Electromembrane extraction of nonpolar acidic analytes from human plasma

Generic method A1

Intended use

Generic method A1 is recommended for nonpolar monoacidic compounds with 1.8<log P<6.0.
A1 is described below for extraction of small molecule pharmaceuticals from human plasma and serum samples. For other types of substances, and other type of samples or sample volumes, modification of A1 conditions may be required.

Chemicals and solutions

- Dodecyl methyl sulfoxide (DDMS)
- Thymol
- 50 mM Phosphate buffer (pH 7.4)
- 50 mM Ammonium bicarbonate buffer (pH 10.0)

Consumables

- Conductive vials, 200 or 600 µL
- PP2E support membrane
- Support membrane union

Procedure

1. Before extraction

- Load sample solution
  - For 200 µL conductive sample vials: transfer 60 µL plasma sample and 60 µL of 50 mM phosphate buffer pH 7.4 (sample diluent) into the sample vial
  - For 600 µL conductive sample vials: transfer 125 µL plasma sample and 125 µL of 50 mM phosphate buffer pH 7.4 (sample diluent) into the sample vial
- Load acceptor solution
  - For 200 µL conductive acceptor vials: transfer 120 µL of 50 mM NH4HCO3 buffer pH 10.0 (acceptor) into the acceptor vial
  - For 600 µL conductive acceptor vials: transfer 250 µL of 50 mM NH4HCO3 buffer pH 10.0 (acceptor) into the acceptor vial
- Place a PP2E support membrane in the support membrane union
- Screw the support membrane union to the acceptor vial, with the supported membrane towards the acceptor vial
- Deposit 9 µL of liquid membrane A1 (see “Liquid membranes and solutions for EME”) onto the support membrane. To ensure an accurate volume, wipe the outside of the pipette tip before dispensing.
- Wait for 30 seconds, and then screw the sample vial into the support membrane union. The extraction cell is now ready for extraction.

2. **Extraction**
3. Place the extraction cell in the 12-position holder, such that the sample vial is in contact with the positive electrode (anode) and the acceptor vial is in contact with the negative electrode (cathode)
4. Perform the extraction at 30 V for 30 min with 800 rpm agitation*

3. After extraction

- Collect the acceptor immediately for injection into LC-MS/MS or a related instrumental technique. Leaving the acceptor solution in contact with the liquid membrane may result in back-extraction of analytes by passive diffusion.

** An optimisation of the volume and rpm are usually needed depending on your sample matrix*

Recovery

Recoveries from human plasma obtained with generic method A1 are summarized below.

Compound	log P	Charge	Recovery (%)
1-naphthoic acid	2.62	-1	88.5
3-indoleacetic acid	1.71	-1	65.2
Bezafibrate	3.99	-1	96.9
Bumetanide	2.30	-1	94.4
Chlorpropamide	1.94	-1	96.4
Diclofenac	4.26	-1	93.6
Diflunisal	3.91	-1	88.1
Enalapril	0.59	-1	93.5
Furosemide	1.75	-1	69.1

Compound	log P	Charge	Recovery (%)
Ketoprofen	3.61	-1	93.4
Ketorolac	2.28	-1	69.5
Mefenamic acid	5.40	-1	91.9
Piroxicam	0.39	-1	79.2
Probenecid	2.44	-1	98.3
Salicylic acid	1.98	-1	77.2
Sulindac	2.93	-1	96.2
THC-acid	5.14	-1	87.0
Warfarin	3.16	-1	96.4

Values for log P and charge at sample pH have been calculated using www.chemicalize.com

Notes

A1 is recommended for analyte of 1.8<log P<6.0, A2 as alternative for more hydrophilic analytes. If extraction efficiency is unsatisfactory, consider increasing voltage or extraction time, or investigate higher pH of the sample and acceptor solution (<12). Expected current for A1 is approximately 10 µA per sample.

Documentation

Generic conditions for electromembrane extraction of acids with low to moderate hydrophilicity in human plasma, Chenchen Song, Samira Dowlatshah, Somayeh Gaznawi, Anne Oldeide Hay, Grete Hasvold, Frederik André Hansen, **ChemRxiv.** 2024; doi:10.26434/chemrxiv-2024-mftbp

Ordering information

Conductive vials, 200 µL	201001-1
Conductive vials, 600 µL	201002-1
Support membrane union	201001-2
PP 2E support membrane	201001-3
Transparent vial holder	201001-4

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Extraction Technologies Norway

Extraction Technologies Norway AS was established in 2013 with a mission to develop a completely different, novel and innovative sample preparation method, which should be groundbreaking in terms of simplicity, speed of method and purity of samples. For this purpose and based on our patented technology, we have developed the world's first commercial instrument that uses electromembrane extraction to prepare samples for analysis. With this EME technology charged molecules can be extracted from difficult matrices like e.g. blood or urine in an unprecedented purity, ready for direct analysis.

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