Archive ouverte UNIGE
https://archive-ouverte.unige.ch

Article scientifique | Article | 2023 | Published version | Open Access

This is the published version of the publication, made available in accordance with the publisher's policy.

Commercially Available Nitrate Ionophores in Potentiometric Sensors are not Superior to Common Ion-exchangers

Damala, Polyxeni; Zdrachek, Elena; Bakker, Eric

How to cite

DAMALA, Polyxeni, ZDRACHEK, Elena, BAKKER, Eric. Commercially Available Nitrate Ionophores in Potentiometric Sensors are not Superior to Common Ion-exchangers. In: Electroanalysis, 2023, vol. 35, n° 2, p. 1–10. doi: 10.1002/elan.202200247

This publication URL: https://archive-ouverte.unige.ch/unige:180007
Publication DOI: 10.1002/elan.202200247

© The author(s). This work is licensed under a Creative Commons Attribution (CC BY 4.0)
https://creativecommons.org/licenses/by/4.0

Research Article

Wiley Online Library

ELECTROANALYSIS

doi.org/10.1002/elan.202200247

Commercially Available Nitrate Ionophores in Potentiometric Sensors are not Superior to Common Ion-exchangers

Polyxeni Damala,[a] Elena Zdrachek,[a] and Eric Bakker*[a]

Abstract: Nitrate sensing is an important application for potentiometry in environmental applications. Its recognition is by ion-exchangers whose selectivity is governed by the lipophilicity of the ions in solution. Yet, considerable research efforts have been dedicated to the development of such ionophores and some have already been commercialized. This work examines two commercially available nitrate ionophores, nitrate ionophores V and VI, and compares their performance with widely used ion-exchangers by determining the resulting membrane selectivity and complexation to nitrate. Unfortunately, adding a nitrate ionophore to the membrane did not result in improved selectivity. Sandwich membrane experiments indicated that binding interaction is too weak to be measurable, with a logarithmic formation constant of just 1.36±0.14 for ionophore V with nitrate. Ways to improve the reporting of relevant data are suggested.

Keywords: nitrate · ionophores · potentiometry · ion-selective electrodes

1 Introduction

Anion recognition chemistry dates to the late 1960s but it was only after two decades that a considerable interest in the complex anion-binding phenomena started to develop. The selective detection of anions through the design of suitable receptors is more challenging compared to that of cations. Several reasons lie behind this inconvenient aspect. The larger size of anionic species gives them a smaller charge-to-radius ratio which does not favor strong electrostatic interactions. Many anions are greatly influenced by pH perturbations as they become protonated at low pH to lose their negative charge. In addition, their geometry varies widely, including spherical, linear, trigonal planar and tetrahedral, making the design of receptors with sizes complementary to the anions a complex procedure. Solvation effects may also influence the anion-receptor interactions. As an example, anions may form strong hydrogen bonds with protic solvents with which the receptors have to compete for complexation. The choice of solvent in this case becomes particularly important. Hydrogen bonding is one type of noncovalent interaction between anions and receptors. Others include electrostatic interactions and coordination to metal ions, as well as combinations between them. Additional critical factors for the selectivity are the hydrophobicity of the anion, the receptor's binding sites and the environment where complexation occurs [1].

Several strategies and recommendations are nowadays available for tailoring the anion-host interactions while designing new receptors. A general approach for designing molecules to coordinate with anions is favoring the hydrogen bonding by adding hydrogen bond donor groups to the backbone of the molecule. Interestingly, electrostatic potential surface studies have shown that nitrate possesses six positions for placing positive charges around the anion. Hence, the ideal nitrate host would provide six sites for hydrogen bonding. However, in practice only half of the sites are usually occupied, likely due to steric crowding [2]. In this context matching the size and shape of the guest ion is an important consideration. In the case of (thio)urea-based receptors (one of the simplest and most widely used neutral receptors for anions) this can be achieved by finding a suitable linker that can organize the urea units in the form of a cavity whose size and shape is complementary to the targeted anion [3]. (Thio)ureas have been suggested as suitable candidates for nitrate recognition, however, the association constant reported for nitrate was relatively small ($K_{11}=17.1\pm0.4\ M^{-1}$) and overall the lowest among acetate, cyanide, bromide and hydrogensulfate [4]. Also, the authors stated that small structural variations of the ionophore can result in complete loss of binding affinity with nitrate. Indeed, an earlier study showed that bis-thioureas selectively bind

---

[a] P. Damala, E. Zdrachek, E. Bakker
Department of Inorganic and Analytical Chemistry, University of Geneva, Quai Ernest-Ansermet 30, CH-1211 Geneva, Switzerland
E-mail: eric.bakker@unige.ch

Supporting information for this article is available on the WWW under https://doi.org/10.1002/elan.202200247

© 2022 The Authors. Published by Wiley-VCH GmbH. This is an open access article under the terms of the Creative Commons Attribution License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited.

dihydrogenphosphate over acetate, chloride, sulfate and nitrate [5]. The enhanced selectivity was attributed to the complex geometry and basicity of the guest anions. Interestingly, the association constant for nitrate was remarkably smaller ($K_{11} < 1\ M^{-1}$) than the one reported in the previous work while in both studies the binding was examined by NMR titration. The fact that the binding affinity of an ion-receptor complex can be completely lost even by minor structural changes underlines how delicate the design process is [3,4]. Another strategy for enhancing complexation is to use the metal-ligand coordination chemistry for initiating conformational changes in the ligand so that its hydrogen-bond donor sites favor the anion binding. Alternatively, metal ions can be used to coordinate ligands and bring together their functional groups that can form hydrogen bonds with the target anion [6].

The majority of the studies reporting on binding affinities of different synthetic receptors for nitrate originate in the field of supramolecular chemistry. In those studies the complexation between the in-house synthetized receptors and nitrate is usually examined in organic solvents such as dimethyl sulfoxide, dichloromethane, acetonitrile and chloroform. The choice of solvent is crucial and can significantly influence the binding interactions. As an example, in the case of a metal-based anion receptor changing the polarity of the solvent led to a shift in the orientation of its –CH and –NH groups and to a subsequent competition between the solvent and anion binding [6]. Receptors examined for nitrate recognition include tripodal thiophene- and urea-based structures, guanidinium- and acyclic amide-based receptors, as well as bicyclic cyclophanes [7–11]. The investigated receptors typically contain a variety of hydrogen bond donor groups. The advantage of hydrogen bonds is that they are directional which, in principle, enables the design of structures including cavities that are complementary to the size and shape of the target ion [2]. The most common techniques for quantifying their binding interactions and stoichiometry of the complexes include ^{1}H NMR titration, isothermal titration calorimetry and X-Ray analysis.

