A Novel Al^{3+}-Selective Potentiometric Sensor Based on Nickel (II) Complex of Bis(Thiosemicarbazone) Macrocyclic Ligand as a Neutral Carrier and its Application in Biological Fluids

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ABSTRACT

A novel PVC membrane electrode for Al^{3+} ion based on nickel(II) complex of bis(thiosemicarbazone) macrocyclic ligand as a suitable ionophore was prepared. The electrode exhibits a Nernstian response for Al^{3+} ion over a wide concentration range (4.0 × 10^{-8} to 1.0 × 10^{-1} M) with a slope of 19.85 ± 0.29 mV/decade. The limit of detection is 2.0 × 10^{-8} M. A response time of 11 seconds is possessed by the electrode, and its useful working pH range extends from 2 to 11. The membrane sensor that has been developed demonstrates excellent discriminating capabilities with regard to the Al^{3+} ion in relation to a number of alkali, alkaline earth transition, and heavy metal ions among others. As an indicator electrode in the potentiometric titration of Al^{3+} ion with EDTA, it was successfully utilized in the determination of aluminum ion in biological fluids.

Keywords: Aluminum(III) sensor; Potentiometry; PVC membrane; Macrocyclic ligand; Biological fluid.

1. INTRODUCTION

In terms of abundance, aluminum is the second most prevalent element in the crust of the planet. In each and every aspect of life, it has applications and implications that are significant. There is an extremely minute amount of it being found in the human body. It is hypothesized that certain neurodegenerative diseases, such as Parkinson's disease, Alzheimer's disease, and dialysis encephalopathy, are caused by an unusually high quantity of aluminum in the brain [1-4]. Due to the fact that aluminum is a highly reactive metal, its distribution in the human body is most likely in the form of its ionic species. As a result, it is extremely important to accurately determine the amount of aluminum ions present. It is not possible to reduce the amount of aluminum ion when there is a presence of H$^+$ ion and ions of both alkali and alkaline earth metals there [5]. Extremely few efforts have been documented in relation to the direct detection of aluminum ions, particularly aluminum ions, by the use of electro-analytical techniques [6]. However, Al^{3+}-selective sensors that have been described in the past have a number of drawbacks, including low selectivity [7-9], considerable interferences from cations (such as Ba^{2+}, Hg^{2+} and Pb^{2+}), a narrow working concentration range, a high reaction time, and a short life duration, among other drawbacks.

In addition to their specific chemical features, double cavity bis(thiosemicarbazone) ligand also serve a specific biological purpose. Their characteristics allow for geometric and cavity control of host–guest complexation, which results in exceptional selectivity, sensitivity and stability for a particular ion. These characteristics could lead to their utilization as a sensing carrier for an ion selective electrode. Researchers started producing the sensor materials themselves as a result of the rising expense of chemicals. Over the past few years, there has been a rise in the significance of the synthesis of ionophore molecules. These molecules are present in the composition of ion-selective sensors and exhibit significant functional groups within their structure.

An Al^{3+}-selective electrode that contains a newly synthesized nickel(II) complex of bis(thiosemicarbazone) macrocyclic ligand as ionophore is described in this study. Additionally, the article discusses the applicability of this electrode in the analysis of biological fluids. Currently available ISE exhibits a higher selectivity towards the Al^{3+} ion, while also exhibiting little interference from the cations of alkali and alkaline earth metals, as well as other heavy metal cations. In addition, it has a quick response time, improved repeatability, a relatively long lifetime, and a wide working concentration range when it comes to identifying the Al^{3+} ion.

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2. EXPERIMENT

All reagents used were of analytical-reagent grade. Doubly distilled deionized water was used throughout. High molecular weight poly(vinyl chloride) (PVC) was used as received from Fluka. The plasticizer, bis(2-ethylhexyl)sebacate (BES), tris(2-ethylhexyl) phosphate (TEHP), benzyl acetate (BA), 2-nitrophenyl octyl ether (NPOE), sodium tetra phenyl borate (NaTPB) and oleic acid (OA) were obtained from Sigma-Adrich (USA), dibutyl (butyl) phosphonate (DBBP) from Mobil (USA), dibutylphthalate (DBP) and dioctylphthalate (DOP) from Reidel (India) were used.

