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[Bis(2-hydroxyl imino)1-phenyl, 2-(2-quinoline)1-ethanone]Aluminium(III) Complex as Carrier for a Salicylate-Sensitive Electrode

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A salicylate-selective electrode based on the complex [bis(2-hydroxyl imino)1-phenyl,2-(2-quinoline)1-ethanone]Aluminium(III) as the membrane carrier was developed. The electrode exhibited a good Nernstian slope of -59.1 ± 0.4 mV / decade (mean value \pm standard deviation, $n = 5$) and a linear range of $1.0 \times 10^{-6} - 1.0 \times 10^{-1}$ mol L⁻¹ for salicylate. The limit of detection was 5.0×10^{-7} mol L⁻¹. The electrode had a fast response time of 15 s and could be used for more than three months. The selectivity coefficients were determined by the fixed interference method (FIM) and could be used in the pH range of 2.0–7.8. It was employed as an indicator electrode for direct the determination of salicylate in pharmaceutical samples.

INTRODUCTION

Carrier-based ion-selective electrodes (ISEs) are well-established analytical tools, which are used routinely to measure a wide variety of different ions selectively and directly in complex clinical, industrial and environmental samples. Compared to other types of ISEs, modern solvent polymer membrane-based devices represent a generic approach to chemical sensing, since their response characteristics rely on ion-extraction and complexation equilibrium in the organic membrane phase.¹

Development of PVC membranes has made the original liquid membrane electrode configuration virtually redundant and has led to potentiometric sensors based on polymer membranes being available commercially to sense ions such as calcium, water hardness, nitrate, and bicarbonate. It should be noted that many of the biologically important ions are included in this list and thus

potentiometric sensors are used extensively in the analysis of biological fluids.

Potentiometric ionophore-based membrane sensors are a preferred measuring tool for a variety of applications. Since the binding selectivity of the lipophilic ionophore dictates, for the most part, the ion-exchange selectivity of the membrane, large cation and anion selectivity variations can be achieved by a suitable choice of the ionophore.²

Construction and application of an ion-selective electrode as a potentiometric sensor offers advantages such as simplicity, fast response, low cost, and wide linear range. These characteristics have inevitably led to construction of sensors for ionic species.³ When the attraction is purely electrostatic, the partition of anions from the aqueous sample solution into the ISE membrane is simply dependent on the lipophilicity of the anions.⁴

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Selectivity of these classical ion exchangers depends on the lipophilicity of the anions, with more lipophilic anions rendering the best response. The most important recognition elements that can be utilized in the development of ISEs involve specific metal-ligand interaction.⁵ The demand for ionophores with either new or improved selectivities in the field of ion-selective electrodes is high, particularly in the area of anion-selective electrodes. A strong interaction between the ionophore and the anion is required in order to successfully complex anions in a selective fashion. Complexes of several metal ions with different ligands, as ionophores for anions, have been observed to show such specific metal ligand interactions and induce anion selectivities in the membranes that differ somewhat from the classical anion exchangers.^{6,7}

Salicylate derivatives are commonly used as effective antimicrobial, antipyretic and analgesic agents. Aspirin, in particular, probably remains one of the most widely used drugs of any kind.⁸ One should realize, however, that salicylates can be quite toxic if taken in large doses. Levels in plasma higher than 2.2 mmol L⁻¹ of salicylates are regarded as being toxic to the patients. Salicylic acid is one of the common metabolites of acetylsalicylic acid (aspirin), which is widely used as an analgesic and anti-inflammatory agent and in cases as a preventive of heart attacks.⁹ The free acid is widely used as an antiseptic and a food preservative, and in cases of acute salicylate poisoning, where knowledge of the plasma salicylate level and of its rate of change provides a valuable indication of the severity of poisoning, it is a very useful guide to the type of treatment required. Aspirin is responsible for more cases of accidental poisoning in children than any other substance. Toxic doses of salicylates initially produce a stimulation of the central nervous system. This may be reflected by hyperventilation, flushing and fever. Unfortunately, an unrecognized case of salicylate poisoning may be thought to be a case of infection and further aspirin may be given in a vain attempt to control the fever. Central nervous system stimulation is followed by depression and a complex disturbance of acid-base balance. Initially a respiratory alkalosis caused by severe hyperventilation occurs, which may be followed, especially in infants, by a metabolic acidosis due in part to the absorbed drug and in part to accumulation of other metabolic acids. Toxicity is relatively common in high dose therapy. The therapeutic range is 15–30 mg/dL. Mild toxic symptoms (tinnitus, dizziness, sweating, nausea, and vomiting) begin at concentrations higher than 30 mg/dL, with severe toxicity (central nervous system effects ranging from irrationality and confusion to convulsions and coma) occurring at concentrations above 50 mg/dL. Salicylates increase the respiratory rate, causing respiratory alkalosis and, at high levels, increased anion gap metabolic acidosis. In children younger than four years, metabolic acidosis usually predominates, while respiratory

alkalosis or a mixed picture is present in adults. The degree of salicylate toxicity correlates with the peak concentration and rate of decline.¹⁰

