Extraction to Injection in a Single Process

MEPS™ – Fast Miniaturized SPE

- Save hours in sample preparation
- Semi or fully automate to improve workflow and increase productivity
- Reduce solvent usage and sample volume

SGE Analytical Science

www.sge.com

MEPS™ Made Simple

MEPS Explained

MEPS is Micro Extraction by Packed Sorbent and is a development for sample preparation and handling. MEPS is the miniaturization of conventional SPE packed bed devices from milliliter bed volumes to microliter volumes.

The MEPS approach to sample preparation is suitable for reversed phases, normal phases, mixed mode or ion exchange chemistries. MEPS is available in a variety of common SPE phases.

The MEPS Barrel Insert and Needle Assembly (BIN), contains the stationary phase, and is built into the syringe needle (Figure 1).

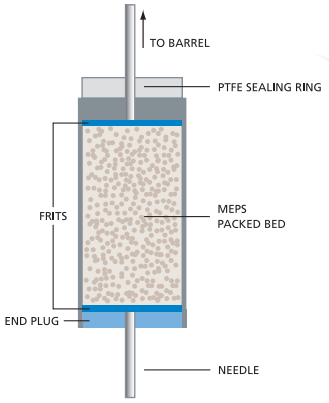


Figure 1
Schematic of the MEPS BIN in the syringe needle.

The Advantage of MEPS

Historically, many sample preparation methods used liquid-liquid extraction (LLE) which required large volumes of sample, solvents and time. Advantages of SPE over LLE include: less time; can be developed into a fully automated technique; requires less solvent, and offers selectivity.

MEPS miniaturizes SPE – removing interfering matrix components and selectively isolating and concentrating analytes. MEPS increases the advantages of conventional SPE in the following ways:

- Significantly reduces the time needed to prepare and inject samples.
- Combined with LC or GC automation - the extraction step and injection step are performed on-line using the same syringe.
- Reduces the volume of solvents needed.
- Works with samples as small as 10 µL versus several hundred µL for SPE.

Sample Size and Sensitivity

Sample volumes may be as little as 10 µL, or by taking multiple aliquots of 100 µL or 250 µL, samples of 1 mL or larger may be concentrated.

Automation

Extract samples and make injections on-line using a single device, reducing sample processing times and the need for operator intervention.

Sorbent Life

BIN life is dependent on the specific matrix being analyzed. For example, C18 analyzing whole plasma samples is conservatively 25-100 samples. BIN life of cleaner samples is significantly longer.

Carryover

The small quantity of phase in the MEPS™ BIN is easily and effectively washed between samples to reduce the possibility of carryover. This washing process is not practical with off-line SPE devices. With automation of MEPS, washing occurs while the previous sample is running.

Flexible and Easy to Use

The dimensions of the sorbent bed ensure performance remains identical to conventional SPE devices when used for extraction of similar samples. Using MEPS BINS for sample volumes as small as 3.6 µL make them well suited to on-line use with LC-MS analysis of volume limited samples.

The MEPS BIN is easily installed in the syringe housing and then secured by the locking nut. Individual labeling of each BIN ensures the use of the correct stationary phase for each extraction.

The amount of sorbent determines the maximum amount of analyte that can be retained. The capacity of non-ionic, silica-based sorbents can be estimated as 3 % to 5 % of the sorbent bed mass.

MEPS has a sorbent bed mass of 4 mg so the capacity is:
4 mg x 3% = **120 µg**
4 mg x 5% = **200 µg**

Conventional silica-based SPE products have a bed volume that can be estimated as 1.5 µL per mg of sorbent. MEPS uses 4 mg of packing so: 1.5 µL x 4 mg = **6 µL bed volume.**

MEPS - Semi or Fully Automated

Semi-automation of MEPS is achieved by coupling MEPS syringes to SGE's eVol® digital analytical syringe, speeding up repetitive SPE, and making it ideal for rapid method development.

