Analytical validation of a cation assay in binary parenteral nutrition with capillary electrophoresis.

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INTRODUCTION:

Individualized binary parenteral nutritions (PN) are daily compounded in our pharmacy for extremely preterm babies. Control process include determination of cations concentration by enzymatic method in the biochemistry laboratory. Several issues have been identified: Na^+ detection limit of 20mM and a lower quality control of 80mM while the majority of the binary mixtures compounded have a theoretical Na^+ concentration between 15 and 40mM. Moreover an interaction between calcium (Ca^{2+}) and magnesium (Mg^{2+}) leads to an overestimation of the Mg^{2+} concentration particularly during high amont of Ca^{2+} *(Chouaou et al. GERPAC 2020).* The objective is to study the feasibility and carry out the validation of a method to dose cations in binary mixtures of parenteral nutrition by capillary electrophoresis according to ICH Q2 (R1) criteria.

MATERIAL AND METHOD:

Performance criteria: linearity, repeatability, intermediate precision, accuracy, lower quantitation limit and matrix effect

- Linearity : 5 concentrations chosen according to the concentrations of ions most frequently found in the mixtures prepared in the unit and taking into account a 1/200 dilution, dosages repeated 3 times in a row
- Repeatability : 3 quality control, dosages repeated 6 times in a row by concentration and by ion
- Intermediate precision : 3 concentrations, dosages repeated 6 times in a row

Calculations: regression coefficient (R^2), mean, standard deviation, coefficient of variation (CV), bias.

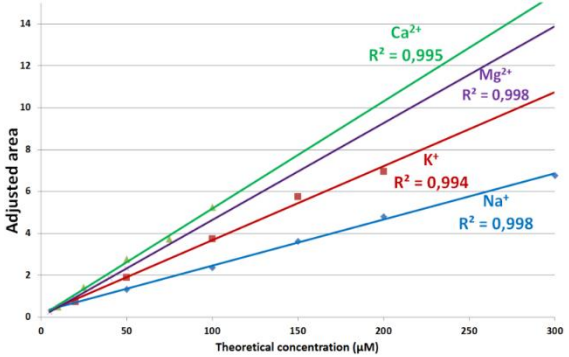
Analysis parameters:

Contactless Conductivity Detector *(C4D)*
Fused silica capillary (conditioned by NaOH)
Buffer solution : Acetic acid /Histidin pH 4,1
Analysis time : 3 minutes
Flushing time : 3 minutes

RESULTS :

Linearity

Adjusted area as a function of ion concentration



Repeatability

Na^+	75 µM	125 µM	250 µM
Mean	74.6	121.8	246.8
CV(%)	2.4	1.7	1.9

K^+	40 µM	75 µM	125 µM
Mean	39.6	74.5	123.6
CV(%)	1.9	1.0	1.3

Ca^{2+}	15 µM	40 µM	90 µM
Mean	15.0	39.7	88.7
CV(%)	3.1	4.4	0.7

Mg^{2+}	15 µM	25 µM	45 µM
Mean	15.5	25.1	44.9
CV(%)	3.9	2.0	1.4

Intermediate precision

Na^+	75 µM	125 µM	250 µM
Mean	74.8	126.6	249.4
CV(%)	2.3	1.3	1.4
Bias (%)	-0.3	1.3	-0.2

K^+	40 µM	75 µM	125 µM
Mean	39.6	74.1	123.1
CV(%)	3.9	2.3	2.6
Bias (%)	-1.0	-1.2	-1.5

Ca^{2+}	15 µM	40 µM	90 µM
Mean	15.1	40.9	91.3
CV(%)	4.3	3.1	4.7
Bias (%)	0.3	2.3	1.4

Mg^{2+}	15 µM	25 µM	45 µM
Mean	15.1	24.8	44.8
CV(%)	2.0	3.5	2.3
Bias (%)	0.4	-0.8	-0.4

Lower quantitation limit:

	Na^+	K^+	Ca^{2+}	Mg^{2+}
Concentration	10 µM	10 µM	5 µM	5 µM
CV (%)	3.8	7.1	8.1	12.6
Bias (%)	8.7	4.1	-5.3	-5.6

Lowest concentration of linearity study, CV<20% and bias<20%

Matrix effect :

We did not highlight any matrix effect after comparing the results of a sample of NP100 (binary mixture) and a control sample

CONCLUSION:

These results allowed us to validate the assay method with a concentration range adapted to our problem. Considering the analysis time of a sample is comparable between the two techniques, it will allow us to overcome the problems encountered with the enzymatic technique. Thus, this technique, adapted to the specific problem of NP, allows us to improve the security of our circuit at the control step.