Recently, several salicylate-selective membrane electrodes involving a variety of ion carriers have been reported.^{11–16} Development of a suitable salicylate-selective electrode would enable the detection of "free" salicylate in samples and could help researchers studying the pharmacological role of this drug.¹⁷

The purpose of the present work was the development of a salicylate-selective electrode based on a poly (vinyl chloride) (PVC) membrane impregnated with the complex [bis(2-hydroxyl imino)1-phenyl,2-(2-quinoline)1-ethanona]Aluminium(III). This sensor is potentially useful for detection of salicylate in biological samples. The proposed sensor displays a low detection limit and high selectivity and sensitivity in salicylate determination in real samples.

EXPERIMENTAL

Reagents

All chemicals used were of analytical reagent grade. Twice distilled water and "grade A" glassware were used throughout. PVC of high relative molecular weight, trioctylmethyl ammonium chloride (TOMAC), and dioctyl phthalate (DOP) were used as received from Aldrich. The ionophore of [bis(2-hydroxyl imino)1-phenyl,2-(2-quinoline)1-ethanona] Aluminium (III) (Figure 1) was synthesized and used after purification. Tetrahydrofuran (THF) and all other chemicals were of the highest purity available from Merck, and were used without further purification, except THF, which was distilled before use. The pH adjustments were made with dilute phosphoric acid and sodium hydroxide. A salicylate stock solution was prepared by dissolving an appropriate amount of sodium salicylate in 100 mL of water. Working solutions were prepared by successive dilutions with water.

Sample Preparation

For the preparation of pharmaceutical samples, three powdered acetylacetic acid tablets (all purchased at local pharmacies) were treated with 50 mL NaOH of 1.0 mol L⁻¹ solution in a 100 ml beaker. The mixture was heated over a

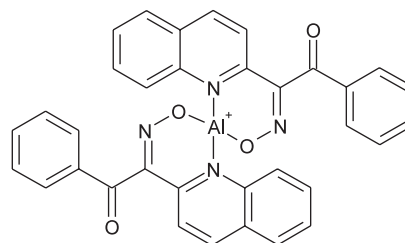


Figure 1. Structural representation of the compound [bis(2-hydroxyl imino)1-phenyl,2-(2-quinoline)1-ethanona]Aluminium(III), AlL_2 , used as ionophore in the PVC-membrane sal^- -selective electrode.

TABLE I. Optimized membrane compositions and their potentiometric response properties in the salicylate-selective electrode. Values given in the table are the percent mass ratio

No.	PVC %	DOP %	Ionophore %	TOMAC %	Slope mV/decade	Linear dynamic range mol L ⁻¹
1	32	62	6	–	–42.1	1.0×10 ⁻⁴ – 1.0×10 ⁻¹
2	33	66	–	1	–12.2	1.0×10 ⁻³ – 1.0×10 ⁻¹
3	31.5	61	7	0.5	–50.3	5.0×10 ⁻⁵ – 1.0×10 ⁻¹
4	32	61	6	1	–52.3	1.0×10 ⁻⁵ – 1.0×10 ⁻¹
5	32	62	5	1	–51.3	1.0×10 ⁻⁵ – 1.0×10 ⁻¹
6	30.5	61	7	1.5	–56.0	5.0×10 ⁻⁶ – 1.0×10 ⁻¹
7	31	61	6	2	–55.0	5.0×10 ⁻⁶ – 1.0×10 ⁻¹
8	30	60	8	2	–59.1	1.0×10 ⁻⁶ – 1.0×10 ⁻¹
9	30.5	60.5	7	2	–56.8	5.0×10 ⁻⁶ – 1.0×10 ⁻¹

boiling water bath for 1 h. The resulting solution was diluted to 250 mL in a volumetric flask and used for determination of the salicylate content by potentiometric and spectrophotometric methods. During measurements, the solutions were agitated with a magnetic stirrer and the temperature was maintained constant.