Synthesis of nickel(II) complex of bis(thiosemicarbazone): 1,10-(4,10-Dimethyl-1,4,7,10-tetraazacyclododecane-1,7-diyl)bis(propan-2-one) (**1**) was synthesized according to previously published methods [10]. In brief, to a solution of compound (**1**) and 4-methyl-3-thiosemicarbazide in EtOH (40 mL) was added 7 drops of glacial acetic acid. The solution was stirred for full two days at room temperature. The precipitate was collected on a vacuum glass frit, washed with EtOAc and Et$_2$O to afford a bright yellowish solid (yield: 35%). In the next step, a solution of bis(thiosemicarbazone) in methanol (10 mL) was added a Ni(NO$_3$)$_2$·6H$_2$O solution and then the solution was left to stir for 17 h at ambient temperature. Then, a solution of sodium tetraphenylborate in methanol (3 mL) was added and the resulting suspension was stirred for an additional 10 h at ambient temperature. The product was collected and washed with diethyl ether.
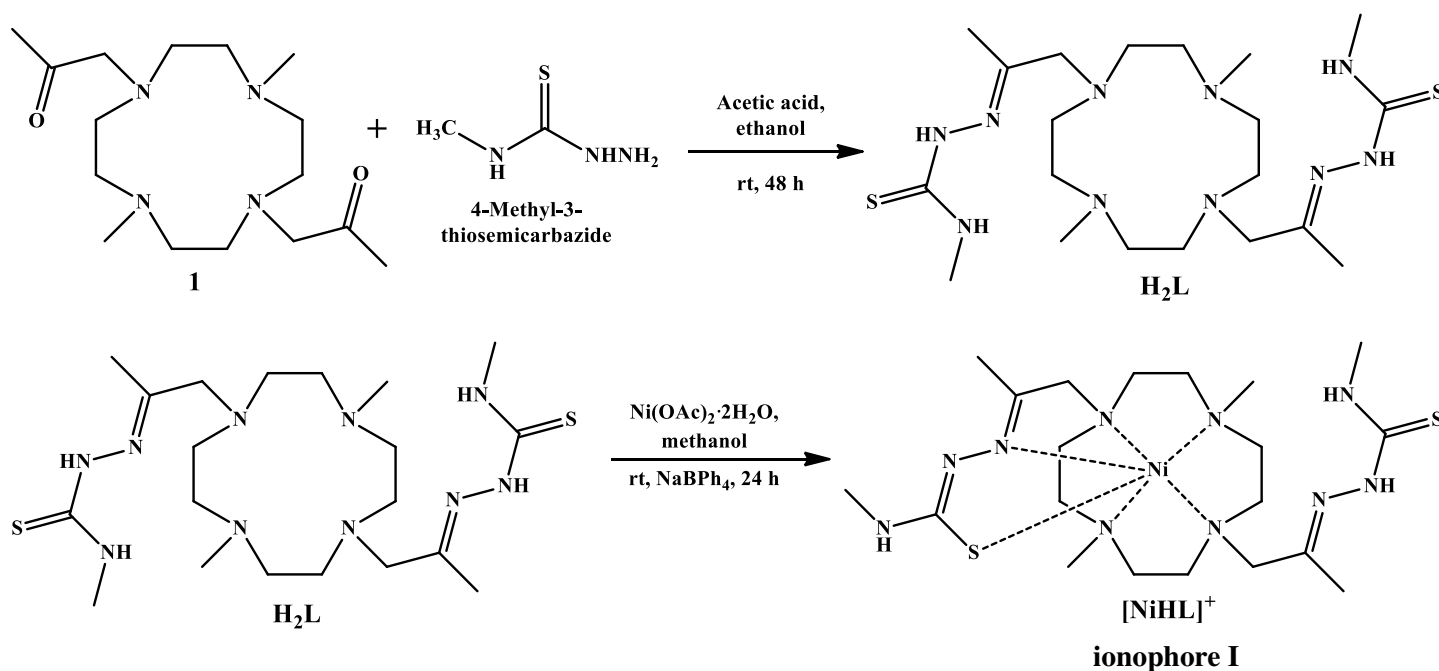
Electrode preparation