In this study we aim to assess the selectivity and complexation of nitrate ionophores and ion-exchangers in potentiometric ion-selective electrodes (ISEs). Such ISEs typically use a plasticized polymeric (typically poly(vinyl chloride)-based) membrane to encapsulate the ionophore or ion-exchanger that is responsible for the selective binding with nitrate. Hence, despite the abundance of studies reporting quantitative data on binding affinities and stoichiometries of several synthetized receptors with nitrate, the practical use of these data is often limited given the different nature of solvents used during the complexation studies. Indeed, complexation studies in solvents of high polarity (methanol, ethanol) have reported lower complex formation constants than those obtained in a typical membrane composition and the differences are attributed to the weak solvation properties of the typically apolar membranes of ISEs [12]. Besides, the methods to examine the complexation and selectivity of ionophores in the fields of organic and analytical chemistry are inherently different. In potentiometry, the selectivity of ISEs was initially described by the Nicolsky equation [13]. Later on, this equation was proved inadequate for ions of different charges and subsequently a new formalism was described for the electrode response in the presence of analytes and interfering ions with different charges [14]. The selectivity coefficients are valid only if Nernstian slopes are observed for both primary and interfering ions. This prerequisite was not always met and efforts to eliminate the factors resulting in the non-Nernstian behavior were made. A procedure was then suggested by conditioning the membrane in the form of the most discriminated ion before any contact with the preferred ion [15,16]. This adapted protocol allowed the determination of improved and unbiased selectivity coefficients.

Most of the studies on potentiometric nitrate selective electrodes examined in this paper use either the separate solution method (SSM) or the fixed interference method (FIM) for the determination of selectivity coefficients. In the first case, the potential of the ISE is recorded in separate solutions for each of the ions tested while in the second case, one solution contains both the primary and interfering ion and the selectivity coefficient is obtained by using separate sections of the calibration curve [17]. In the present study we used the modified separate solution method (mSSM), an extension of the classic SSM where entire calibration curves need to be recorded for each ion tested and use the potentials that fall in the Nernstian section of the curves. In order to avoid frequent biases made with this method, we applied the recommendations provided in the literature [15,16] and thus calculated the selectivity coefficients by using the highest concentration of interfering ions and avoiding the contact of membranes with the primary ion before measuring all the interfering ions.

For the determination of the complex formation constant, a potentiometric technique referred as the segmented sandwich membrane method is typically employed. The method, originally proposed by Russian researchers [18,19], requires the use of a two-layer membrane from which only one contains the ionophore. By recording the initial membrane potential of this sandwich membrane one may obtain information on the ion activity ratio in both aqueous-membrane phases and calculate the resulting complex formation constant [20]. Many studies using the sandwich method are available in the literature examining both cation- [21–26] and anion-selective [27–31] ionophores. Nevertheless, none of them addresses nitrate-selective receptors. With the classic segmented sandwich membrane method, two distinct cases are examined: one that considers strong ion-pairing in the membrane and one that neglects it. Experiments with plasticized PVC membranes have shown that ions are completely associated in the membrane. However, the

15214109, 2023, 2, Downloaded from https://analyticalsciencejournals.onlinelibrary.wiley.com/doi/10.1002/elan.202200247 by Bibliothèque de l'Université de Genève, Division de l'information, Wiley Online Library on [17/09/2024]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

ion-pairs formed are rather non-specific and their effect on the ion-extraction equilibria can be neglected considering that the respective ion-pair formation constants will have similar values [20]. In that case, the calculated complex formation constants are expected to be close to the true values. This assumption was made in many of the above mentioned studies where ion-pairing is neglected [21,24,25,27,28,31]. The sandwich method distinguishes the cases where ion-pairing is strong or weak but it does not allow for the estimation of ion-pair formation constants. Modified versions of the method were consequently suggested to address this issue enabling the successful quantification of ion-pairing formation constants in membranes of variant compositions [32,33].

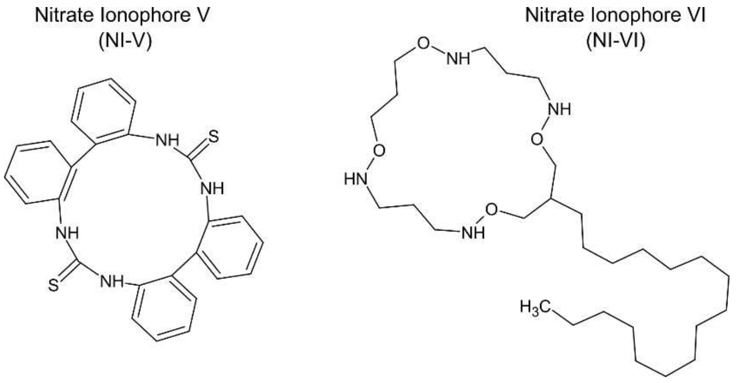
Despite the considerable importance of nitrate measurements, especially in the environmental context, the existing research on nitrate ionophores (which has been ongoing since the 90s) has not found a wider application. Up until the end of the 1990s, the field of potentiometric nitrate sensing was dominated by the use of ion-exchangers, mainly nickel(II)-based ones [34]. This trend has not changed much until today with the main difference being the use of different ion-exchangers which are usually tetralkylammonium-based salts [35,36]. Ion-exchangers are used as the main components for ion-recognition when selective ionophores are lacking. The resulting selectivity order is named the Hofmeister sequence based on the studies of Franz Hofmeister who originally studied the effect of salts on the coagulation of proteins [37]. Despite the plethora of studies examining nitrate-selective electrodes using tetralkylammonium-based ion-exchangers [38–46], there are a few exceptions. These include studies using ionophores that have been identified as nitrate-selective and are commercially available (Scheme 1) [47–50] as well as a few others that have been synthesized in-house [51–53] and whose selectivity has been examined with the same methods used in this study.

Here we aim to compare the performance of those nitrate ionophores and ion-exchangers in terms of their selectivity and complexation to nitrate. The interest for realizing this study was initially triggered by the roughly tenfold price difference between the commercially available nitrate ionophores (namely nitrate ionophores V and VI) and the commonly used ion-exchangers, and our desire to prioritize responsible spending of available resources. In addition, we aim to provide an overview of the potentiometric nitrate sensors developed during the last two decades focusing on the available selectivity and complexation data and highlight the improvements that can be made when reporting such information.

2 Experimental

Reagents. Tridodecymethylammonium chloride (TDMAC) ≥ 97.0 % was purchased from Fluka, 9,11,20,22-tetrahydrotetrabenzo[1,3,8,10]tetraazacyclotetradecine-10,21-dithione (Nitrate Ionophore V, or else NI–V) ≥ 98.0 % was purchased from Santa Cruz Biotechnology Inc., 9-hexadecyl-1,7,11,17-tetraoxa-2,6,12,16-tetraazacycloeicosane (Nitrate Ionophore VI, or else NI-VI), tridodecymethylammonium nitrate (TDMAN) ≥ 99.0 %, tetradodecylammonium tetrakis(4-chlorophenyl)borate (ETH500), 2-nitrophenyl octyl ether ≥ 99.0 % (NPOE), bis(2-ethylhexyl)phthalate (DEHP), dibutyl phthalate (DBP), high molecular weight poly(vinyl chloride) (PVC) and tetrahydrofuran ≥ 99.5 % (THF) were of Selectophore grade and purchased from Sigma Aldrich, tetradodecylammonium chloride (TDDAC) ≥ 97.0 %, sodium nitrate (≥ 99 %), sodium chloride (≥ 99.5 %), sodium nitrite (≥ 97 %), sodium bromide (≥ 99 %), sodium iodide (≥ 99 %), sodium thiocyanate (≥ 98 %), and sodium perchlorate (≥ 98 %) were purchased from Sigma Aldrich. Aqueous solutions were prepared by dissolving the respective salts in Milli-Q water (18.2 MΩ cm).