Preparation of Aluminum Complex

Synthesis of bis(2-hydroxyl imino)1-phenyl,2-(2-quinolile)1-ethanona. – The 2-ketomethyl quinoline (1 mmol, 0.27 g), sodium nitrite (3 mmol, 0.22 g), and silica sulfuric acid (0.3 g) in dichloromethane (10 mL) were vigorously stirred at 0 °C. The progress of the reaction was followed by TLC. The reaction was completed after 0.5–1 h. The yellow solid precipitate of the ligand was filtered, washed with dichloromethane (20 mL) and dried. 1-Phenyl-2-quinolin-2-yl-ethane-1,2-dione-2-oxime (C₁₇H₁₂N₂O₂), yellow powder; m.p. 156–158 °C; IR (KBr) ν/cm^{-1} : 3600–2200 ($\nu_{\text{N-H}}$), 1640 ($\nu_{\text{C=O}}$), 1590 ($\nu_{\text{C=N}}$), 1495 (ring vibration), 1025 (ring vibration) cm^{-1} ; ¹H NMR (500.1 MHz, CDCl₃) δ/ppm : 7.45 (t, $J = 7.8$ Hz, CH), 7.50 (d, $J = 7.5$ Hz, 2CH), 7.62 (t, $J = 7.3$ Hz, CH), 7.69 (t, $J = 7.9$ Hz, CH), 7.82 (dt, $J = 8.0$ and $J = 0.9$ Hz, CH), 7.88 (t, $J = 8.0$ Hz, CH), 7.99 (d, $J = 8.4$ Hz, CH), 8.08 (d, $J = 8.4$ Hz, CH), 8.13 (d, $J = 7.9$ Hz, CH), 8.36 (d, $J = 8.7$ Hz, CH), 18.25 (br. s, OH). ¹³C NMR (125.8 MHz, CDCl₃) δ/ppm : 151.25 (C=NOH), 193.82 (C=O). MS: m/z (%) = 276 (M⁺, 22), 231 (62), 171 (100), 154 (20), 128 (20), 105 (64), 77 (76), 51 (28). Anal. Calcd. for C₁₇H₁₂N₂O₂: C 73.91, H 4.34, N 10.14. Found: C 73.78, H 4.12, N 9.85.

Synthesis of [bis(2-hydroxyl imino)1-phenyl,2-(2-quinolile)1-ethanona]Aluminium(III). – Ligand (2 mmol) and Lewis acid (1 mmol, AlCl₃) were ground in a pestle and mortar for the required time. The reaction completed after 0.5–1 h in 70–80 °C. Crystallization of the solid from dichloromethane (10 mL) produced analytically pure complex. IR (KBr) ν/cm^{-1} : 3100 ($\nu_{\text{N-H}}$), 1630 ($\nu_{\text{C=O}}$), 1580 ($\nu_{\text{C=N}}$). Fw: 577 g mol⁻¹. Anal. Calcd. for C₃₄H₂₄N₄O₄Al: C 70.71, H 3.83, N 9.7, Al 4.67. Found: C 70.35, H 3.78, N 9.75, Al 4.73.

Electrode Preparation

The membrane ion-selective electrodes were prepared according to a previously reported method.^{18,19} A mixture of PVC, DOP as plasticizer and TOMAC as an additive with lipophilic cation were dissolved in a minimal amount of tetrahydrofuran (THF). The PVC-THF solution was mixed with [bis(2-hydroxyl imino)1-phenyl,2-(2-quinolile)1-ethanona]Aluminium(III) (AlL₂). The resulting mixture was poured into a small flat bottom dish, covered with a filter paper and the solvent was allowed to evaporate at room temperature. The resulting membrane (ca. 0.2 mm thick) was then sectioned with a cork borer and mounted across the opening of a PVC tube of about 7 mm i.d. and 1.5 cm length using a glue of PVC in THF. The PVC tube with the membrane was then incorporated into a silver-silver chloride wire electrode. The electrode was then filled with an internal solution of 0.1 mol L⁻¹ KCl and sodium salicylate 1.0 × 10⁻⁵ mol L⁻¹.

Potential Measurement and Calibration

The electrode was equilibrated for 22 h in 1.0 × 10⁻⁵ mol L⁻¹ salicylate solution. The potential measurements were carried out by setting up the following cell assembly: Ag|AgCl|internal solution (KCl 0.1 mol L⁻¹, 1.0 × 10⁻⁵ mol L⁻¹ NaSal)|PVC membrane|test solution||SCE

All potentials were measured at 25 ± 1 °C using a Metrohm model 691 pH/mV meter. A saturated calomel electrode (SCE, Metrohm) with a fiber junction was used as the external reference electrode. Calibration curves were constructed by plotting the potential, E , vs. the logarithm of the concentration of salicylate at constant pH. Activities were calculated according to the Debye-Hückle procedure.²⁰ However, concentration instead of activity was used for the calibration curve. The pH of the sample solution was monitored simultaneously with a conventional glass pH electrode (Metrohm).

The performance of the electrode was investigated by measuring its potential in sodium salicylate solutions prepared in the concentration range 1.0 × 10⁻⁷ – 1.0 mol L⁻¹ by

serial dilution at a constant pH = 7. All solutions were freshly prepared by dilution from the standard stock solution, 2.0 mol L⁻¹, with doubly distilled water. The solutions were stirred and potential readings were recorded when they became stable. The data were plotted as the observed potential *vs.* the logarithm of the salicylate concentration.

