

## Pharmacology 2018: Electro membrane extraction combined with capillary electrophoresis for the determination of metoclopramide and ondansetron in urine samples - Ehsan Sadeghi- Shahid Beheshti University

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### Abstract

Electro membrane extraction (EME) was inspired by solid-phase microextraction and developed from hollow fiber liquid-phase microextraction in 2006 by applying an electrical field over the supported liquid membrane (SLM). EME provides rapid extraction, efficient sample clean-up and selectivity supported the character of the SLM and therefore the electrical field. EME has been applied for the separation of ionizable compounds from complex samples, and EME is currently considered as a lively research topic within the area of sample preparation and analytical chemistry. We expect that EME will play important roles in future analytical laboratories. This review summarizes and highlights the advancements in EME from 2006 to 2016 with focuses on 1) fundamental aspects, 2) device and operation modes, 3) performance, and 4) hyphenation to other analytical sample preparation techniques. Meanwhile, this review indicates that the most objectives for future EME are to determine EME as tool for routine applications, and to stimulate for further research on sophisticated systems based on the EME principle.

The scientific interest for EME is said to many unique conceptual properties. First, extraction selectivity are often manipulated by the direction and magnitude of the electrical field. The direction of the electrical field is controlled by the external power supply, and is employed to tune the extraction system for either cationic or anionic analytes. The magnitude of the electrical field is additionally controlled by the external power supply, and research has demonstrated that extraction selectivity depends on the magnitude of the electrical field [10]. Second, extraction selectivity is controlled by the chemical composition of the SLM. The SLM are often tuned for non-polar analytes, polar analytes, or for highly selective extraction of certain analytes supported molecular recognition and complexation. Third, extraction selectivity is controlled by the pH conditions within the sample and acceptor solution.

Additional advantages of EME include efficient sample clean-up, Due to the non-polar nature of the SLM, many matrix components present in aqueous samples such as biological fluids are unable to pass the SLM, and that they remain within the sample. In addition, anionic species will remain within the

sample during extraction of cationic analytes, and the other way around, thanks to the direction of the electrical field. Acceptor solutions in EME are (in most cases) aqueous; therefore, they can be injected directly into liquid chromatography (HPLC), liquid chromatography–mass spectrometry (LC–MS), and capillary electrophoresis (CE). Thus, there is no need for evaporation of extracts and reconstitution, as is often the case with traditional sample preparation methods. Normally, the volume of sample in EME exceeds the volume of acceptor solution; therefore analytes can be pre-concentrated during the process. In one example, EME from 3.5 mL samples and into 20  $\mu$ L acceptor solution resulted in 74 times the target analyte pre-concentration. Finally, the volume of organic solvent used for the SLM is in the range of 3–15  $\mu$ L, and this represents the total volume of organic solvent required per sample. Thus, EME represents a green chemistry approach to analytical sample preparation

### Highlights

- Advances on the device and operation modes in electro membrane extraction are emphasized.
- Selective, exhaustive and soft extractions using electro membrane extraction are summarized.
- Hyphenation of electro membrane extraction to other sample preparation technique is reviewed.
- Electrolysis, stability, and mass transfer in electro membrane extraction are discussed.
- The main objectives for future electro membrane extraction are identified.

Capillary electrophoresis (CE) may be a separation technique that separates molecules in an electrical field consistent with size and charge. CE is performed during a small glass tube called a capillary that's crammed with an electrolyte solution. Analytes are separated due to differences in electrophoretic mobility, which varies with charge, solvent viscosity, and size. Traditional electrophoresis in gels is restricted within the amount of voltage which will be applied because Joule heating effects will ruin the gel and therefore the separation. Capillaries have a large surface area-to-volume ratio and thus

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dissipate heat better. Therefore, the voltages applied for a capillary electrophoresis experiment are quite large, often 10,000–20,000 V.

Capillary electrophoresis is useful for high-performance separations. Compared to liquid chromatography, CE separations are often faster and more efficient. However, capillary electrophoresis works best to separate charged molecules, which isn't a limitation of liquid chromatography. CE features a greater peak capacity than high-performance liquid chromatography (HPLC), meaning the separations are more efficient and more peaks are often detected. The instrumentation can be very simple. However, HPLC is more versatile and many stationary and mobile phases have been developed for different types of molecules.

Electro membrane extraction (EME) is a sample preparation technique in pharmaceutical, chemical, clinical and environmental analysis. This technique uses electromigration across artificial liquid membranes for selective extraction of analytes and sample enrichment from complex matrices. This method has many advantages such as simplicity, rapid, low-cost, low LOD, high preconcentration factor and high recovery.