Preparation of Ion-Selective Electrodes. For the selectivity study, six different nitrate-selective membranes were tested which are referred with the numerals (I) to (IV) and have the following compositions: (I) 4.1 mmol kg^{-1} TDDAC, PVC:DBP (1:1), (II) 100.6 mmol kg^{-1} NI-VI, 4.1 mmol kg^{-1} (4.1 % mol) TDDAC, PVC:DBP (1:1) (composition similar to manufacturer's recommendation), (III) 22 mmol kg^{-1} NI-VI, 11 mmol kg^{-1} (50 % mol) TDMAC, PVC:DEHP (1:2),



Scheme 1. Commercially available nitrate ionophores V and VI.

15214109, 2023, 2, Downloaded from https://analyticalsciencejournals.onlinelibrary.wiley.com/doi/10.1002/elan.202200247 by Bibliotheque de l'Universite de Geneve, Division de l'information, Wiley Online Library on [17/09/2024]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

(IV) 11 mmol kg^{-1} TDMAC, PVC:NPOE (1:2), (V) 22 mmol kg^{-1} NI–V, 11 mmol kg^{-1} (50 % mol) TDMAC, PVC:NPOE (1:2) (composition used in [50]) and (VI) 11 mmol kg^{-1} TDMAC, 15 mmol kg^{-1} ETH500, PVC:DEHP (1:2). The PVC:plasticizer ratios refer to membrane masses. For each composition 200 mg membrane solution was prepared and dissolved in 2 mL THF. The membrane components mixture was poured to a 22 mm glass ring attached on a glass plate and left to dry overnight in ambient air. Then, three circular pieces of 8 mm were cut from the dried membrane and mounted in three OSTEC electrode bodies manually. The same procedure was followed for all membrane compositions and the resulting electrodes were filled with their respective inner filling solutions and conditioned before use. For the complexation study, four of the above mentioned membranes were prepared afresh, namely membranes (I) and (II) (without and with nitrate ionophore VI), and membranes (IV) and (V) (without and with nitrate ionophore V). In addition, two new membrane compositions were prepared to determine whether the ion-exchangers TDMAC and TDDAC can be used interchangeably in the ion-selective membrane solutions. These had the following compositions: 10 mmol kg^{-1} TDDAC, PVC:DEHP (1:2) and 10 mmol kg^{-1} TDMAC, PVC:DEHP (1:2). More details on the concentrations of the solutions used for the selectivity and complexation studies are given in the respective sections below.

Electrochemical equipment and corrections in potential. A high impedance input 16-channel EMF monitor (Lawson Laboratories, Malvern, PA) was used for the potentiometric measurements. The potential values were corrected for the liquid junction potentials arising from the double junction reference electrode (Ag/AgCl/3 M KCl/1 M LiOAc, Metrohm, Switzerland) used in the selectivity study based on the Henderson equation (detailed numbers provided in the Supporting Information).

Selectivity coefficients and data processing. The selectivity study was performed with the modified separate solution method (mSSM) as follows: a 1 mM NaCl solution was used both as the inner filling and conditioning solution of the electrodes which were conditioned for 4 h prior to the study. Then, the electrodes were immersed sequentially in separate solutions of nitrate and interfering anions with the order of the Hofmeister series and their potentials were recorded for the tested concentrations (starting from 10^{-4} M up to 10^{-1} M). The selectivity coefficients were calculated using the following general equation adapted for nitrate: $\log K^{pot}_{NO_3^-,j} = \frac{\left(E_{NO_3^-} - E_j\right)}{s} + \log\frac{a_{NO_3^-}}{a_j}$ where $E_{NO_3^-}$ and E_j are the corrected potential values corresponding to 0.1 M solution of nitrate or interfering anion respectively, $a_{NO_3^-}$ and a_j are the activities of nitrate and interfering anions respectively corresponding to 0.1 M ion solutions (detailed numbers provided in the Supporting Information), and is the average slope calculated for each membrane composition from the individual Nernstian slopes of the tested ions using the two highest activities tested (log$a$ equal to −1.4 and −1.1.). The ions with slopes that were far from Nernstian even at these high activities (having values above −55 mV dec^{-1} or below −64 mV dec^{-1}) were excluded from the averaging process and a relevant mention is made in the respective tables below. As a result, the values of the average slopes corresponding to the membranes (I)–(VI) were ranging between 56 mV dec^{-1} and 60 mV dec^{-1} (see Table 1 & Table 2). For each membrane composition the average slope was subsequently used to perform a linear fit of the experimental data (after being corrected for the junction potentials) which resulted in a new set of fitted equations, all having the same slope (see red lines in Figure 2 and Figure 4).

Complex formation constants. The complex formation constants of the commercially available nitrate ionophores V and VI were examined using the segmented sandwich membrane method [20]. In the case of nitrate ionophore V, the freshly prepared membranes (IV) and (V) were conditioned overnight in a solution of 10 mM $NaNO_3$ and 0.1 mM NaCl. The same composition was used for the inner filling solution and measuring solution. The membranes were firstly conditioned overnight. After conditioning, they were mounted in OSTEC bodies and immersed in the measuring solution to record the potentials corresponding to the single membranes under unstirred conditions. Subsequently, the electrodes were taken out of solution and were disassembled to re-obtain the single membranes which were gently dried and swiftly pressed together to obtain a fused two-layer membrane (one layer with the examined ionophore and one without). The two-layer membrane, or else sandwich membrane, was then mounted back to the electrode making sure that the layer containing the ionophore was the one to face the measuring solution and not the inner filling solution. The re-assembled electrodes were again immersed in the measuring solution and potentials were recorded for approximately 2 h. The same procedure was followed for nitrate ionophore VI with the membranes (I) and (II). A similar experiment was performed with membranes containing the TDDAC and TDMAC ion-exchangers (see section with preparation of ISEs for their detailed composition) to examine the potential differences observed in the single and sandwich membranes and to determine whether they can be used interchangeably. The complex formation constant$\beta_{IL}$was calculated combining the difference of the membrane potentials that correspond to the sandwich and single membranes, and the charge balances at the individual segments. Detailed calculations are provided in the Supporting Information.

3 Results and Discussion

The selectivity of nitrate ionophore VI (NI-VI) was evaluated based on the membrane composition recommended by the manufacturer [54] which in this study is

© 2022 The Authors. Electroanalysis published by Wiley-VCH GmbH

15214109, 2023, 2, Downloaded from https://analyticalsciencejournals.onlinelibrary.wiley.com/doi/10.1002/elan.202200247 by Bibliothèque de l'Université de Genève, Division de l'information, Wiley Online Library on [17/09/2024]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

denoted as membrane (II). This composition has an uncommonly low proportion of ion-exchanger with respect to the ionophore which is typically maintained at a molar percentage around 50 % as opposed to the 4 % recommended. For comparison purposes, a membrane with the same composition but without ionophore (denoted as membrane (I)) and one with the same ionophore in different concentration and with different plasticizer (denoted as membrane (III)) were also prepared and tested. As shown in Figure 1 and Table 1 the selectivity coefficients among the three membrane compositions do not show significant differences. More importantly, the composition which lacks the ionophore presents the best results in terms of selectivity towards chloride which is the most common interfering ion in most applications.