RESULTS AND DISCUSSION

It is believed that the potentiometric response of the membranes doped with macrocyclic complexes of metal ions is based on the coordination of analyte anions as an axial ligand to the metal center of the carrier molecule. Hence, it is possible that additional investigations of the interaction between metal ion complexes and anions will lead to the development of anion sensing ligands for an ISE. We examined ALL₂ as potential sensing material in construction of PVC membrane. Preliminary experiments revealed that the PVC-based membrane electrode, incorporating ALL₂ ionophore, generate a stable potential response in salicylate solutions of varying concentrations. The membrane without the ionophore (blank membrane) exhibits insignificant potentiometric response to salicylate and other anions.

Influence of Membrane Composition

The effect of membrane composition on the potentiometric response of the electrode was investigated by varying the proportions of the membrane active phase and the plasticizer to PVC ratio. Table I presents the compositions of several typical membranes, along with their other characteristics. The electrode suffered from long response times and potential drift, which was assumed to be due to high membrane resistance. The response of the electrode was improved by addition of lipophilic salts such as TOMAC to the membrane; it not only reduced the membrane resistance but also enhanced the response behavior and selectivity and reduced interferences from lipophilic sample anions.^{21,22} Although the ISE membrane can work properly with a very small amount of ionic sites (*e.g.* as polymer impurities), addition of ionic sites is highly advisable. The presence of lipophilic ionic sites keeps constant total concentration of the measuring ion in the membrane phase, and can be used to adjust optimal stoichiometry of the ion-ionophore complex and membrane selectivity. Preferential response to salicylate is believed to be associated with the coordination of salicylate with the central metal ion of the carrier and the lipophilicity of the anion. It is well-known that the sensitivity and selectivity obtained for a given ionophore depend significantly on the membrane condition.^{23–25} Irrespective of ionophore concentration, the slope was relatively larger when DOP / PVC weight ratio was 2.0. It was also observed that the potentiometric response of the electrode to salicylate ion was dependent to the concen-

tration of the ionophore incorporated within the membrane. Increasing the percentage of ALL₂, up to 8 % results in larger slopes and wider linear range of membranes.

The potentiometric response of the membrane was greatly improved by the presence of the lipophilic cationic additive, TOMAC. Better response characteristics, *i.e.* Nernstian response and improved selectivity, were usually observed with an ionophore/TOMAC weight ratio of approximately 4.0, which corresponds to a mole ratio of approximately 2.8. The presence of lipophilic ionic sites is beneficial for both the neutral carrier and charged carrier-based ion-selective electrodes.^{26,27}

Among the different compositions studied (Table I), the best response was recorded for the membrane containing 30 % PVC, 60 % DOP, 2 % additive and 8 % ALL₂. This composition was, therefore, used to study the performance of the electrode, *viz.*, working concentration range, sensitivity, selectivity, life time, response time, and effect of pH. The characteristic properties of the optimized membrane are summarized in Table II.

Over the concentration range $1.0 \times 10^{-6} - 1.0 \times 10^{-1}$ mol L⁻¹ of salicylate in the calibration solution, the electrode potential response was linear with the salicylate concentration. The calibration curve slope was -59.1 ± 0.4 mV / p [Sal] and the detection limit, calculated as recommended by the IUPAC, was 5.0×10^{-7} mol L⁻¹.²⁷ It is below the normal salicylate concentration in whole blood, plasma and serum. In practice, slopes of between -55 and -59 mV decade⁻¹ are referred to as Nernstian for analytical purposes.^{28,29} The potentiometric response characteristics of the plasticized PVC-based electrode, incorporating [bis(2-hydroxyl imino)1-phenyl,2-(2-quinolile)1-ethanona]Aluminium(III), to salicylate ion are shown in Figure 2.

Response Characteristics of the Electrodes

The influence of the concentration of the internal solution on the potential response of the salicylate-selective elec-

TABLE II. Characteristics of optimized Sal⁻-ISE

Linear range / mol L ⁻¹	$1.0 \times 10^{-6} - 1.0 \times 10^{-1}$
Slope \pm standard deviation / mV decade ⁻¹	-59.1 ± 0.4
pH range	2.0–7.8
Precision	At concentrations of 1.0×10^{-2} , 1.0×10^{-3} and 1.0×10^{-4} mol L ⁻¹ sal ⁻ standard deviations were ± 0.3 , ± 0.4 and ± 0.7 mV, respectively.
Detection limit / mol L ⁻¹	5.0×10^{-7}
Life time / month	3
Response time / s	10–15

