Electromembrane extraction of non-polar basic analytes from human plasma

Generic method B1

Intended use

Generic method B1 is recommended for mono- and dibasic analytes (charge +1 or +2) with 2.0<log P<6.0. B1 is described below for extraction of small molecule pharmaceuticals from human plasma and serum samples. For other types of substances, and other volumes or type of samples, modification of B1 conditions may be required (see Notes).

Chemicals and solutions

- 2-Nitrophenyl octyl ether (NPOE)
- 100 mM Formic acid
- 500 mM Formic acid

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 500 mM formic acid in water (sample diluent) into the sample vial
  - For 600 µL conductive sample vials: transfer 125 µL plasma sample and 125 µL of 500 mM formic acid in water (sample diluent) into the sample vial
- Load acceptor solution
  - For 200 µL conductive acceptor vials: transfer 120 µL of 100 mM formic acid (acceptor) into the acceptor vial
  - For 600 µL conductive acceptor vials: transfer 250 µL of 100 mM formic acid (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 pure 2-nitrophenyl octyl ether (NPOE) 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 of the EME apparatus, 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 100 V for 30 min with 1000 rpm agitation*

3. After extraction

- Collect the acceptor immediately for direct 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 B1 are summarized below.

Compound	log P	Charge	Recovery (%)
Alprenolol	2.69	+1	83
Amitriptyline	4.81	+1	94
Chlorpromazine	4.54	+1	87
Chlorprothixene	5.07	+1	86
Cinnarizine	5.88	+1.7	83
Clomipramine	4.88	+1	91
Clotrimazole	5.84	+1	66
Cocaine	2.28	+1	91
Diltiazem	2.73	+1	91
Doxepin	3.84	+1	92
Droperidol	3.01	+1	93
Fluoxetine	4.17	+1	92
Haloperidol	3.66	+1	90
Hydroxyzine	3.41	+1	98
Lidocaine	2.84	+1	60
Loperamide	4.77	+1	98
Methadone	5.01	+1	95
Mianserin	3.83	+1	90
Nortriptyline	4.43	+1	90
Noscapine	2.58	+1	92
Oxprenolol	2.17	+1	75
Omeprazole	2.43	+1	76

Compound	log P	Charge	Recovery (%)
Papaverine	3.08	+1	90
Perphenazine	3.69	+1.9	76
Pethidine	2.46	+1	95
Pimozide	5.83	+1	80
Prochlorperazine	4.38	+2	90
Promazine	3.93	+1	93
Promethazine	4.29	+1	92
Propranolol	2.58	+1	85
Pyrilamine	3.04	+2	81
Quinine	2.51	+2	55
Raloxifene	5.47	+2	86
Reserpine	3.53	+1	98
Telmisartan	6.13	+1.9	77
Thioridazine	5.47	+1	87
Trimipramine	4.76	+1	94
Venlafaxine	2.74	+1	83
Verapamil	5.04	+1	92

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

Notes

NPOE is a very stable liquid membrane, and the current is normally below 5 µA per sample at 50 V. B1 provides high recovery for most analytes within 2.0<log P<6.0, but may even be efficient for some analytes outside this range.

Documentation

Generic Liquid Membranes for Electromembrane Extraction of Bases with Low or Moderate Hydrophilicity, Chen Zhou, Samira Dowlatshah, Anne Oldeide Hay, Maria Schüller, Stig Pedersen-Bjergaard, Frederik André Hansen, **Analytical Chemistry** 95 (2023) 8982-8989

Optimization of generic conditions for electromembrane extraction of basic substances of moderate or low polarity, Chenchen Song, Chen Zhou, Frederik André Hansen, Anne Oldeide Hay, Stig Pedersen-Bjergaard, **Journal of Separation Science** 47 (2024) 2300801

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

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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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