MEPS can also be fully automated by using MEPS XCHANGE® syringes on autosamplers such as the CTC PAL* for on-line SPE and injection.

** Contact your CTC distributor for configuration and hardware requirements.*

Meet Mighty MEPS™! Fast Miniaturized SPE

Together eVol® XR + MEPS™ = Mighty MEPS™

Mighty MEPS offers improvements in workflow and resource savings. eVol XR custom programming semi-automates MEPS – you control the speed and volume of each step making Mighty MEPS ideal for:

- Sample preparation.
- Method development.
- Sample clean up.

How To Use Mighty MEPS

eVol®
The world's first digital analytical syringe

R&D 100 2010

MEPS Performance

Sample preparation for complex biological samples is readily adapted to MEPS, reducing the volumes of sample and reagents required for extraction. The extraction of xanthine metabolites from raw human urine using a MEPS BIN packed with C18, prior to GC-MS analysis, is shown in Figure 2. The extraction of anaesthetics from rat plasma using a MEPS BIN packed with C2, prior to LC-MS analysis is shown in Figure 3.

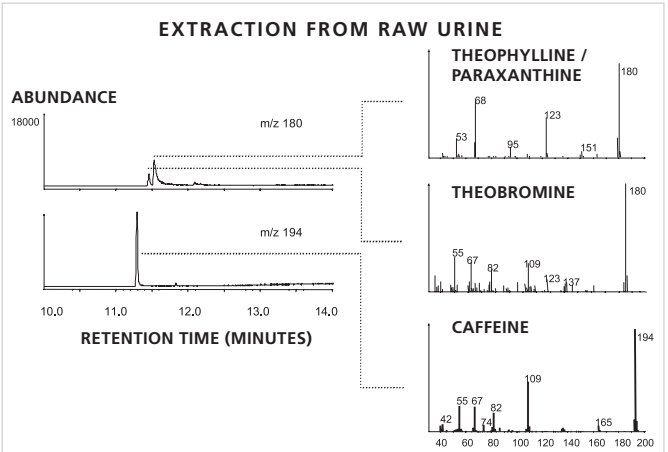


Figure 2
Difficult matrices such as human urine are easily processed using MEPS. In this example 100 µL of human urine was aspirated through a C18 MEPS BIN (conditioned with methanol and water, water wash). Bound xanthines were eluted with 30 µL methanol, 2 µL injected on a BPX5 column for GC-MS analysis.

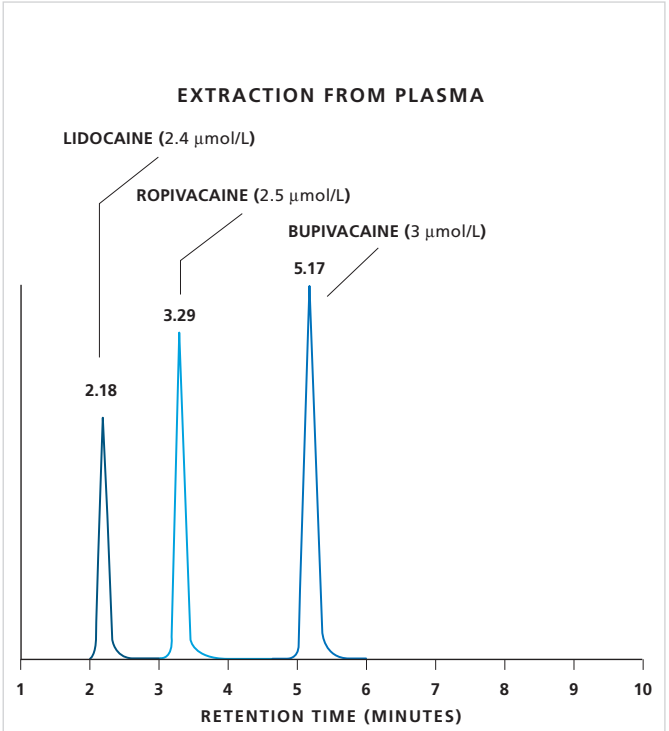


Figure 3
Local anaesthetics were spiked into rat plasma samples - final concentrations: Lidocaine 2.4 µmol/L, Ropivacaine 2.5 µmol/L and Bupivacaine 3.0 µmol/L. 50 µL of the spiked plasma was aspirated through a C2 MEPS BIN, washed with water and eluted using 0.1% HCOOH in 25% Acetonitrile + 75% water onto a C18, 100 X 2.1 mm column.