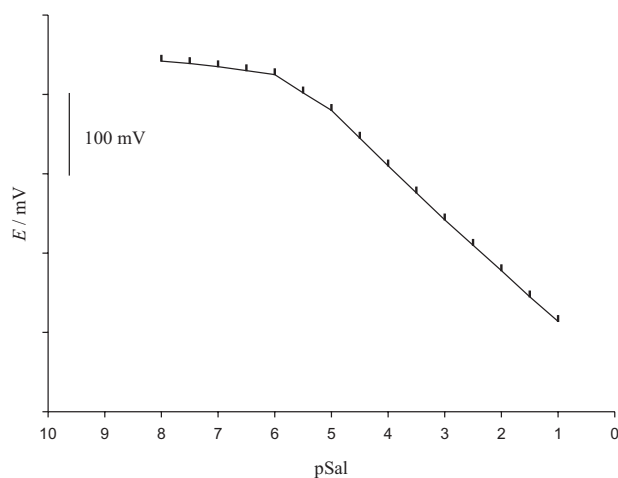


Figure 2. Potentiometric response of the salicylate-selective electrode to salicylate using optimized membrane electrode.

trode was studied and the results showed the concentration of the internal solution did not cause any significant difference in the potential response of the electrodes, except for an expected change in the intercept of the resulting Nernstian plots.

The effect of pH of the test solution on the response of the membrane electrodes was examined at three salicylate concentrations. As illustrated in Figure 3 for 1.0×10^{-4} , 1.0×10^{-3} and 1.0×10^{-2} mol L⁻¹ of salicylate, the potentials remain constant at pH of about 2.0–7.8. The results show that the sensor is suitable for salicylate determination in wide pH range of 2.0–7.8. In high pH media, OH⁻ will probably compete with the salicylate ion, whereas in acidic media (pH < 2.0), the drift in the potential may be due to the instability of the ionophore (complex of the aluminum with the ligand) due to the oxygen sites protonation. The working pH range over which the electrode can be used (2.0–7.8) covers the physiological conditions (pH = 7.2–7.6).

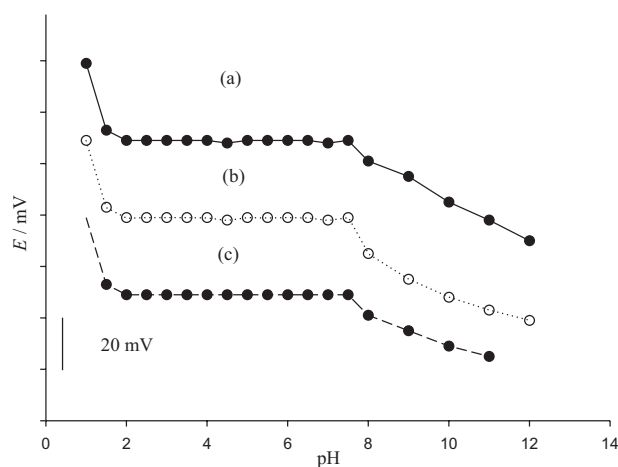


Figure 3. The pH response of the membrane electrode at: a) 1.0×10^{-4} mol L⁻¹, b) 1.0×10^{-3} mol L⁻¹, and c) 1.0×10^{-2} mol L⁻¹ salicylate concentrations.

TABLE III. Stability and reproducibility of the salicylate-selective electrode ($n = 5$)

Time day	Slope mV/decade	Linear range mol L ⁻¹	Correlation of coefficients
1	-59.1	1.0×10^{-6} – 1.0×10^{-1}	0.998
7	-58.6	1.0×10^{-6} – 1.0×10^{-1}	0.998
20	-58.0	5.0×10^{-6} – 1.0×10^{-1}	0.997
25	-57.5	5.0×10^{-6} – 1.0×10^{-1}	0.999
40	-57.0	5.0×10^{-6} – 1.0×10^{-1}	0.998
55	-56.0	5.0×10^{-6} – 1.0×10^{-1}	0.999
75	-55.4	5.0×10^{-6} – 1.0×10^{-1}	0.997
95	-55.0	1.0×10^{-5} – 1.0×10^{-1}	0.993
115	-55.0	1.0×10^{-5} – 1.0×10^{-1}	0.991

Stability and reproducibility of the electrodes were also tested. Standard deviations of 20 replicate measurements for the PVC sensor at 1.0×10^{-2} , 1.0×10^{-3} and 1.0×10^{-4} mol L⁻¹ salicylate were ± 0.3 , ± 0.4 and ± 0.7 mV, respectively. Long-term stability of the electrode was studied by periodical recalibration in standard solutions and by calculating the response slope over the range of 1.0×10^{-7} – 1.0×10^{-1} mol L⁻¹. The detection electrode was very stable and could be used over a period of at least 3 months. The slopes of the electrode response decreased from -59.1 to -55.0 mV / decade over a period of three months (Table III). The lifetime of solvent polymeric ion-selective electrodes is limited by leaching of membrane components into the sample solutions. Since ionic sites of high lipophilicity are available, loss of ionic sites is, in general, not a problem. It is, therefore, assumed here that the co-transported or ion-exchanging ions are primary or interfering ions forming complexes with the ionophore.

