Use of CE-C4D for quality control of pharmaceutical formulations produced in hospital pharmacy

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Introduction
Pharmaceutical formulations produced in hospital pharmacy are submitted to a quality control before patient administration. Capillary electrophoresis (CE) appears to be a technique of choice to quantify drugs present in preparations due to its high efficiency, low solvent consumption and rapid method development. Capacitively coupled contactless conductivity detection (C4D) is an attractive alternative to optical detection techniques in CE for the analysis of inorganic ions or organic molecules without chromophore groups. In our laboratory, two simple CE-C4D methods were developed for the quantitative determination of suxamethonium (SUX) in an intravenous formulation and for inorganic cations (K, Na, Mg and Ca) in total parenteral nutrition.

Methods
HP3DCE system (Agilent Technologies, Germany) & TraceDec detector (Innovative Sensor Technologies GmbH, Austria)

Suxamethonium analysis

Experimental conditions
BGE: 100 mM Tris-acetate at pH 4.2: acetonitrile (90:10, v/v)
Temp.: 25°C
Injection: 40 mbar for 10s
Voltage: 30 kV
Capillary: 50 µm i.d., 375 µm o.d.
C4D: output frequency: 75 kHz, output voltage: 80 Vpp

Analysis of a sample containing SUX (0.2 mg.mL−1), choline (0.2 mg.mL−1) and K (internal standard, 0.02 mg.mL−1) in an aqueous solution (in presence of Na 0.07 mg.mL−1).

Degradation products:
A complete separation (Rs > 1.5) between suxamethonium, Na and its degradation products (choline, succinic acid and succinylmonocholine) was achieved. tR succinic acid > tR EOF and tR succinylmonocholine > 4 min.

Validation results
Quantitative performance was estimated by 3 series with 2 calibration standards at 1 level and 4 validation standards at all concentration levels: for Na and K: 1-4 mM and for Ca and Mg: 0.5-2 mM. 3 series with 2 calibration standards at 1 level and 4 validation standards at all concentration levels.

Applications
• For the stability study and quality control of intravenous solutions of SUX produced by the HUG pharmacy
• For a stability study of succinylmonocholine in commercially available pharmaceutical products (Lysthenon®, Succinomil®)

Inorganic ions analysis

Experimental conditions
BGE: 100 mM Tris-acetate at pH 4.5: acetonitrile (80:20, v/v)
Temp.: 25°C
Injection: 40 mbar for 10s
Voltage: 30 kV
Capillary: 50 µm i.d., 375 µm o.d.
C4D: output frequency: 150 kHz, output voltage: 40 Vpp

Analysis of a sample containing Na, K (2 mM), Ca, Mg (1 mM) and lithium (internal standard, 1.25 mM) in an aqueous solution.

Validation results
For each ion, the method was validated to cover the range of usually measured concentrations: for Na and K: 1-4 mM and for Ca and Mg: 0.5-2 mM. 3 series with 2 calibration standards at 1 level and 4 validation standards at all concentration levels.

Applications
• For the quality control of total parenteral nutrition produced by the HUG pharmacy

Conclusion
The CE-C4D methods were found suitable for the quantification of suxamethonium and the four inorganic cations in pharmaceutical formulations and they were successfully applied in routine analyses at the pharmacy of Geneva University Hospitals.

References