Short communication

Selectivity coefficients of ion-selective magnesium electrodes used for simultaneous determination of magnesium and calcium ions

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A B S T R A C T

Membrane ion-selective magnesium electrodes are commonly used to determine ionized magnesium concentration in blood serum and intracellular fluid by potentiometric clinical analyzers. The selectivity of these electrodes against calcium ion is typically insufficient to avoid calcium interference in blood serum analysis. For this reason the selectivity coefficient for calcium ion has to be studied to make possible any mathematical corrections for calcium ion influence. Existing methods relate to the thermodynamic concept of ISE response which suggest a single constant value of the selectivity coefficient and slope that are stable over the concentration ranges of calcium and magnesium ions in the samples. Unfortunately, this rarely happens, and we rather observe dependences on solution and membrane composition, readout time, matrices (anticoagulant, vial coats) that justify usage of apparent selectivities and slopes. To get the practical insight into the response of magnesium ion-selective electrodes a novel method for estimating the selectivity coefficients and the slope of the electrode characteristics is proposed. This method is an effective starting point for selecting electrodes and designing transient signal software in a potentiometric clinical analyzer. The method allows obtaining the ionized magnesium concentration in blood serum with minimal possible error by addressing the assessed targets, i.e. apparent selectivity and slope. The method is based on computer simulation and on the Nicolsky–Eisenman equation. Usually only a few iterations are needed to obtain stable congruent results. The method presented is particularly useful in conditions where is not possible to obtain calibration curve, which is typical for clinical analyzer where at most three point calibration is performed.

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1. Introduction

The selectivity coefficients of ion-selective electrodes are determined in several ways [1–5]. The simplest and fastest method is based on measurements of the ion-selective electrode potential in separate solutions of $0.1\,mol\,L^{-1}$ solutions of the main and the interfering ion (separate solutions method – SSM). Then the selectivity coefficient (K_{ij}^{Pot}) can be calculated from the Nikolsky–Eisenman semiempirical equation:

$$E = \mathrm{const} + \frac{RT}{z_i F} \log(a_i + K_{ij}^{Pot} a_j^{z_i/z_j}) \qquad (1)$$

where a_i and a_j denote activity of the main and interfering ions and z_i and z_j – their charge, respectively. R, F are gas and Faraday constant and T denotes absolute temperature.

A similar but fully empirical equation can be given as:

$$E = \mathrm{const(app)} + S(\mathrm{app}) \log(a_i + K_{ij}^{Pot}(\mathrm{app})a_j^{z_i/z_j}) \qquad (2)$$

where index "app" means apparent.

Another method, called the mixed solution method (MSM), uses the measurements in solutions containing both the main and interfering ions. Usually, the concentration of the interfering ion is constant (fixed interference method FIM) and that of the main ion is changing, which leads to a calibration curve with a plateau caused by the interfering ion. Then K_{ij}^{Pot} is found using the SIMPLEX method (or other analogous) from the Nicolsky–Eisenman equation where "const", slope ($RT/z_i F$) and K_{ij}^{Pot} are the parameters. In the Gadzekpo and Christian method, the selectivity refers to the concentration of interfering ion, which changes by 10% the potentiometric response of the electrode for the main ion. A thorough discussion of these methods is given in the IUPAC recommendation [1]. Bakker [2] proposed measuring the selectivity of the electrodes with plastic ion-selective membranes not containing the main ion. The results obtained were more similar to the thermodynamic values expected from the stability constants of complexes

Table 1
Composition of the calibration solutions (mmol L^{-1}).

Component	STD 1	STD 2	STD 3
NaCl	140.0	120.0	150.0
KCl	4.5	6.0	3.0
CaCl$_2$	1.25	0.75	1.75
MgCl$_2$	0.75	0.50	1.50
TES	5 (pH 7.4)	5 (pH 7.0)	5 (pH 7.8)