Response time of the electrode was measured after successive immersion in a series of salicylate solutions, in each of which the salicylate concentration increased tenfold, from 1.0×10^{-6} to 1.0×10^{-1} mol L⁻¹. The static response time thus obtained was 10 s for the 1.0×10^{-1} mol L⁻¹ salicylate concentration. At lower concentrations, however, the response time was longer and reached 15 s for a salicylate concentration of 1.0×10^{-5} mol L⁻¹. The actual potential *versus* time traces is shown in Figure 4. The potentials remained constant for approximately 5 min, after which a very slow change within the resolution of the meter was recorded. The sensing behavior of the membrane electrode did not depend on whether the potentials were recorded from low to high concentrations or *vice versa*. In fact, the measured potential virtually immediately follows the activity changes in both phases at the membrane interface, and the rate-limiting step is the establishment of the equilibrium between the activities in the aqueous phases at the surface layer and in the bulk of

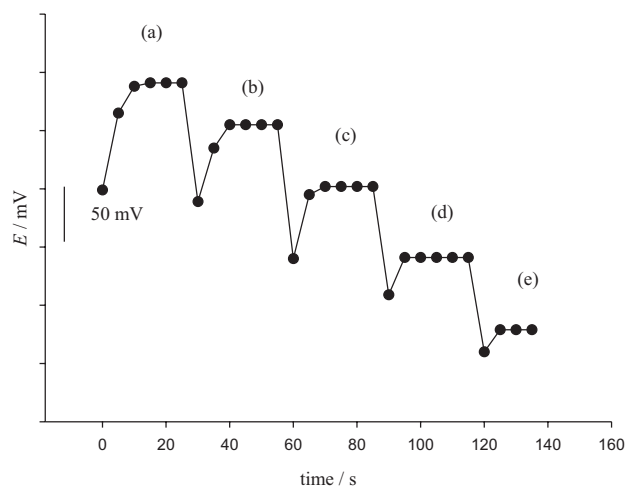


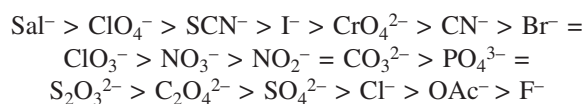
Figure 4. Response time of the membrane electrode for salicylate with a change in concentration from: a) $1.0 \times 10^{-6} \text{ mol L}^{-1}$ to $1.0 \times 10^{-5} \text{ mol L}^{-1}$, b) $1.0 \times 10^{-5} \text{ mol L}^{-1}$ to $1.0 \times 10^{-4} \text{ mol L}^{-1}$, c) $1.0 \times 10^{-4} \text{ mol L}^{-1}$ to $1.0 \times 10^{-3} \text{ mol L}^{-1}$, d) $1.0 \times 10^{-3} \text{ mol L}^{-1}$ to $1.0 \times 10^{-2} \text{ mol L}^{-1}$, and e) $1.0 \times 10^{-2} \text{ mol L}^{-1}$ to $1.0 \times 10^{-1} \text{ mol L}^{-1}$.

the sample. The three possible time limiting processes are (1) the interfacial ion exchange, (2) the diffusion-controlled equilibration of the sample with the aqueous side of the phase boundary and (3) the membrane side of the phase boundary with the membrane bulk. As a consequence, a virtually immediate shift of the phase boundary potential is expected after a change of activity in either of the phases at the membrane surface. Therefore, potential drifts arise as a consequence of slow equilibration of the corresponding surface layers with the bulk of the solution and/or membrane upon a change of the sample.³

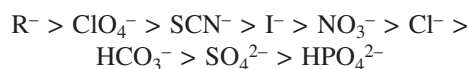
Selectivity of the Electrode

Selectivity of solvent polymeric membrane ion-selective electrodes is quantitatively related to equilibria at the interface between the sample and the electrode membrane. Potentiometric selectivity coefficients, describing the preference by the membrane for an interfering ion A^- relative to salicylate, were determined by the fixed interference method. The selectivity coefficient should be preferably evaluated by measuring the response of an ion selective electrode in solutions of the primary ion, salicylate, and interfering ion, (fixed interference method). Selectivity coefficient ($K^{\text{Pot}}_{\text{sal},A^-}$) for various anions were evaluated by the mixed solution method with a fixed concentration of interference ion, and varying amounts of salicylate concentrations. Table IV lists the potentiometric selectivity coefficient data of the sensor for several anions compared to salicylate. The selectivity coefficients clearly indicate that the electrode is selective to salicylate over a number of other inorganic and organic anions. In this work, interference studies were made for F^- , Cl^- , Br^- , I^- , CH_3COO^- , SCN^- , CN^- , CrO_4^{2-} , CO_3^{2-} , PO_4^{3-} and other ions.