The general procedure to prepare the PVC membrane was to thoroughly mix 40 mg powdered PVC and 50 mg plasticizer DBP in 10 ml THF. To this mixture was added 20 mg oleic acid and 10 mg ionophore and the solution was mixed well. The resulting mixture was transferred into a glass dish of 2 cm diameter. The THF was evaporated slowly until an oily concentrated mixture was obtained. A Pyrex tube (3–5 mm o.d.) was dipped into the mixture for about 10 s so that a non-transparent membrane of about 0.3 mm thickness was formed. The tube was then pulled out of the solution and kept at room temperature for 1 h. The tube was filled with internal filling solution 1.0×10^{-1} M Al(NO$_3$)$_3$. The electrode was finally conditioned for 24 h by soaking in a 1.0×10^{-1} M solution of aluminum. A silver/silver chloride coated wire electrode was used as an internal reference electrode.

EMF measurements

All the potentiometric measurements were made with an Elico-LI-Model-120 pH meter. The electrochemical system was as follows:

Ag–AgCl/1.0×10^{-1} M Al(NO$_3$)$_3$/PVC membrane / test solution / Ag–AgCl

Stated solutions of Al(NO$_3$)$_3$ were obtained by dilution of 0.1 M Al(NO$_3$)$_3$ solution. As the pH of pure solutions lies in the functional range of the sensor, one does not require any pH adjustment.

Preparation of sample solution

Sucralfate, which is used for the treatment of peptic ulcer disease, is purchased from Ranbaxy Pharmaceutical Co., India. The sample solution was prepared by soliciting one tablet sucralfate (0.25 g) in 250 ml and further diluted 100 times in order to get the final solution.

3. RESULTS & DISCUSSION

Several parameters were investigated in order to evaluate the performance of the aluminum(III) ion-selective electrodes based on ionophore I in terms of membrane composition, calibration curve slopes, reproducibility, linear range, limit of detection, response time, selectivity and sample analysis. The influence of the concentration of internal solution in the PVC based ionophore I membrane electrode on its potential response was studied. The Al(NO$_3$)$_3$ concentration was changed from 1.0×10^{-4} to 1.0×10^{-2} M and the emf pAl^{3+} plots were obtained. It was found that the variation of the concentration of the internal Al^{3+} solution does not cause any significant difference in the potential response, except for an expected change in the intercept of the resulting Nernstian plots. A 1.0×10^{-3} M concentration of the reference solution is quite appropriate for smooth functioning of the system.

The optimum equilibration time, in a 1.0×10^{-3} M solution of Al(NO$_3$)$_3$, for the PVC based ionophore I membrane electrode is 48 h, after which they generate stable potentials when placed in contact with Al^{3+} solutions. The critical response characteristic of Al^{3+} electrode was assessed according to the IUPAC recommendations [11]. The emf responses of the membrane sensor at varying concentration of aluminum ions (Fig. 2) shows linear range from 4.0×10^{-8} to 1.0×10^{-1} M (slope 19.58 ± 0.3 mV dec^{-1}). The limit of detection, as determined from the intersection of the two extrapolated segment of the calibration of the calibration graph was 2.0×10^{-8} M.

The membrane containing no plasticizer (membrane no. 1) gave a working concentration range of 7.9×10^{-6} – 1.0×10^{-1} M with a slope of 18.6 ± 0.5 mV/decade of activity. All other membranes containing amount of ionophores and PVC but one or another type of plasticizers used in this study (in same quantity), except TEHP, exhibited slopes in the close vicinity of recommended range for various metal ions. As far as response time is concerned, it was 15 s for the membrane without plasticizer and 12, 10, 10, 10, 12, 10, 15 and 13 s for membranes nos. 2, 3, 5, 6, 7, 8, 9 and 10, respectively, but for TEHP containing membrane (no. 4), the response time was 25 s. Also as seen, among the different plasticizers used, BA was found to be the most effective solvent mediator in preparing the Al^{3+}, ion-selective electrode, although the use of NPOE as plasticizer is also promising (No. 9 and 10, respectively). However, the use of NPOE was found to largely increase the interfering effect of some other cations of higher charge density like Cu^{2+}, Cd^{2+} and Sm^{3+} ions. The nature of plasticizer is known to influence both the dielectric constant of the membrane and the mobility of ionophore and its cation complex [12,13].

