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

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Introduction

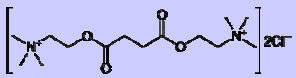
Pharmaceutical formulations produced in hospital pharmacy are submitted to a quality control before patient administration.

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 (C^4D) 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-C^4D methods were developed for the quantitative determination of suxamethonium (SUX) in an intravenous formulation[1] and for inorganic cations (K, Na, Mg and Ca) in total parenteral nutrition.

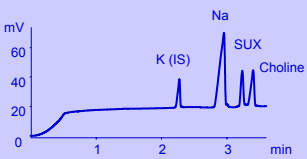
Methods: HP3DCE system (Agilent Technologies, Germany) & TraceDec detector (Innovative Sensor Technologies GmbH, Austria)

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.
total length: 64.5 cm, effective length: 50 cm
C^4D: 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}).

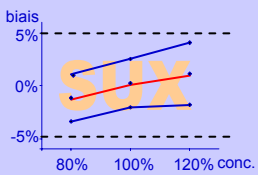
Degradation products:

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

Validation results

Quantitative performance was estimated by 3 series with 2 calibration standards and 4 validation standards at 3 concentration levels: 80, 100 and 120% of the target value (0.2 mg.mL^{-1}) according to STP PHARMA Pratiques [2].

Concentration level	Trueness	Repeatability	Intermediate precision
80%	98.8%	1.1%	1.2%
100%	100.2%	1.3%	1.3%
120%	101.1%	0.6%	1.6%



As shown in the accuracy profile the total error did not exceed 5% for all concentration levels.

Applications

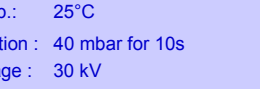
- For the stability study and quality control of an intravenous solution of suxamethonium at 10 mg.mL^{-1} produced by the HUG pharmacy
- For a stability study of suxamethonium in commercially available pharmaceutical products (Lysthenon®, Succinolin®).

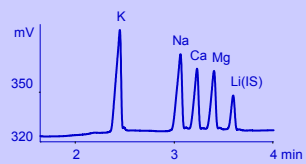
Inorganic ions analysis

Experimental conditions

11 23 Na sodium	19 39 K potassium	20 40 Ca calcium	12 24 Mg magnesium

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.
total length: 64.5 cm, effective length: 50 cm
C^4D: output frequency: 150 kHz, output voltage: 40 Vpp

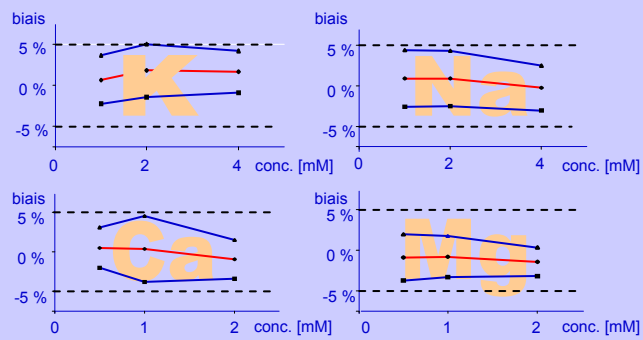




Analysis of a sample containing Na, K (2 mM), Ca, Mg (1 mM) and lithium (internal standard, 1.25 mM) in an aqueous solution.

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 [2].



As shown in the accuracy profile the total error did not exceed 5% in the tested concentration range for each cation.

Applications

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

Conclusion

The CE-C^4D 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.

(1) Nussbaumer, S., Fleury-Souverain, S., Bonnabry, P., Rudaz, S., Veuthey, J.-L., Journal of Pharmaceutical and Biomedical Analysis 49 (2009) 333-337.
(2) Hubert, P., Nguyen-Huu, J. J., Boulanger, B., Chapuzet, E., et al., STP PHARMA PRATIQUES (2003), 13, 101-138.