As can be seen from Table IV, the interfering effect of the ions is in the following order:



The sequence is characterized by the Hofmeister series:



The reason that the selectivity coefficients of this electrode do not comply with the Hofmeister series, and show an anti-Hofmeister behavior, is thought to be the possible interaction of the anions with Al .^{30,31} However, the selectivity coefficients of the salicylate-selective electrode compared to the other anions investigated are in good compliance with the literature data. Certainly, an obvious advantage of this electrode in comparison with other salicylate selective electrodes is its good selectivity coefficient.

As evident from the data in Table IV, the AlL_2 -doped membrane electrode displayed substantially improved selectivity for salicylate compared to several other anions. Most of these anions would be expected to interfere seriously with the classical anion-exchanger-type membrane electrodes. The high selectivity for salicylate compared to perchlorate, thiocyanate and iodide clearly deviates from the conventional Hofmeister anion response pattern and suggests that salicylate is directly interacting with the AlL_2 as an axial ligand. The strength of this interaction, relative to other anions, dictates the observed selectivity pattern of the electrode. The hard metal center in ionophore endows a strong oxophilic character to the complex and interacts strongly with the carboxylate group of salicylate, which acts as a hard base. This correlates well with the stability constant of salicylate complex with

TABLE IV. Selectivity of coefficients, determined by the fixed interference method, for the salicylate-selective electrode

Interfering ion	$\log K^{\text{Pot}}_{\text{sal},A^-}$	Interfering ion	$\log K^{\text{Pot}}_{\text{sal},A^-}$
F^-	-5.9	PO_4^{3-}	-4.6
Cl^-	-5.3	CO_3^{2-}	-4.5
Br^-	-4.1	ClO_3^-	-4.1
I^-	-3.1	SO_4^{2-}	-5.0
CN^-	-4.0	$S_2O_3^{2-}$	-4.6
SCN^-	-3.0	ClO_4^-	-2.8
OAc^-	-5.6	CrO_4^{2-}	-3.8
NO_3^-	-4.2	NO_2^-	-4.5
$C_2O_4^{2-}$	-4.9	-	-

TABLE V. Comparison of the potentiometric parameters of the proposed Sal⁻-selective electrode with other Sal⁻-selective electrodes

A ⁻	Nernstian slope mV decade ⁻¹	Linear range mol L ⁻¹	Limit of detection mol L ⁻¹	Response time s	Interfering ions $K_{\text{sal}^-, \text{A}^-}^{\text{pot}} > 1.0 \times 10^{-2}$
The proposed Sal-ISE	-59.1 ± 0.4	1.0×10 ⁻⁶ – 1.0×10 ⁻¹	5.0×10 ⁻⁷	10–15	–
Ref. 11	-54.3	5.0×10 ⁻⁶ – 1.0×10 ⁻¹	1.9×10 ⁻⁶	60	ClO ₄ ⁻ , SCN ⁻
Ref. 13 Ionofores ^(a)				20–30	
I	-58.9	1.0×10 ⁻⁶ – 1.0×10 ⁻¹	1.0×10 ⁻⁶		ClO ₄ ⁻ , I ⁻ , SCN ⁻ , OH ⁻
II	-59.0	1.0×10 ⁻⁵ – 1.0×10 ⁻¹	4.0×10 ⁻⁶		SCN ⁻ , OH ⁻
Ref. 17	-55	1.0×10 ⁻⁵ – 1.0×10 ⁻¹	1.0×10 ⁻⁵	120–1200	IO ₄ ⁻ , I ⁻ , SCN ⁻ , ClO ₄ ⁻ , Br ⁻
Ref. 21 Ionofores ^(b)				–	
I	-50 ± 2	2.5×10 ⁻⁴ – 1.0×10 ⁻¹	8.0×10 ⁻⁵		–
II	-54 ± 1	1.0×10 ⁻⁴ – 1.0×10 ⁻¹	4.0×10 ⁻⁵		ClO ₄ ⁻ , SCN ⁻ , I ⁻
III	-53 ± 2	8.0×10 ⁻⁵ – 1.0×10 ⁻¹	1.3×10 ⁻⁵		ClO ₄ ⁻
IV	-41 ± 1	3.0×10 ⁻⁴ – 1.0×10 ⁻¹	8.0×10 ⁻⁵		ClO ₄ ⁻
V	-41 ± 1	3.0×10 ⁻⁴ – 1.0×10 ⁻¹	8.0×10 ⁻⁵		ClO ₄ ⁻ , SCN ⁻
Ref. 32	-60 ± 2	1.0×10 ⁻³ – 1.0×10 ⁻¹	6.0×10 ⁻⁴	30–300	I ⁻ , Benzoate
Ref. 33	-59.1	1.0×10 ⁻⁷ – 1.0×10 ⁻¹	1.0×10 ⁻⁷	20	I ⁻ , ClO ₄ ⁻ , N ₃ ⁻ , NO ₂ ⁻ , NO ₃ ⁻ , SCN ⁻
Ref. 34	-59.6 ± 1.0	1.0×10 ⁻⁶ – 1.0	5.0×10 ⁻⁷	5–10	–

^(a) Ionofores I and II are Al(salophen) and Sn(salophen), respectively.