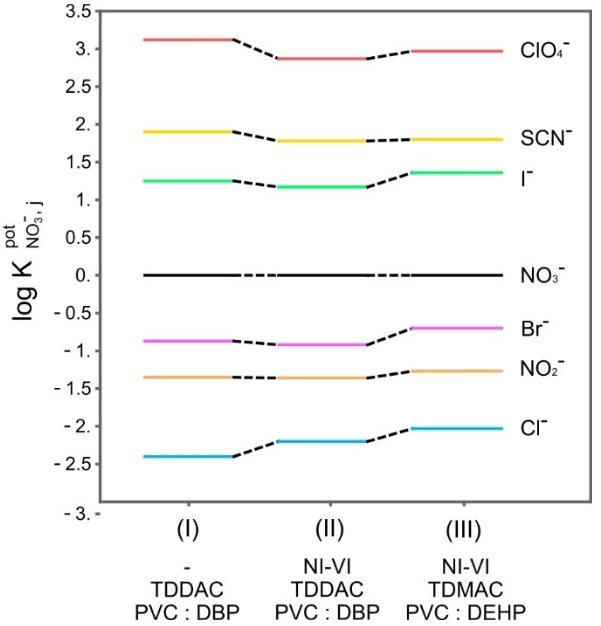


Fig. 1. Selectivity coefficients ($\log K^{pot}_{NO_3^-,j}$) for plasticized PVC membranes with compositions (I) 4.1 mmol kg^{-1} TDDAC, PVC:DBP (1:1), (II) 100.6 mmol kg^{-1} NI-VI, 4.1 mmol kg^{-1} (4.1 % mol) TDDAC, PVC:DBP (1:1) (same to manufacturer's recommendation) and (III) 22 mmol kg^{-1} NI-VI, 11 mmol kg^{-1} (50 % mol) TDMAC, PVC:DEHP (1:2).

For membrane (II), chloride did not show a Nernstian behavior even at high concentrations ($s = -42.4$ mV dec^{-1}) hence the reported selectivity coefficient should be regarded as an approximation of the actual value. With the exception of three other similar cases (see Table 1) all ions showed a potentiometric response that correlated well with the calculated average slope of each composition, as shown from their individual curves in Figure 2. Moreover, the calculated selectivity coefficients are close to the reported values provided by the manufacturer (logarithmic selectivity coefficients equal to –2.5, –1.2 and –1.1 for chloride, nitrite and bromide respectively) confirming the validity of the reported data [54] for which no reference is available.

Only one study was found in the literature reporting on NI-VI [47]. The separate solutions method was used for the calculation of selectivity coefficients which were shown significantly improved compared to the ones obtained here. More specifically, the logarithmic selectivity coefficients for chloride, nitrite, bromide and perchlorate were calculated as –3.6, –1.9, –2.9 and 2.8. The membrane composition used was 39 mmol kg^{-1} NI-VI, 50 % mol TDMAC and PCV:NPOE at a ratio 1:2, which is similar to the composition of membrane (III) examined here with the exception of the plasticizer used. The goal of that study was to examine the performance of solid-contact electrodes using thiol-functionalized reduced graphene oxide as transducer but it is unclear whether these electrodes or the traditional liquid-based electrodes were used for the selectivity study. Nevertheless, even in the first case, the use of a solid-contact electrode for the selectivity study should not significantly influence the results. This was demonstrated in two separate studies [43,45] where selectivity results based on solid-contact electrodes were compared with the ones from liquid-based electrodes confirming the absence of influence of the transducer on selectivity. Hence, the differences in selectivity are expected to be based on the membrane composition rather than the transducer.

Table 1. Selectivity coefficients for nitrate-selective membranes with and without NI-VI.

Ion j		$\log K^{pot}_{NO_3^-,j}$ [(a)]	
	(I) (slope -57.8 ± 1.6 mV dec^{-1})[(b)]	(II) (slope $= -56.2 \pm 0.7$ mV dec^{-1})[(b)]	(III) (slope $= -60.7 \pm 1.2$ mV dec^{-1})[(b)]
Cl^-	-2.40 ± 0.10	-2.20 ± 0.15[(c)]	-2.03 ± 0.00
NO_2^-	-1.35 ± 0.04	-1.36 ± 0.10	-1.27 ± 0.01
Br^-	-0.87 ± 0.04	-0.92 ± 0.09	-0.70 ± 0.00
NO_3^-	0.00	0.00[(c)]	0.00
I^-	1.25 ± 0.05	1.17 ± 0.01	1.36 ± 0.01[(c)]
SCN^-	1.90 ± 0.03	1.78 ± 0.02	1.80 ± 0.01
ClO_4^-	3.12 ± 0.03	2.87 ± 0.02[(c)]	2.97 ± 0.01

[(a)] Average and standard deviations from three electrodes, [(b)] Slope: average value of the individual Nernstian slopes of the examined ions between log$a$ –1.4 and –1, [(c)] The slopes for these ions were far from Nernstian and thus excluded from the calculation of the average slope (see section of "Selectivity coefficients and data processing" for more information).

© 2022 The Authors. Electroanalysis published by Wiley-VCH GmbH

15214109, 2023, 2, Downloaded from https://analyticalsciencejournals.onlinelibrary.wiley.com/doi/10.1002/elan.202200247 by Bibliotheque de l'Universite de Geneve, Division de l'information, Wiley Online Library on [17/09/2024]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

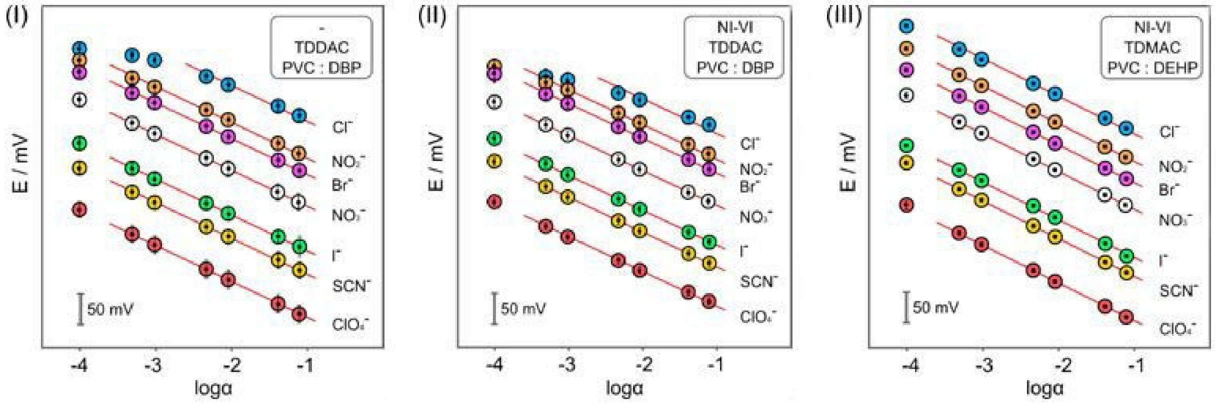


Fig. 2. EMF responses of plasticized PVC membranes with compositions (I), (II) and (III) with the modified separate solutions method.

