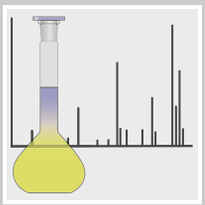
doi:10.2533/chimia.2013.665



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Non-aqueous Capillary Electrophoresis for the Analysis of Pharmaceutical Acidic Compounds Using Negative ESI-MS

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Keywords: Capillary electrophoresis · CE-MS · NACE · Negative ESI · Sheathless interface · Sheath liquid interface

Non-aqueous capillary electrophoresis (NACE) is an attractive capillary electrophoresis (CE) mode in which the conventional aqueous background electrolyte (BGE) is replaced by organic solvents. This substitution modifies several physicochemical properties (pK_a, dielectric constant, viscosity, zeta potential, and conductivity) resulting in a modification and often an improvement of the CE separation performance. NACE is particularly well adapted to mass spectrometry (MS) detection due to the high volatility of solvents that improves the formation of easily evaporable droplets with the electrospray ionization (ESI) source, increasing ionization efficiency while ensuring a stable spray.

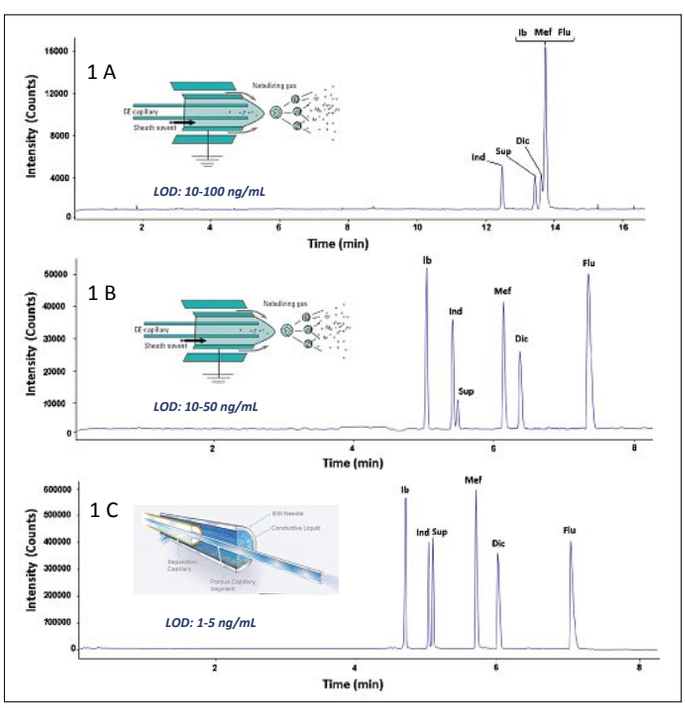

Fig. 1. CE-MS separation of non-steroidal anti-inflammatory drugs with aqueous electrolyte and sheath liquid interface (A), with organic electrolyte and sheath liquid interface (B), and with organic electrolyte and sheathless interface (C).

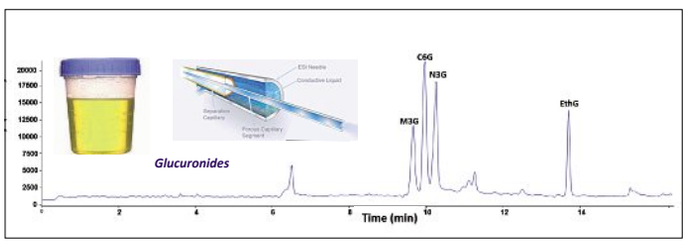

Fig. 2. CE-MS separation of four glucuronides in diluted urine with organic electrolyte and sheathless interface.

We studied the use of NACE coupled to negative ESI-MS for the analysis of acidic compounds with two CE-MS interfaces (sheath liquid and sheathless). First, the NACE mode was compared to the aqueous CE mode for the analysis of non-steroidal anti-inflammatory drugs (NSAIDs) that represent an important pharmacological class commonly used for their analgesic and antipyretic properties. As shown in Fig. 1A, the NSAIDs were not separated when an aqueous BGE was used, whereas an organic BGE (acetonitrile, methanol and ammonium acetate) allowed a complete separation (Fig. 1B) and led to a 1–10-fold improvement of the detection sensitivity. Separation performance as well as detection limit could be further improved using the sheathless interface without modifying the BGE composition (Fig. 1C).

These results indicate that the NACE-ESI-MS method could be considered an attractive tool for the analysis of very polar phase II metabolites such as glucuronides. The latter are infrequently analyzed using aqueous BGE due to their amphoteric properties. Additionally, glucuronides are present at low concentrations in urine (ng/mL range); therefore, NACE-ESI-MS with the sheathless interface could provide the benefit of increased sensitivity, particularly when a minimal sample preparation such as simple urine dilution is used. As presented on the Fig. 2, a complete separation of four glucuronides was achieved using a sheathless interface. Concentration limits down to 500 ng/mL in urine (corresponding to 25 ng/mL injected concentration) were obtained without the presence of any significant matrix effect, while a simple and rapid sample pre-treatment (dilution 1:20 with the BGE) was applied.

NACE is an interesting alternative to the CE aqueous mode, especially because of the improved selectivity, sensitivity, and spray stability when used in combination with ESI-MS.

Received: July 1, 2014

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