MEPS Applications

MEPS has been used successfully in these industries:

Environment

Environmental (Example: Determination of organic priority pollutants and emerging compounds in wastewater and snow samples)

Forensics

Forensics (Example: Contribution of microextraction in packed sorbent for the analysis of cotinine in human urine by GC-MS)

Pharmaceuticals

Pharmaceutical (Example: Liquid chromatographic analysis of oxcarbazepine and its metabolites in plasma and saliva)

Food

Food and Flavor (Example: Determination of 2,4,6-trichloroanisole and 2,4,6-tribromoanisole in Wine)

Life Sciences

Life Sciences (Example: Rapid and Sensitive Method for Determination of Cyclophosphamide in Patients Plasma Samples).

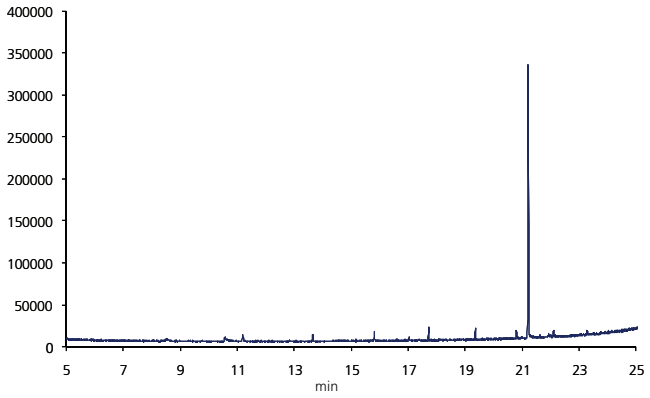
For an up to date list of published MEPS applications visit **www.sge.com/products/meps**

Mighty MEPS Custom Programmed Method

Mighty MEPS Example Method - Caffeine Extraction from Saliva

Step	Mode	Amount (µL)	Speed
Methanol Conditioning			
1	Aspirate	20	4 (20 µL/sec)
2	Dispense	20	4
3	Aspirate	20	4
4	Dispense	20	4
5	Aspirate	20	4
6	Dispense	20	4
H_2O Equilibration			
7	Aspirate	20	4
8	Dispense	20	4
9	Aspirate	20	4
10	Dispense	20	4
11	Aspirate	20	4
12	Dispense	20	4
Sample Bind			
13	Aspirate	50	4
14	Dispense	50	4
15	Aspirate	50	4
16	Dispense	50	4
17	Select Mix x8	50	4
H_2O Wash			
18	Aspirate	20	4
19	Dispense	20	4
Saturated sodium tetraborate			
20	Aspirate	20	4
21	Dispense	20	4
H_2O Wash			
22	Aspirate	20	4
23	Dispense	20	4
Air Dry			
24	Aspirate	50	4
25	Dispense	50	10 (83 µL/sec)
26	Aspirate	50	4
27	Dispense	50	10
28	Aspirate	50	4
29	Dispense	50	10
Methanol Elute			
30	Aspirate	20	4
31	Dispense	20	4
32	Aspirate	20	4
33	Dispense	20	4