To further investigate the binding properties of NI-VI, the sandwich membrane method was employed for the determination of its complex formation constant. This is a potentiometric method used to examine the complexation of ionophores in solvent polymeric membranes [20] the details of which are presented in the Experimental section. The membranes used in the sandwich technique are schematically presented in Figure 5 where (A) shows one of the two single homogenous membranes and (B) shows the two membranes fused together to obtain the two-layer confirmation that is subsequently used to measure the membrane potential. Unfortunately, the results obtained did not allow for the calculation of the constant due to the increased potential observed after immersing the sandwich membrane in the measuring solution (Figure 5, curve (i)). In general, when the sandwich membrane is immersed in the solution of the measuring ion *i*, the activity of *i* at the membrane-sample interface is expected to be lower than the one at the membrane-inner solution due to the ion-ionophore complexation. Based on the well-known phase-boundary potential model, in the case of anions this should result in a measured sandwich membrane potential that is lower than the measured potential of the single membrane segments. For nitrate ionophore VI the sandwich membrane potential was somewhat higher than the potentials of the individual segments which made the calculation of the complex formation constant meaningless.

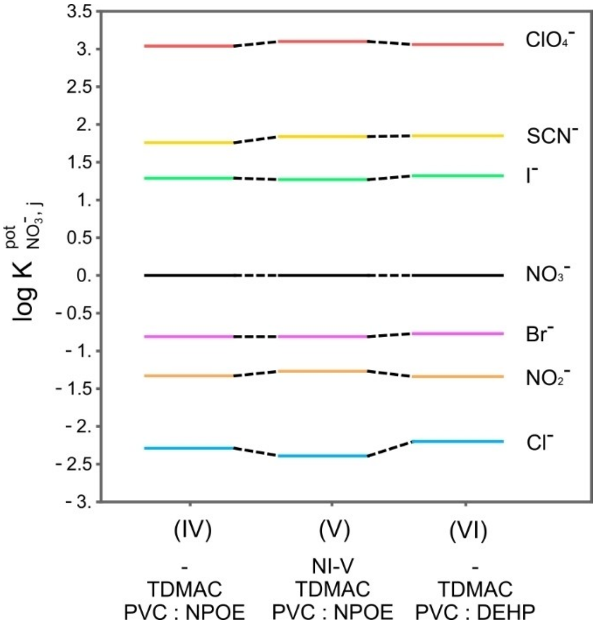


Fig. 3. Selectivity coefficients ($\log K^{pot}_{NO_3^-,j}$) for plasticized PVC membranes with compositions (IV) 11 mmol kg^{-1} TDMAC, PVC:NPOE (1:2), (V) 22 mmol kg^{-1} NI–V, 11 mmol kg^{-1} (50 % mol) TDMAC, PVC:NPOE (1:2) (same to reference [50]) and (VI) 11 mmol kg^{-1} TDMAC, 15 mmol kg^{-1} ETH500, PVC:DEHP (1:2).

The selectivity of nitrate ionophore V (NI–V) was evaluated based on a membrane composition found in the literature showing significant selectivity over chloride ($\log K^{pot}_{NO_3^-,Cl^-} = -3.5$) reported in a study which is used here as a reference (Figure 3) [50]. This composition is represented by membrane (V). Similarly, two other compositions were tested for comparison purposes, one with the same composition but without ionophore (denoted as membrane (IV)) and one with the composition we typically use in our group for nitrate sensing [55–58] (denoted as membrane (VI)) with the exception that TDMAC was used instead of TDMAN to avoid the presence of nitrate in the membrane. As shown in Table 2 the selectivity coefficient obtained here ($\log K^{pot}_{NO_3^-,Cl^-} = -2.4$) is worse than the one reported in the abovementioned reference study. In our case the slope for chloride response was equal to −53.0 mV dec^{-1}, which is close to Nernstian. In contrast, the slope for chloride presented in [50] was −47.8 mV dec^{-1} which, despite the uncertainty on whether this slope was used for the calculation selectivity coefficient, raises concerns on the validity of the reported values. Also, the authors reported

© 2022 The Authors. Electroanalysis published by Wiley-VCH GmbH

15214109, 2023, 2, Downloaded from https://analyticalsciencejournals.onlinelibrary.wiley.com/doi/10.1002/elan.202200247 by Bibliotheque de l'Universite de Geneve, Division de l'information, Wiley Online Library on [17/09/2024]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Selectivity coefficients for nitrate-selective membranes with and without NI–V.

Ion j	$\log K^{pot}_{NO_3^-,j}$ [(a)]		
	(IV) (slope = -59.2 ± 1.0 mV dec^{-1})[(b)]	(V) (slope = -58.2 ± 1.6 mV dec^{-1})[(b)]	(VI) (slope = -59.9 ± 0.7 mV dec^{-1})[(b)]
Cl^-	-2.29 ± 0.02	-2.39 ± 0.01[(c)]	-2.20 ± 0.01
NO_2^-	-1.33 ± 0.03	-1.27 ± 0.00[(c)]	-1.34 ± 0.01
Br^-	-0.81 ± 0.01	-0.81 ± 0.00	-0.77 ± 0.00
NO_3^-	0.00	0.00	0.00
I^-	1.29 ± 0.01	1.27 ± 0.01	1.32 ± 0.00[(c)]
SCN^-	1.76 ± 0.02	1.84 ± 0.01	1.85 ± 0.00
ClO_4^-	3.04 ± 0.03	3.10 ± 0.02	3.06 ± 0.00

[(a)] Average and standard deviations from three electrodes, [(b)] Slope: average value of the individual Nernstian slopes of the examined ions between log*a* −1.4 and −1, [(c)] The slopes for these ions were far from Nernstian and thus excluded from the calculation of the average slope (see section of "Selectivity coefficients and data processing" for more information).

data for a membrane composition without ionophore which are close to our reported values (membrane (IV) in Table 2). One aspect that should be taken into consideration and could explain the observed differences is that the nitrate ionophore in the above study was synthetized in-house in contrast to our case where the ionophore was purchased by a manufacturer.

Two more studies (both from the same research group) were found in the literature that reported on the ionophore NI–V [48,49]. As in our case, the ionophore was purchased and according to the cited reference [17] the modified separate solutions method was used for the determination of selectivity coefficients. Also, the same membrane compositions were used in both studies, including 24 mmol kg^{-1} NI–V, 50 % mol TDMAC (with respect to ionophore) and PCV: NPOE at a ratio 1:2. This composition is very similar to the one of the abovementioned reference study and the comparison of all the reported results should be straightforward. In their more recent study [49] the selectivity coefficients for chloride and nitrite are somewhat better than the ones reported in Table 2 with approximate average values of $\log K^{pot}_{NO_3^-,Cl^-} = -2.9$ and $\log K^{pot}_{NO_3^-,NO_2^-} = -1.6$, respectively. These are approximate values estimated from the bar graph provided by the authors. The selectivity coefficients reported in their older study [48] for chloride and nitrite are even more improved with their logarithmic values ranging between −3.3 to −3.5 and −3.0 to −3.4 respectively. The authors attribute the improved selectivity to the addition of an intermediate tetrathiafulvalene (TTF) layer which is oxidized in the presence of nitrate during the preparation of the electrodes. It is also stated that the selectivity is improved when increasing the number of cycles performed during TTF oxidation. However, this protocol raises some concerns since the described procedure introduces nitrate in the layer which risks leaching to the sensing membrane and become potential determining, thereby introducing a bias in the measurements. According to the modified separate solutions method [17] the membrane should not come in contact with the primary ion before all of the interfering ions are examined. This condition is violated in case nitrate is present in the membrane beforehand, as it happens in the study above, where TTF is oxidized in a concentrated solution of nitrate that consequently introduces the primary ion in the transducing layer. In such circumstances, the knowledge of the slopes obtained for all ions during the selectivity study would be valuable.

