymeric sorbent (Fig. 4a). In the case of phenol it was difficult to determine optimal range of flow rate – about 1 mL/min (Fig. 4b). In the case of caffeine the flow rate had no significant effect on the sorption process (Fig. 4c).

3.4. Solvent selection

To select an appropriate solvent, series of extraction processes were carried out (Fig. 5). In most cases the use of ethanol and dichloromethane allowed to obtain the recovery of analytes at high level. Because of the high toxicity of dichloromethane, ethanol was chosen as eluent in all the tests.

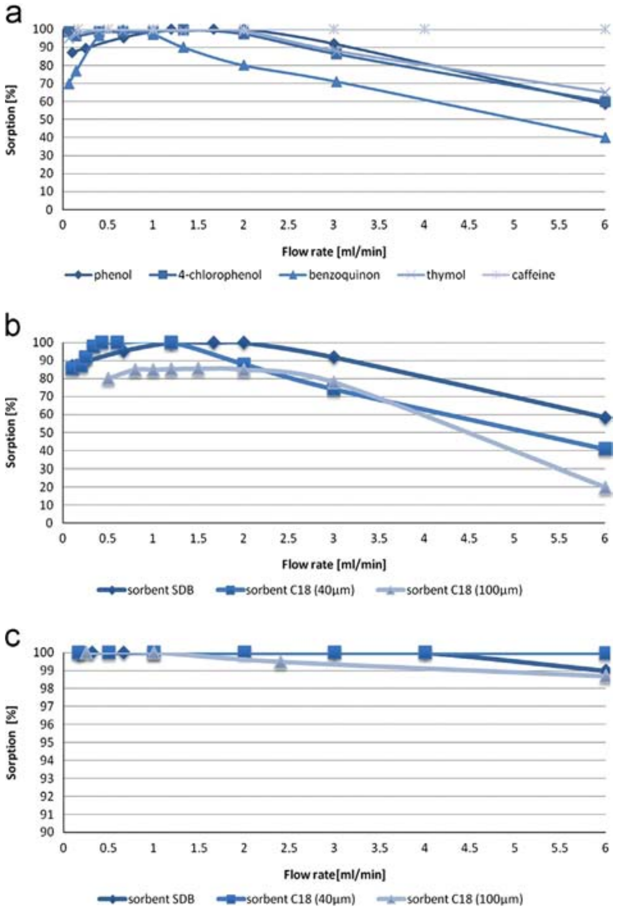

Fig. 4. Influence of flow rate on the sorption percentage determined for (a) a needle filled with SDB, (b) sample containing phenol, and (c) sample containing caffeine; volume of the solvent (ethanol) was 1 mL.

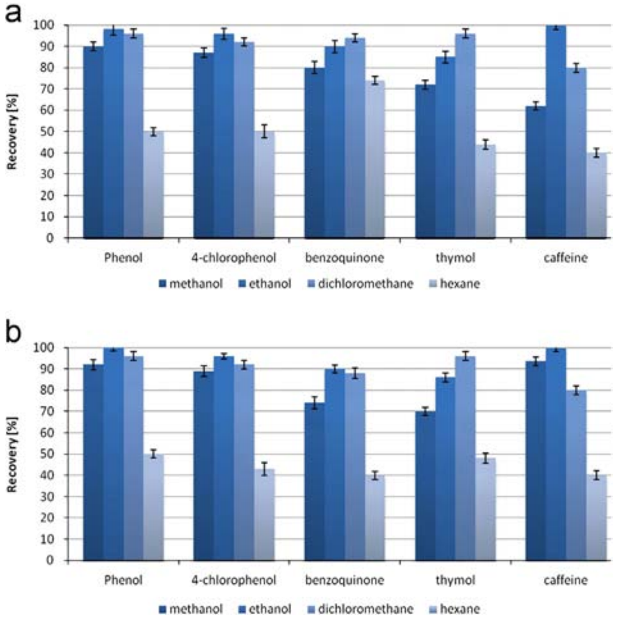

Fig. 5. Influence of the solvents on recovery level for (a) silica sorbent and (b) SDB sorbent; sample flow rate was 1 mL/min and volume of the solvent was 1 mL.

The volume of solvent required to elute analytes from the sorbent material was determined (Fig. 6). First 400 μL of solvent is sufficient to elute almost completely the analytes from the silica sorbent. However, in the case of SDB sorbent, required volume of