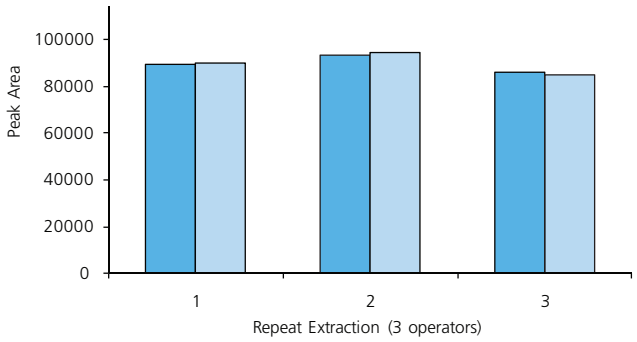
Caffeine in Saliva Mighty MEPS C18 Extraction



Caffeine extraction using Mighty MEPS method:

- 100 µL eVol MEPS syringe
- C18 MEPS BIN
- 8 separate prompted functions
- 33 steps
- Total time: ~ 3 minutes

Interoperator Repeatability



Three different operators, two independent extractions, same day, same MEPS cartridge.

6 injections = 4.17 % RSD*

** auto injector repeatability on 6 standard injections = 2.94 % RSD*

Comparing MEPS

Accuracy and Precision

The precision and accuracy results obtained analyzing Ropivacaine by four sample preparation methods: MEPS , Liquid-Liquid Extraction (LLE), conventional SPE and Solid Phase Microextraction (SPME) are shown in Table 1. MEPS demonstrates improved precision and accuracy while taking significantly less time than SPME to process each sample.

The accuracy, precision, limits of detection and extraction time of MEPS with two other µSPE techniques, SPME and SBSE are compared in Table 2. The results from the MEPS and SBSE techniques are significantly better than SPME but MEPS processes each sample 100 times faster than SBSE.

Table 1: Comparison of accuracy and precision between MEPS and other methods for ropivacaine (local anesthetics)

Method	Ropivacaine LOD (nM)	Accuracy (%) Inter-assay)	Precision (RSD%)	Handling Time
([1] MEPS / GC-MS	2	105	5.0	1 min
[2] LLE / GC-MS	2	101	3.8	20 min
[3] SPE / LC-UV	100	101	3.0	20 min
[4] SPME / GC-MS	5	110	6.3	40 min

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Table 2 : Comparison of accuracy and precision of MEPS , SPME and SBSE for the analysis of PAH's in water.

Compound	Accuracy (%)		
	MEPS	SPME	SBSE
Anthracene	**84**	81	99
Chrysene	**107**	81	100
Fluoranthene	**100**	84	100
Fluorene	**103**	96	97
Pyrene	**115**	86	100

Compound	Precision (RSD%)		
	MEPS	SPME	SBSE
Anthracene	**12**	3	6
Chrysene	**1**	4	5
Fluoranthene	**9**	4	4
Fluorene	**5**	5	4
Pyrene	**7**	3	3

Compound	Limit of detection (ng/L)		
	MEPS	SPME	SBSE
Anthracene	**5**	100	1.2
Chrysene	**5**	90	0.2
Fluoranthene	**5**	100	1.2
Fluorene	**1**	40	0.7
Pyrene	**1**	40	0.7

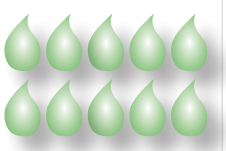
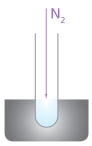
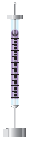
Compound	Extraction time (min)		
	MEPS	SPME	SBSE
Anthracene	**2**	30	200
Chrysene	**2**	30	200
Fluoranthene	**2**	30	200
Fluorene	**2**	30	200
Pyrene	**2**	30	200