Overall, the three membrane compositions examined in this study exhibit similar values of selectivity coefficients for all tested ions. This indicates that NI–V does not offer significant advantages. As mentioned earlier, most studies on nitrate sensors found in the literature use the tetralkylammonium-based ion-exchangers as the nitrate sensing component and rely on the selectivity governed by the Hofmeister sequence of ions. Narrowing the selection to the studies using the separate solution method, the following logarithmic values of selectivity against chloride ($\log K^{pot}_{NO_3^-,Cl^-}$) were reported: −2.0 [39], −2.5 [40], −2.2 [41], −2.5 [42], −1.7 (reported as minimum value) [43], −2.2 [44] and −1.9 [45]. Again, these values are similar to the ones obtained here for membranes (IV) and (VI) where TDMAC is used as ion-exchanger for nitrate recognition (Figure 4).

Apart from the studies using either tetralkylammonium-based ion-exchangers or the nitrate ionophores V and VI examined here, there are three other cases where nitrate ionophores synthetized in-house were examined for their selectivity using potentiometric techniques [51–53]. Interestingly, two of them reported excellent selectivity over any anion tested, including the lipophilic perchlorate and thiocyanate ions. These were not included in the comparisons made above since they used either the fixed interference method (FIM) or the matched potential method (MPM) for the calculation of the selectivity coefficients and a direct comparison with the results obtained from the SSM cannot be made.

Next, the sandwich membrane method was employed for the determination of the complex formation constant of nitrate ionophore V. The data suggest that a mere 31 % of the nitrate ions in the membrane are complexed by the ionophore (see Supporting Information for details), giving

© 2022 The Authors. Electroanalysis published by Wiley-VCH GmbH

15214109, 2023, 2, Downloaded from https://analyticalsciencejournals.onlinelibrary.wiley.com/doi/10.1002/elan.202200247 by Bibliotheque de l'Universite de Geneve, Division de l'information, Wiley Online Library on [17/09/2024]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

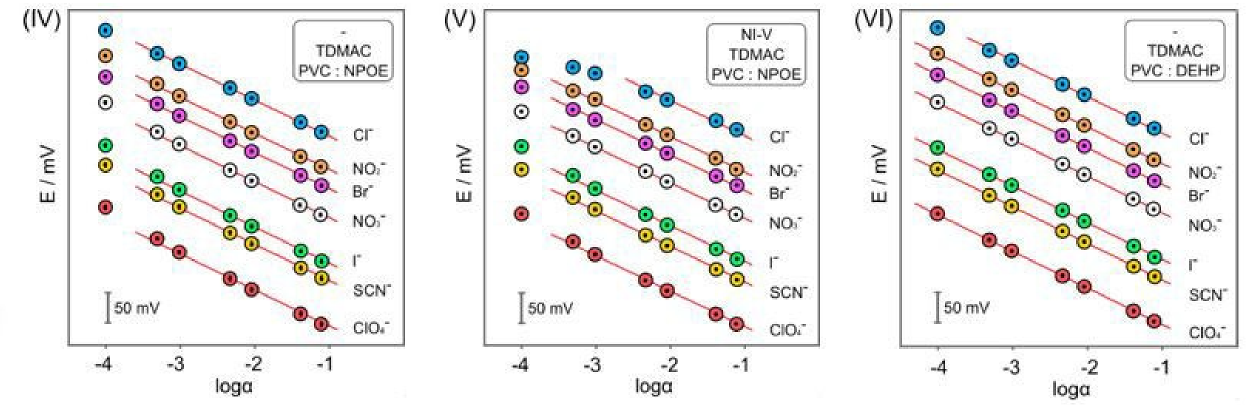


Fig. 4. EMF responses of plasticized PVC membranes with compositions (IV), (V) and (VI) during the modified separate solutions method.

a very small complex formation constant of just $\log\beta_{NO_3^-L} = 1.36 \pm 0.14$.

The weak complexation is also evident in the graph of Figure 5 (curve (ii)) where the sandwich membrane potential is shown to be almost equal to the single membrane, in contrast to what is expected when the interaction between an ionophore and ion is strong. In the latter case, the potential difference is expected to be large owing to the large ratio in concentrations of the uncomplexed primary ion between the two segments. In that case, the concentration of uncomplexed ions in the layer with the ionophore is expected to be significantly lower than the one in the layer without due to their complexation with the ionophore. An example of a strong interaction is given by the valinomycin-potassium complex. To make a direct comparison with the results obtained here, the membrane potential difference for this complex has been calculated to approximately 400 mV giving a value for the complex formation constant of $\log\beta_{K^+L} = 10.0$ [20]. Hence, as demonstrated, the complexation of nitrate ionophore V with nitrate is not superior to the one offered by the common ion-exchangers. Unfortunately, none of the studies mentioned above have investigated the complex formation constant of ionophores using the sandwich technique.

Membranes (I) to (VI) included either TDDAC or TDMAC as ion-exchangers. To examine whether there were any differences in the electrostatic interaction between these two ion-exchangers and nitrate which could result in potential differences, a similar sandwich membrane technique was employed. Here, the single membrane contained either TDDAC or TDMAC alone and the sandwich membrane contained both membrane segments, the one with TDDAC pressed together with the