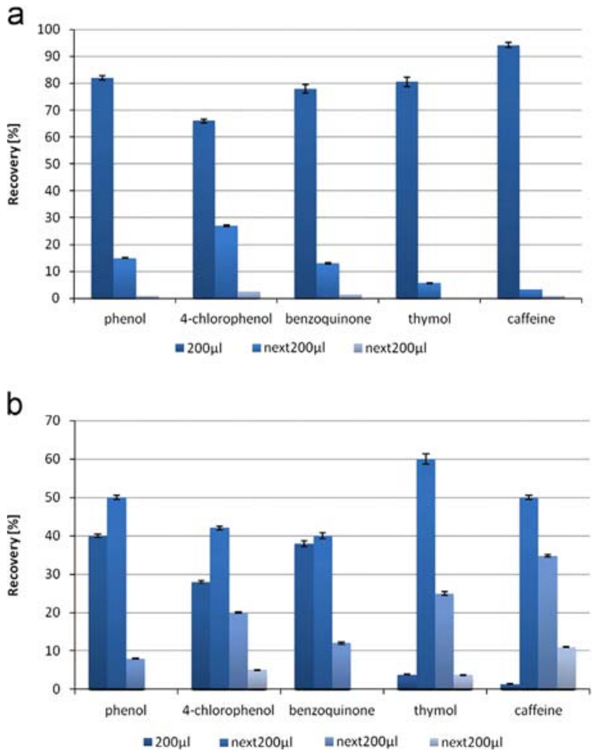

Fig. 6. Influence of solvent volume for (a) silica sorbent and (b) SDB sorbent.

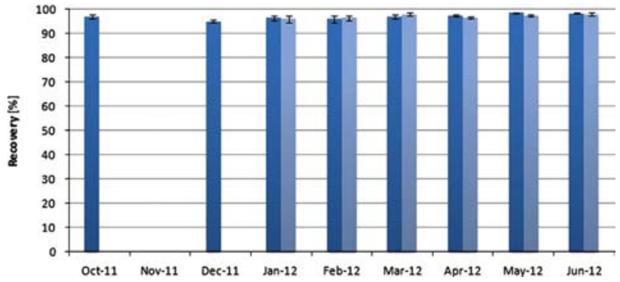

Fig. 7. Repeatability of the method using two identical needles filled with silica sorbent (grain size 40 µm); sample flow rate was 1 mL/min and volume of the solvent (ethanol) was 1 mL.

solvent rises to 600 µL or even 800 µL. Therefore, 1 mL of ethanol was used for desorption step in this paper.

3.5. Repeatability

The repeatability of the method (extraction for two identical needles) was acceptable and RSD values varied between 2% and 5% (Fig. 7). The limit of quantification for the compounds estimated were 0.4 µg for phenol, 1 µg for 4-chlorophenol and 6 µg for p-benzoquinone.

Percentage recovery of phenol for two identical needles remained at the same high level. This demonstrates the fact that the needle prepared had identical extraction properties and also the repeatability of carried extraction is high and after more than a hundreds of sorption/desorption process the extraction properties did not change.

4. Conclusions

Applying the P_{IN} parameter allowed the selection of in-needle devices enabling analyte isolation under the sample flow rate in the range of 0.1–6 mL/min.

Extraction properties of needles filled with commercial materials were examined. Sorbent materials were analyzed in several ways, e.g. breakthrough volume and the sorption capacity. The experiments results allowed to estimate the following optimal extraction process conditions:

- flow rate of the sample through the sorbent material should be in the range of 0.5–2 mL/min, and the suggested rate is 1 mL/min;
- in most cases, the use of 600 µL of eluent allow to complete elution of the analytes; and
- the concentration level of the analytes is a result of the sorption capacity and breakthrough volume, the extraction efficiency therefore depends on that, which of the limiting factors will be first exceeded.

The final result of extraction level is affected by many factors. Influence of the concentration of the analyte on the recovery is related to the breakthrough volume and the sorption capacity. Therefore, it must be taken into account that the obtained recovery value is a result of all factors. Obviously, the sorption efficiency is influenced by the contact time of the liquid sample, and the desorption efficiency is affected by the type and volume of solvent. Decrease of the recovery of the analyte will be observed even if only one of the limiting factors will be exceeded.

Acknowledgments

This work was supported by the National Science Center 2011/01/N/ST5/05549 grant.