M. Abdel-Rehim / J. Chromatog. A 1114 (2006) 234-238

MEPS Extraction Comparison of LLE and SPE with MEPS

Description	Liq-Liq Extraction	Liq-Solid Extraction	MEPS Extraction
Concentration of sample	5 ng/mL	5 ng/mL	5 ng/mL
Extraction volume	1000 mL	20 mL	1 mL
Volume of solvent used	150 mL DCM	3 mL DCM	0.04 mL DCM
Concentration in solvent	33.33 ng/mL	33.33 ng/mL	125.00 ng/mL
Final volume of extract	1 conc vol (mL)	0.2 conc vol (mL)	NO CONCENTRATION STEP REQUIRED
Concentration in final volume	5000 ng/mL	500 ng/mL	
Injection volume	1 µL inj	2 µL inj	2 µL inj
Concentration of injection volume	5 ng per µL	0.5 ng per µL	0.125 ng per µL
Concentration injection on column	5 ng	1 ng	0.25 ng
Approx. time to prepare	Extraction to injection ~2-3 hours	Extraction to injection ~40-60 min	Extraction to injection ~5-10 min
Approx. volume of waste generated	Waste Generated ~1+ Liter	Waste Generated ~50 mL	Waste Generated <2 mL

Comparison Table SPE versus MEPS

	Sample Volume	Time	Price	Solvents	Evaporation Step
SPE					
MEPS					

Devices used for SPE are traditionally considered to be single use. The precision engineering used in the design and manufacture of MEPS allows for simple wash steps and consequently the re-use of the device. To demonstrate this, phenols were extracted from waste water and the carryover measured between experiments.

The chromatograms for the three 10 µL extractions are shown in Figure 4. Clearly all of the phenols were eluted in the first 10 µL of Methanol used.

One of the most often stated reasons for the use of disposable SPE BINS is the issue of carryover. Results from five studies are summarized in Table 3. With a series of washes, carryover was virtually eliminated. With a cycle time measured in seconds for MEPS this washing takes less than five minutes. To accomplish the same for conventional SPE takes an hour or more and uses significant quantities of solvents.

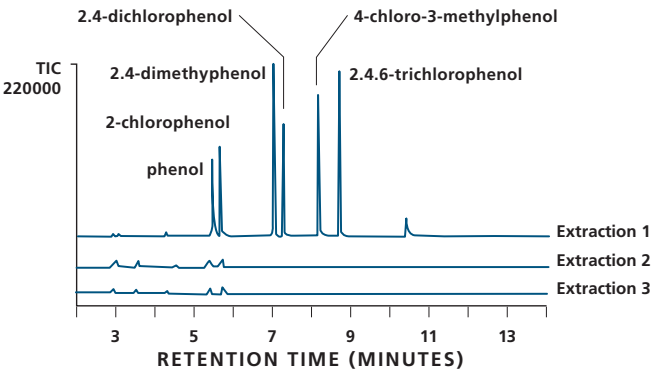


Figure 4
Phenols at 25 ppb in alkane contaminated water. 10 x 100 µL cycles on C18 MEPS BIN (conditioned with methanol and water). Sample was eluted with methanol 10 µL, 2 µL injected onto a BPX5 column and analyzed by GC-MS.

Summary

Table 4 summarizes the comparison of MEPS, SPME and conventional SPE. MEPS requires much less time than either SPE or SPME, and shows much better recovery and sensitivity than SPME. MEPS also eliminates any intermediate steps between the sample preparation steps and the injection into a GC or LC system.

Table 3 : Comparison of carryover and wash regime.

	Wash Volume (uL)	# of Washes and Wash Solution	Carry-over	Source
PAHs in water	50 µL	4x methanol, 5x water	0.2% - 1%	M. Abdel-Rehim / J. Chromatog. A 1114 (2006) 234-238
Anesthetics in human serum	50 µL	4x methanol, 4x water	~ 0.2% (I.S.)	M. Abdel-Rehim / J. of Chromatography B, 801 (2004) 317-321
Roscovitine in plasma and urine	50 µL	5x methanol/water (95:5, v/v) 5x water/methanol (90:10, v/v)	<0.1%	M. Abdel-Rehim / J. of Chromatography B, 817 (2005) 303-307
Roscovitine in human plasma	50 µL	4x methanol, 4x water	<0.01%	M. Abdel-Rehim / J. Mass Spectrom. 204; 39: 1488-1493
Olomoucine in human plasma	50 µL	5x methanol/water (95:5, v/v) 5x water/methanol (90:10, v/v)	<0.1%	M. Abdel-Rehim et al. / Analytica Chimica Acta 2005

Table 4 : Comparison of MEPS BINs, SPME and conventional SPE.