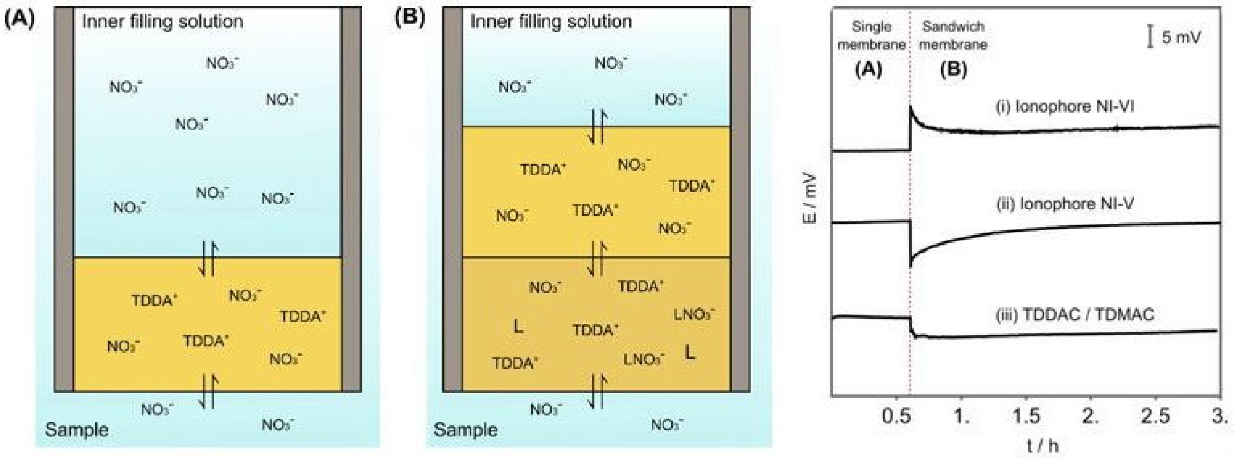


Fig. 5. Schematic generic representation of single membrane segment without ionophore (A) and combined sandwich membrane with both segments (without and with ionophore L) (B), and graph of recorded potentials for the single and sandwich membranes from experiments performed with (i) ionophore NI-VI (with composition similar to membrane (II)), (ii) ionophore NI–V (with composition similar to membrane (V)) and (iii) TDDAC / TDMAC (see section of "Preparation of ISEs" for information on the membrane composition).

15214109, 2023, 2, Downloaded from https://analyticalsciencejournals.onlinelibrary.wiley.com/doi/10.1002/elan.202200247 by Bibliothèque de l'Université de Genève, Division de l'information, Wiley Online Library on [17/09/2024]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

one with TDMAC. As shown in Figure 5 (curve (iii)), the potential difference between the single and sandwich membrane segments was very small (6.3 ± 2.7 mV) which confirmed that both ion-exchangers can be used interchangeably without contributing to significant potential differences.

4 Conclusions

After a detailed examination of the studies reporting selectivity data on nitrate ionophores and ion-exchangers, there are some observations worth to be discussed. The majority of the studies limit the information provided to the type of the method used and the values of the calculated coefficients. For the studies using SSM, there is often missing information on the conditioning protocol (duration, type of solution, etc.) and the type of electrodes used for the study (solid- or liquid-contact ones). More importantly, it is essential to report the experimental electrode slopes based on which the selectivity coefficients are calculated and to mention the activity range to which they correspond. When the slopes are not Nernstian, it should be clearly stated. With the exception of one study [43] this practice has not been followed for most of the investigated ISEs. Also, it should be mentioned whether the theoretical slope is used for the calculations and even in these cases, the experimental slopes should be provided. In order to provide selectivity coefficients which are not biased, emphasis should be given on ensuring that the response for all investigated ions is Nernstian [17]. One recommendation is to avoid exposing the membrane to the primary ion before bringing it in contact with the most discriminated ions. This prerequisite cannot be met in the cases where TDMAN is used as ion-exchanger. Additionally, a more frequent use of the sandwich membrane method for the determination of complex formation constants is recommended. As a simple potentiometric technique, it does not require specialized equipment and can be used as a valuable tool for the determination of binding properties in solvent polymeric membranes.

Overall, the selectivity of commercially available nitrate ionophores is not superior to the one provided by the common tetralkylammonium-based ion-exchangers, a finding that can hardly justify their tenfold price. The selectivity coefficients over chloride determined in this study are $\log K^{pot}_{NO_3^-,Cl^-}=-2.4$ and -2.2 for nitrate ionophore V and VI respectively, with the equivalent values found in the literature equal to $\log K^{pot}_{NO_3^-,Cl^-}=-3.5$ [50] and -2.5 [54]. It is unclear where the differences in the reported coefficients come from. Another study reports an equally low selectivity coefficient over chloride for nitrate ionophore VI with a value of $\log K^{pot}_{NO_3^-,Cl^-}=-3.6$ [47] which is more than an order of magnitude lower than the one obtained in this study. For both nitrate ionophores examined here, the selectivity data for all investigated ions are similar to the ones obtained using just ion-exchangers. Finally, a complex formation constant of $\log\beta_{NO_3^- L}=1.36\pm0.14$ is found for nitrate ionophore V underlying a weak complexation with nitrate that is also in agreement with the results from the selectivity study.

Acknowledgements

This work was financially supported by a European Union Eurostars program (E! 113301 AQISE) with funding from Innosuisse. Open access funding provided by Universite de Geneve.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

References

[1] P. D. Beer, P. A. Gale, *Angew. Chem. Int. Ed.* **2001**, *40*, 486–516; *Angew. Chem.* **2001**, *113*, 502–532.
[2] Hay, B. P. Hay, M. Gutowski, D. A. Dixon, J. Garza, R. Vargas, B. A. Moyer, *J. Am. Chem. Soc.* **2004**, *126*, 7925–7934.
[3] C. Jia, W. Zuo, D. Zhang, X.-J. Yang, B. Wu, *Chem. Commun.* **2016**, *52*, 9614–9627.
[4] R. Herges, A. Dikmans, U. Jana, F. Köhler, P. G. Jones, I. Dix, T. Fricke, B. König, *Eur. J. Org. Chem.* **2002**, *2002*, 3004–3014.
[5] S. Nishizawa, P. Bühlmann, M. Iwao, Y. Umezawa, *Tetrahedron Lett.* **1995**, *36*, 6483–6486.
[6] D. J. Mercer, S. J. Loeb, *Chem. Soc. Rev.* **2010**, *39*, 3612–3620.
[7] A. P. Bisson, V. M. Lynch, M.-K. C. Monahan, E. V. Anslyn, *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 2340–2342.
[8] M. Işiklan, M. A. Saeed, A. Pramanik, B. M. Wong, F. R. Fronczek, A. Hossain, *Cryst. Growth Des.* **2011**, *11*, 959–963.
[9] P. Blondeau, J. Benet-Buchholz, J. de Mendoza, *New J. Chem.* **2007**, *31*, 736.
[10] A. S. Singh, S.-S. Sun, *J. Org. Chem.* **2012**, *77*, 1880–1890.
[11] M. M. Watt, L. N. Zakharov, M. M. Haley, D. W. Johnson, *Angew. Chem. Int. Ed.* **2013**, *52*, 10275–10280; *Angew. Chem.* **2013**, *125*, 10465–10470.
[12] E. Bakker, P. Bühlmann, E. Pretsch, *Chem. Rev.* **1997**, *97*, 3083–3132.
[13] E. Pungor, K. Tóth, A. Hrabéczy-Páll, *Pure Appl. Chem.* **1979**, *51*, 1913–1980.
[14] E. Bakker, R. K. Meruva, Erno. Pretsch, M. E. Meyerhoff, *Anal. Chem.* **1994**, *66*, 3021–3030.
[15] E. Bakker, *J. Electrochem. Soc.* **1996**, *143*, L83–L85.
[16] E. Bakker, *Anal. Chem.* **1997**, *69*, 1061–1069.
[17] E. Bakker, E. Pretsch, P. Bühlmann, *Anal. Chem.* **2000**, *72*, 1127–1133.
[18] O. K. Stefanova, *Electrokhimiya* **1979**, *15*, 1707–1710.
[19] K. N. Mikhelson, *Sens. Actuators B* **1994**, *18*, 31–37.
[20] Y. Mi, E. Bakker, *Anal. Chem.* **1999**, *71*, 5279–5287.
[21] Y. Qin, Y. Mi, E. Bakker, *Anal. Chim. Acta* **2000**, *421*, 207–220.
[22] K. M. Mikhelson, J. Bobacka, A. Ivaska, A. Lewenstam, M. Bochenska, *Anal. Chem.* **2002**, *74*, 518–527.