References

[1] M. Ogawa, Y. Saito, S. Shirai, Y. Kiso, K. Jinno, Anal. Bioanal. Chem. 388 (2007) 619–625.
[2] F. Raschdorf, Chimia 32 (1978) 478–483.
[3] M.E. McComb, R.D. Oleschuk, E. Giller, H.D. Gesser, Talanta 44 (1997) 2137–2143.
[4] S. Shojania, R.D. Oleschuk, M.E. McComb, H.D. Gesser, A. Chow, Talanta 50 (1999) 193–205.
[5] P. Přikryl, R. Kubinec, H. Jurdáková, J. Ševčík, I. Ostrovský, L. Soják, V. Berezkin, Chromatographia 64 (2006) 65–70.
[6] J. Hrivňák, P. Tölgyessy, E. Král'ovičová, J. Chromatogr. A 1216 (2009) 4815–4816.
[7] P. Tölgyessy, J. Hrivňák, E. Král'ovičová, D. Barloková, Chromatographia 71 (2010) 953–955.
[8] J.A. Koziel, M. Odziemkowski, J. Pawliszyn, Anal. Chem. 73 (2001) 47–54.
[9] V.G. Berezkin, E.D. Makarov, B.V. Stolyarov, J. Chromatogr. A 985 (2003) 63–65.
[10] A. Wang, F. Fang, J. Pawliszyn, J. Chromatogr. A 1072 (2005) 127–135.
[11] H. Jurdáková, R. Kubineca, M. Jurčišinová, Ž. Krkošová, J. Blaško, I. Ostrovský, L. Soják, V.G. Berezkin, J. Chromatogr. A 1194 (2008) 161–164.
[12] I.-Y. Eom, V.H. Niri, J. Pawliszyn, J. Chromatogr. A 1196 (2008) 10–14.
[13] I.-Y. Eom, A. Tugulea, J. Pawliszyn, J. Chromatogr. A 1196 (2008) 3–9.
[14] Y. Gong, I.-Y. Eom, D.-W. Lou, D. Hein, J. Pawliszyn, Anal. Chem. 80 (2008) 7275–7282.
[15] D. Lou, X. Lee, J. Pawliszyn, J. Chromatogr. A 1201 (2008) 228–234.
[16] I. Eom, J. Pawliszyn, J. Sep. Sci. 31 (2008) 2283–2287.
[17] M. Mieth, S. Kischkel, J.K. Schubert, D. Hein, W. Miekisch, Anal. Chem. 81 (2009) 5851–5857.
[18] V.H. Niri, I.-Y. Eom, F.R. Kernami, J. Pawliszyn, J. Sep. Sci. 32 (2009) 1075–1080.
[19] I. Ueta, Y. Saito, M. Hosoe, M. Okamoto, H. Ohkita, S. Shirai, H. Tamura, K. Jinno, J. Chromatogr. B 877 (2009) 2551–2556.
[20] X. Li, G. Ouyang, H. Lord, J. Pawliszy, Anal. Chem. 82 (2010) 9521–9527.
[21] J.D. Crom, S. Claeys, A. Godayola, M. Alonso, E. Anticó, J.M. Sanchez, J. Sep. Sci. 33 (2010) 2833–2840.
[22] H. Bagheri, Z. Ayazi, A. Aghakhani, Anal. Chim. Acta 683 (2011) 212–220.
[23] M. Alonso, A. Godayol, E. Antico, J.M. Sanchez, J. Sep. Sci. 34 (2011) 2705–2711.
[24] X. Lee, D. Huang, D.A. Lou, J. Pawliszyn, J. Sep. Sci. 35 (2012) 1675–1681.
[25] P. Trefz, S. Kischkel, D. Hein, E.S. James, J.K. Schuberta, W. Miekischa, J. Chromatogr. A 1219 (2012) 29–38.
[26] H.L. Lord, W. Hang, J. Pawliszyn, Anal. Chim. Acta 677 (2010) 3–18.
[27] Y. Saito, K. Jinno, M. Nojiri, M. Imaizumi, Y. Nakao, Y. Morishima, H. Kanehara, H. Matsuura, K. Kotera, H. Wada, J. Chromatogr. A 975 (2002) 105–112.

[28] Y. Saito, M. Imaizumi, K. Ban, A. Tahara, H. Wada, K. Jinno, J. Chromatogr. A 1025 (2004) 27–32.
[29] Y. Saito, K. Jinno, M. Imaizumi, M. Ogawa, Chromatographia 63 (2006) 459–463.
[30] Y. Saito, I. Ueta, M. Ogawa, K. Jinno, Anal. Bioanal. Chem. 388 (2007) 619–625.
[31] M. Ogawa, Y. Saito, S. Shirai, Y. Kiso, K. Jinno, Chromatographia 69 (2009) 685–690.
[32] Y. Saito, I. Ueta, M. Ogawa, K. Jinno, Anal. Bioanal. Chem. 386 (2006) 725–732.
[33] Y. Saito, I. Ueta, M. Ogawa, N. Ghani, K. Yogo, A. Abe, S. Shirai, K. Jinno, J. Chromatogr. A 1216 (2009) 2848–2853.
[34] Y. Saito, I. Ueta, M. Ogawa, A. Abe, K.A. Yogo, S. Shirai, K. Jinno, Anal. Bioanal. Chem. 393 (2009) 861–869.
[35] Y. Saito, I. Ueta, M. Ogawa, M. Hayashida, K. Jinno, J. Pharm. Biomed. A 44 (2007) 1–7.
[36] K. Ridgway, S.P.D. Lalljie, R.M. Smith, J. Chromatogr. A 1174 (2007) 20–26.
[37] K. Sieg, E. Fries, W. Püttmann, J. Chromatogr. A 1178 (2008) 178–186.
[38] M. Pietrzynska, A. Voelkel, K. Héberger, K. Bielicka-Daszkiewicz, M. Kaczmarek, Anal. Chim. Acta 751 (2012) 182–188.
[39] M. Kaczmarek, A. Voelkel, M. Pietrzyńska, J. Chromatogr. A 1278 (2013) 181–183.
[40] M. Pietrzynska, A. Voelkel, K. Bielicka-Daszkiewicz, Anal. Chim. Acta 776 (2013) 50–56.
[41] David B. Rorabacher, Anal. Chem. 63 (1991) 139–146.