Factor	MEPS BIN	SPE	SPME
Amount sorbent	0.5-2 mg	50-2000 mg	thickness 150 mm
Sample prep. time	1-2 min	10-15 min	10-40 min
BIN use	40 to 100 extractions	Once	50-70 extractions
Recoveries	Good	Good	Low
Sensitivity	Good	Good	Low

M. Abdel-Rehim / J. of Chromatography B, 801 (2004) 317-321

MEPS BIN Assembly Options for LC and GC Use

Phase	# per Pack	LC Needle Part No.	GC Needle Part No.
Agilent 7693A - syringe P/N 005292 and 006293			
C18	5	–	2900601
Silica	5	–	2900602
C8+SCX*	5	–	2900603
C2	5	–	2900604
C8	5	–	2900606
MEPS Development Kit (contains 1 each of C18, C8, C2, Silica and C8+SCX)	1	–	2900605
Thermo Scientific, HTA 300A Plus & Varian 8400 systems - syringe P/N 005291 and 006291			
C18	5	2900401	2900101
Silica	5	2900402	2900102
C8+SCX*	5	2900403	2900103
C2	5	2900404	2900104
C8	5	2900406	2900106
SCX	5	2900408	–
SAX	5	2900409	–
MEPS Development Kit (contains 1 each of C18, C8, C2, Silica and C8+SCX)	1	2900405	2900105
CTC Analytics systems - syringe P/N 005291 and 006291			
C18	5	2900501	2900301
Silica	5	2900502	2900302
C8+SCX*	5	2900503	2900303
C2	5	2900504	2900304
C8	5	2900506	2900306
SCX	5	2900508	–
SAX	5	2900509	–
MEPS Development Kit (contains 1 each of C18, C8, C2, Silica and C8+SCX)	1	2900505	2900305

Base material is silica with mean particle size of 45 µm and pore size of 60Å.
**C8+SCX BINS are labelled as M1.*

For LC applications, needle is 22 gauge, 0.72 mm OD, dome point style. For GC applications, needle is 23 gauge, 0.63 mm OD, cone point style.

For an up to date list of published MEPS methods visit **www.sge.com/products/MEPS**

Mighty MEPS

1. Choose your eVol XR - Electronic Syringe

Description	Part No.
eVol XR Electronic Syringe Starter Kit Contains: • eVol XR Electronic Syringe • 3 eVol XR Syringes – 5 µL, 100 µL and 1 mL. • Stand. • Universal Charger. • Comprehensive Instruction Manual. • Disc with Manual in Multiple Languages.	2910200
eVol XR Electronic Syringe	2910205

2. Choose your eVol MEPS Syringe by Volume

Description	Replacement Plunger Part No.	# per Pack	Syringe Part No.
50 µL for MEPS applications*	2910382	1	2910027
100 µL for MEPS applications*	2910383	1	2910028
500 µL for MEPS applications*	2910384	1	2910026

** The 50 µL, 100 µL and 500 µL eVol MEPS syringes can be used with the range of MEPS BINs.*

3. Choose your eVol MEPS BINs by Phase

Phase	LC Needle Part No.	GC Needle Part No.
C18	2900701	2900711
C8	2900702	2900712
C2	2900707	2900717
APS - amino-propyl silane	2900703	2900713
DVB - hydrophobic polystyrene-divinylbenzene copolymer	2900705	2900715
SDVB - styrene-divinylbenzene	2900706	2900716

All LC needles are 55.5 mm in length, 22 gauge and dome tipped. All GC needles are 55.5 mm in length, 23 gauge and cone tipped. All packs contain 5 MEPS BINs and can be used with 50, 100 and 500 µL eVol MEPS syringes.

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