© 2022 The Authors. Electroanalysis published by Wiley-VCH GmbH

15214109, 2023, 2, Downloaded from https://analyticalsciencejournals.onlinelibrary.wiley.com/doi/10.1002/elan.202200247 by Bibliotheque de l'Universite de Geneve, Division de l'information, Wiley Online Library on [17/09/2024]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

[23] V. M. Lutov, K. N. Mikhelson, *Sens. Actuators B* **1994**, *19*, 400–403.
[24] Y. Mi, E. Bakker, *Electrochem. Solid-State Lett.* **2000**, *3*, 159–161.
[25] Z. Szigeti, A. Malon, T. Vigassy, V. Csokai, A. Grün, K. Wygladacz, N. Ye, C. Xu, V. J. Chebny, I. Bitter, R. Rathore, E. Bakker, E. Pretsch, *Anal. Chim. Acta* **2006**, *572*, 1–10.
[26] Z. Jarolímová, M. Vishe, J. Lacour, E. Bakker, *Chem. Sci.* **2016**, *7*, 525–533.
[27] A. Ceresa, Y. Qin, S. Peper, E. Bakker, *Anal. Chem.* **2003**, *75*, 133–140.
[28] V. Gupta, R. Goyal, R. Sharma, *Talanta* **2008**, *76*, 859–864.
[29] S. Makarychev-Mikhailov, A. Legin, J. Mortensen, S. Levitchev, Y. Vlasov, *Analyst* **2004**, *129*, 213–218.
[30] L. Li, Y. Zhang, Y. Li, Y. Duan, Y. Qian, P. Zhang, Q. Guo, J. Ding, *ACS Sens.* **2020**, *5*, 3465–3473.
[31] A. K. Singh, U. P. Singh, S. Mehtab, V. Aggarwal, *Sens. Actuators B* **2007**, *125*, 453–461.
[32] M. A. Peshkova, A. I. Korobeynikov, K. N. Mikhelson, *Electrochim. Acta* **2008**, *53*, 5819–5826.
[33] V. V. Egorov, P. L. Lyaskovski, I. V. Il'inchik, V. V. Soroka, V. A. Nazarov, *Electroanalysis* **2009**, *21*, 2061–2070.
[34] P. Bühlmann, E. Pretsch, E. Bakker, *Chem. Rev.* **1998**, *98*, 1593–1688.
[35] C. Jiang, Y. He, Y. Liu, *Analyst* **2020**, *145*, 5400–5413.
[36] S. Singh, A. G. Anil, V. Kumar, D. Kapoor, S. Subramanian, J. Singh, P. C. Ramamurthy, *Chemosphere* **2022**, *287*, 131996.
[37] F. Hofmeister, *Arch. Exp. Pathol. Pharmakol.* **1888**, *24*, 247–260.
[38] M.-Y. Kim, J.-W. Lee, D. J. Park, J.-Y. Lee, N. V. Myung, S. H. Kwon, K. H. Lee, *J. Electroanal. Chem.* **2021**, *897*, 115553.
[39] H. Wang, B. Yuan, T. Yin, W. Qin, *Anal. Chim. Acta* **2020**, *1129*, 136–142.
[40] T. Fayose, L. Mendecki, S. Ullah, A. Radu, *Anal. Methods* **2017**, *9*, 1213–1220.
[41] C. Wardak, M. Grabarczyk, *J. Environ. Sci. Health Part B* **2016**, *51*, 519–524.
[42] M. Cuartero, G. A. Crespo, E. Bakker, *Anal. Chem.* **2015**, *87*, 8084–8089.
[43] D. Yuan, A. H. C. Anthis, M. Ghahraman Afshar, N. Pankratova, M. Cuartero, G. A. Crespo, E. Bakker, *Anal. Chem.* **2015**, *87*, 8640–8645.
[44] B. Paczosa-Bator, L. Cabaj, R. Piech, K. Skupień, *Anal. Chem.* **2013**, *85*, 10255–10261.
[45] W. Tang, J. Ping, K. Fan, Y. Wang, X. Luo, Y. Ying, J. Wu, Q. Zhou, *Electrochim. Acta* **2012**, *81*, 186–190.
[46] G. A. Khripoun, E. A. Volkova, A. V. Liseenkov, K. N. Mikhelson, *Electroanalysis* **2006**, *18*, 1322–1328.
[47] Y. Liu, Y. Liu, Z. Meng, Y. Qin, D. Jiang, K. Xi, P. Wang, *Talanta* **2020**, *208*, 120374.
[48] M. Pięk, R. Piech, B. Paczosa-Bator, *J. Electrochem. Soc.* **2015**, *162*, B257.
[49] M. Pięk, R. Piech, B. Paczosa-Bator, *J. Electrochem. Soc.* **2018**, *165*, B60.
[50] A. S. Watts, V. G. Gavalas, A. Cammers, P. S. Andrada, M. Alajarín, L. G. Bachas, *Sens. Actuators B* **2007**, *121*, 200–207.
[51] V. K. Gupta, L. P. Singh, S. Chandra, S. Kumar, R. Singh, B. Sethi, *Talanta* **2011**, *85*, 970–974.
[52] H. K. Lee, K. Song, H. Ran Seo, S. Jeon, *Talanta* **2004**, *62*, 293–297.
[53] M. Mazloum Ardakani, M. Salavati-Niasari, M. Jamshidpoor, *Sens. Actuators B* **2004**, *101*, 302–307.
[54] "Nitrate Ionophore VI Selectophore, function tested 1196157-85-3," can be found under http://www.sigmaaldrich.com/, **n.d.**.
[55] E. Zdrachek, T. Forrest, E. Bakker, *Anal. Chem.* **2022**, *94*, 612–617.
[56] E. Zdrachek, E. Bakker, *Anal. Chem.* **2020**, *92*, 2926–2930.
[57] M. Cuartero, G. Crespo, T. Cherubini, N. Pankratova, F. Confalonieri, F. Massa, M.-L. Tercier-Waeber, M. Abdou, J. Schäfer, E. Bakker, *Anal. Chem.* **2018**, *90*, 4702–4710.
[58] N. Pankratova, G. A. Crespo, M. Ghahraman Afshar, M. Coll Crespi, S. Jeanneret, T. Cherubini, M.-L. Tercier-Waeber, F. Pomati, E. Bakker, *Environ. Sci. Process. Impacts* **2015**, *17*, 906–914.

Received: May 27, 2022
Accepted: July 10, 2022
Published online on August 3, 2022

15214109, 2023, 2, Downloaded from https://analyticalsciencejournals.onlinelibrary.wiley.com/doi/10.1002/elan.202200247 by Bibliotheque de l'Universite de Geneve, Division de l'information, Wiley Online Library on [17/09/2024]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License