^(b) Ionofores I, II, III, IV and V are aluminium tetrakis-*tert*-butylphthalocyanine chloride (PcAlCl), PcCu, PcSnCl₂, PcLuOAc, and PcDyOAc, respectively. Pc: tetrakis-*tert*-butylphthalocyanine chloride.

Al^{III}, log $K_1 = 12.9$. From the data given in Table IV, it is immediately obvious that the salicylate-ISE is highly selective compared to other inorganic and organic anions. This is most probably due to the weak interaction between these anions and the ionophore.

It seems that the complex [bis(2-hydroxyl imino)1-phenyl,2-(2-quinolile)1-ethanona]Aluminium(III) exists as [Al(L)₂(H₂O)₂]⁺ in aqueous solutions and that H₂O groups occupy the axial position of an octahedral coordination environment around the central metals. The following mechanism may be proposed for the potentiometric response of the membranes to salicylate.¹³

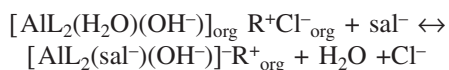
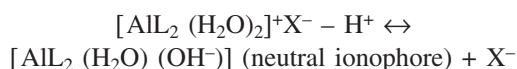
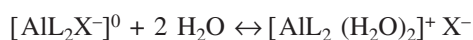


Table V lists the linear range, detection limit, slope, response time and selectivity coefficients of some of other salicylate-selective electrodes against the proposed salicylate-selective electrode for comparative purposes.^{11,13,17,21,32–34} As can be seen from the table, the selectivity coefficients obtained for the proposed electrode are superior to those reported for other salicylate-selective electrodes listed in Table V. It is noteworthy that the limit of detection, linear range, slope and response time of the proposed electrode show somewhat similar, in most cases considerably improved performance compared to those of the previously reported salicylate-selective electrodes.

Analytical Applications

The proposed electrode was used for determination of the salicylate content of hydrolyzed pharmaceutical preparations. Tablets of different aspirin samples were treated according to the procedure described above, and the resulting solutions were used to determine the salicylate

TABLE VI. Determination of salicylate in different aspirin tablets ($n = 10$).

Aspirin samples mg/tablet	Spectrophotometric methods	ISE
100	97.2 ± 0.3	97.4 ± 0.3
325	323.0 ± 0.2	323.4 ± 0.3
500	472.0 ± 0.7	463.0 ± 0.9

content by potentiometric and spectrophotometric methods. The results are compared with the standard spectrophotometric method.³⁵ The results obtained by the electrode method (Table VI) are in good agreement with those obtained by the spectrophotometric method, emphasizing the potentials of the proposed analytical procedure.

CONCLUSION

The results of this study show that the AIL₂ based membrane electrode may provide an attractive alternative for salicylate detection. This electrode is very easy to prepare and use, and shows a Nernstian response. Very low detection limit, wide dynamic range, good selectivity, rapid response time and relatively long term stability make this electrode suitable for measuring the concentration of salicylate in real samples, without the need of preconcentration or pretreatment steps and without any significant interaction from other anionic species present in the samples.

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SAŽETAK**Kompleks Al^{III} i bis(2-hidroksilimino)1-fenil, 2-(2-kunolile)1-etanona kao neutralni prenositelj za elektrodu selektivnu na salicilatni anion****M. Mazloun Ardakani, A. Sadeghi, J. Safari i F. Shibani**

Razvijena je elektroda selektivna na salicilatni anion koja se zasniva na kompleksu Al^{III} s bis(2-hidroksilimino)1-fenil,2-(2-kunolile)1-etanonom kao neutralnom prenositelju u membrani. Elektroda pokazuje dobar nagib od -59.1 ± 0.4 mV/dekadi (srednja vrijednost \pm standardna devijacija, $n = 5$) i raspon linearnosti od 1.0×10^{-6} do 1.0×10^{-1} mol/L salicilata. Granica detekcije je 5.0×10^{-7} mol/L. Vrijeme odziva elektrode je 15 s, a stabilna je dulje od tri mjeseca. Koeficijenti selektivnosti su određeni metodom fiksne interferencije i mogu se koristiti u pH području od 2.0 do 7.8. Elektroda je primijenjena za određivanje salicilata u farmaceutskim pripravcima.