In the present work, simultaneous preconcentration and determination of two basic drugs namely metoclopramide (MCP) and ondansetron (OSN) were studied using EME as a suitable extraction method, followed with capillary electrophoresis (CE) using ultraviolet (UV) detection as separation technique. The drugs were extracted from 4 ml sample solutions, through a supported liquid membrane (SLM) consisting 2-nitrophenyloctylether (NPOE) impregnated in the walls of a polypropylene hollow fiber, and into a 20  $\mu$ L acidic aqueous acceptor solution present inside the lumen of the hollow fiber with a potential difference applied over the SLM. The variables of interest, such as chemical composition of the organic liquid membrane, stirring speed, extraction time and voltage, pH of donor and acceptor phases and salt effect in the EME process were investigated and optimized. Under optimal conditions NPOE as SLM, stirring rate of 1000 rpm, 200 V potential differences, 20 min as the extraction time, acceptor phase HCl (pH 1.0) and donor phase HCl (pH 1.5).

After the microextraction process, the extracts were analyzed by CE with optimum conditions phosphate running buffer (pH 2.0), applied voltage of 20 kV and 25°C. Under the optimum conditions, limits of detection (LOD) and quantification (LOQ) for MCP and OSN were 2.31-2.68 and 7.72-8.91 ng mL<sup>-1</sup> respectively. Preconcentration factor and RSD for five replicates of each drugs were calculated to be 200

and 4.06-3.93 respectively. Finally, the applicability of this method was studied by the extraction and determination of these drugs in urine samples with recovery percentages of 87–92%.

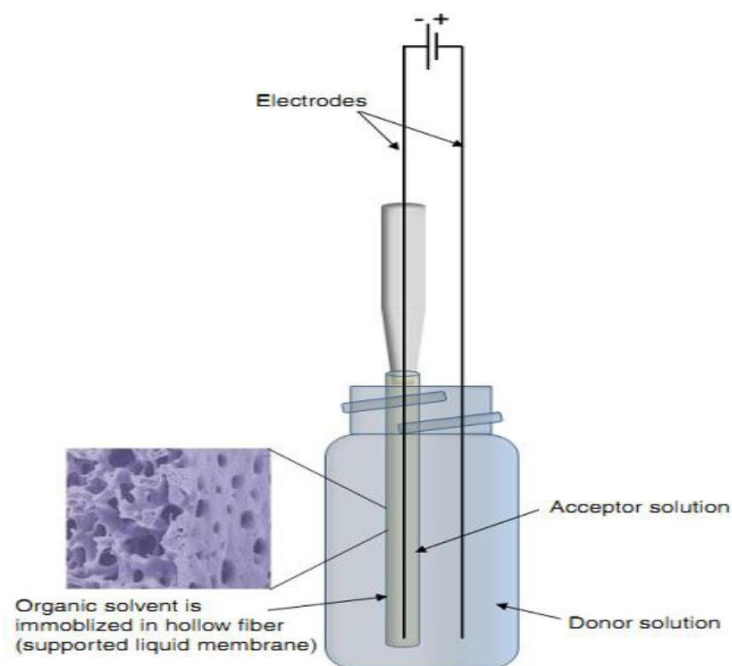


Figure 1. Schematic illustration of the electromembrane extraction (EME) set-up.

#### Recent Publications

1. Tabani, H., Fakhari, A.R. and Shahsavani, A., 2013. Simultaneous determination of acidic and basic drugs using dual hollow fibre electromembrane extraction combined with CE. *Electrophoresis*, 34(2), pp.269-276.
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3. Middelthon-Bruer, T.M., Gjelstad, A., Rasmussen, K.E. and Pedersen-Bjergaard, S., 2008. Parameters affecting electro membrane extraction of basic drugs. *Journal of separation science*, 31(4), pp.753-759.
4. Nojavan, S. and Fakhari, A.R., 2010. Electromembrane extraction combined with capillary electrophoresis for the determination of amlodipine enantiomers in biological samples. *Journal of separation science*, 33(20), pp.3231-3238.
5. Kjelsen, I.J.Ø., Gjelstad, A., Rasmussen, K.E. and Pedersen-Bjergaard, S., 2008. Low-voltage electromembrane extraction of basic drugs from biological samples. *Journal of Chromatography A*, 1180(1), pp.1-9.
6. Rezazadeh, M., Yamini, Y. and Seidi, S., 2011. Electromembrane extraction of trace amounts of

naltrexone and nalmeferne from untreated biological fluids. *Journal of Chromatography B*, 879(15), pp.1143-1148.

7. Kiplagat, I.K., Doan, T.K.O., Kubáň, P. and Boček, P., 2011. Trace determination of perchlorate using electromembrane extraction and capillary electrophoresis with capacitively coupled contactless conductivity detection. *Electrophoresis*, 32(21), pp.3008-3015.

### Biography

He received the B.S. degree in applied chemistry from Khajeh Nasir Toosi University of Technology and was started analytical chemistry at Shahid Beheshti University under the guidance of

prof. Alireza Fakhari in 2015. The Fields of research in prof. Fakhari's lab include sample preparation, enantioseparation, microextraction, electrochemistry, capillary electrophoresis and chromatography. Ehsan has experiences in the field of several extraction and purification techniques such as electromembrane extraction, Headspace solid-phase and dispersive liquid-liquid microextraction in real samples such as urine and plasma and waste water. His current research interests include evaluation and separation of achiral and chiral drug by variety chiral selector such as cyclodextrin, maltodextrin, antibiotic compounds and so on as additive to background electrolyte in CE-based analysis.