of the ions with ionophores used in the membranes. Similar values were obtained when the sample solution with buffered main ion [3] or especially designed electrodes with lowered detection limit [4] were used to determine the selectivity coefficients with SSM. All these methods assumed idealized time-independent selectivity coefficient and slope. For this reason the experimental procedures were recently re-elaborated involving generalized ISE response theory [5].
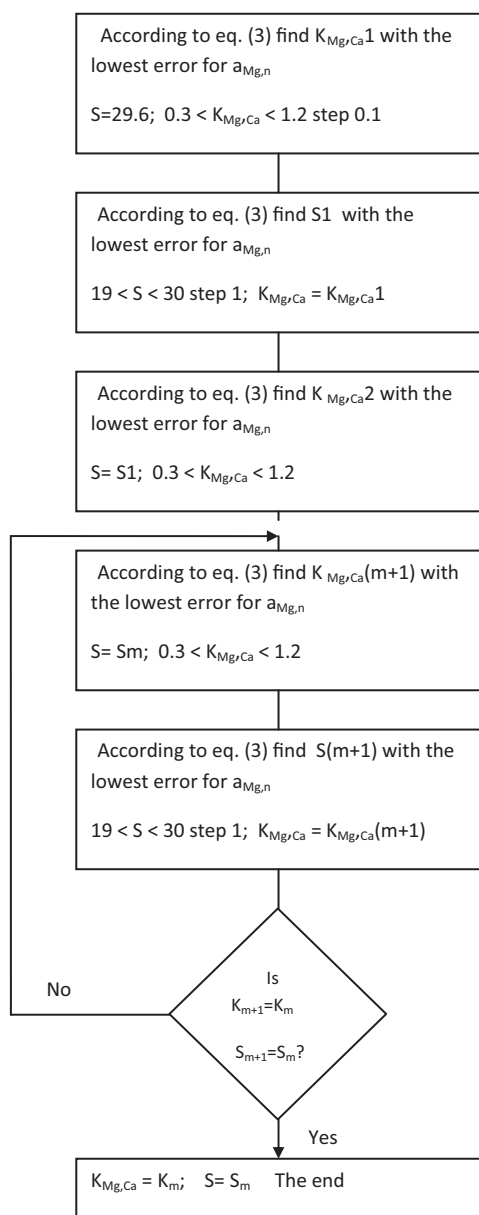
Conventional methods, as introduced by IUPAC, are good enough for comparing various electrodes in the determination of the main ion. However, nowadays there are more and more analyses where the selectivity coefficient value is needed to calculate the activity of the main ion. A good example of such a situation is the determination of lithium and magnesium ions in blood serum. In the case of lithium ion, the influence of sodium could be quantitatively assessed due to a stable and matrix-independent $K_{\text{Li,Na}}$ selectivity coefficient value and independent measurement of sodium [6]. The influence of calcium on magnesium ion-selective electrode was found to be more complex [7]. It was observed that over short readout times the selectivity is time-dependant. More importantly, it was noticed that these time-dependent effects disappear after certain periods of read-out, although not necessarily the same selectivity coefficient and slopes were observed for these readouts over analytical concentration ranges of magnesium and calcium ions. The challenge in this case is to select the electrodes with acceptable apparent selectivities that are able to provide analytical sounded results for magnesium in blood (in the range 0.2–3.0 mmol L^{-1} and CV < 2%) irrespective of possible calcium ionized concentration changes in blood (in the range 0.5–2.5 mmol L^{-1}). This is a background of a method described here which is a way to estimate the apparent selectivity coefficients and the slopes of the electrode characteristics "on fly" in the environment of a real multiparameter clinical analyzer (see Scheme 1).

2. Experimental

The magnesium ion-selective membrane composition was as follows: 1% (w/w) ionophore ETH 5220 synthesized according to [6–8], 70 mol-% to ionophore potassium tetrakis-p-chloroborate (Sigma, Switzerland), 65% (w/w) plasticizer [electrode 1: o-nitrophenylphenyl ether (NPPE)/chloroparaffin (60% Cl) (ClP) = 1 + 1 (vol + vol); electrode 2: o-nitrophenyloctyl ether (NPOE)/ClP = 1 + 1 (vol + vol); electrode 3: NPOE; NPPE was from Kodak, USA; NPOE – from Sigma; ClP – from Scientific Polymer Products, USA], and 33% (w/w) poly(vinyl chloride) (PVC high molecular, Sigma). The membrane was placed in a flow-through electrode body manufactured by Kone Instruments, Finland. Potentiometric measurements were taken at 37 °C in a clinical analyzer

Scheme 1. Flow chart of computer simulation of S(app) and $K_{\text{Mg,Ca}}$(app).

Table 3
The selectivity coefficients and the slopes chosen from simulated curves (±SD), $K_{\text{Mg,Ca}}^{\text{Pot}}$ from SSM and MSM.

Electrode	$K_{\text{Mg,Ca}}^{\text{Pot}}$ (sim.) $n = 24$	S (sim.) mV/dec $n = 24$	$K_{\text{Mg,Ca}}^{\text{Pot}}$ SSM $n = 3$	$K_{\text{Mg,Ca}}^{\text{Pot}}$ MSM $n = 3$
1	0.74 ± 0.10	23.7 ± 2.5	0.66 ± 0.15	0.72 ± 0.20
2	0.89 ± 0.06	24.8 ± 2.3	0.84 ± 0.28	0.89 ± 0.25
3	1.85 ± 0.20	25.5 ± 1.5	0.94 ± 0.38	1.81 ± 0.35

Table 2
Composition of 24 aqueous solutions (mmol L^{-1}) containing cNaCl = 140.0 mmol L^{-1}, cTES = 5 mmol L^{-1}, pH 7.4, and varying concentration of MgCl$_2$ and CaCl$_2$.

cCaCl$_2$	cMgCl$_2$								
	0.50	0.60	0.75	0.90	1.00	1.10	1.25	1.50	
0.75	1	4	7	10	13	16	19	22	Number of
1.25	2	5	8	11	14	17	20	23	solution
1.75	3	6	9	12	15	18	21	24	