Also as seen in Table-1, in the absence of a proper lipophilic additive, the sensitivity of the PVC-membranes is quite low (Nos. 1-3). However, the presence of some 5% OA (No. 8) or 3% NaTPB (No. 9) resulted in increased sensitivity and a more or less Nernstian behaviour of the membrane sensor, as expected [14-18]. Meanwhile, it was found that, maximum membrane selectivity towards aluminum(III) ion can be obtained in the presence of 5% OA as a suitable additive. As it is seen from Table-1, membrane No. 8 with a PVC:BA:OA:I percent ratio of 60:33:5:2 resulted in the Nernstian behavior of the membrane electrode over a very wide concentration range.
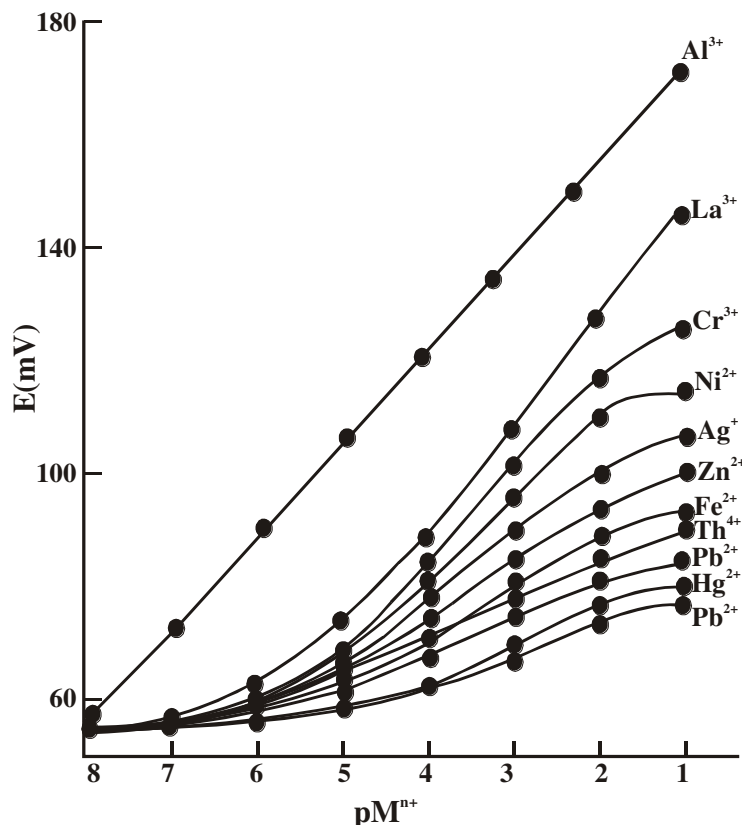
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Figure 2: Potential response of various ion selective membrane electrodes based on ionophore I

Effect of non-aqueous solvent

The Nernst equation ($E = E^o + R/nF\theta$) is obeyed is as many organic solvents as in water. It has been observed that the constant E^o is more negative in the presence of organic solvents than in pure aqueous medium, and its value depends on both the nature of the solvent and the pH of the medium. The shift is mainly due to the asymmetric potential across the membrane of the electrode because of the presence of different solvents on either side of its. The Membrane electrodes containing plastic matrixes should be used in organic solvents, which might affects the working of the membrane electrode. In present work, the studies of PVC-based membrane electrodes in different non-aqueous media have been carried out. Therefore, the partially non-aqueous solutions using organic solvents were prepared for each membrane. Their potentials were measured for a series of primary ion concentration to ensure the effect on working concentration range as well as its slope. Thus, the electrode response for Al^{3+} as a representative case was studied in different mixed-aqueous media-methanol, ethanol, acetone and dioxane water (30–70% v/v) (Table-2). The calibration plot is plotted in each case and the slope of the curve is compared with the aqueous system (Table-2). It is observed that the electrodes are stable in methanol and ethanol systems media up to 50%, but the matrix swelled continuously in higher proportions of methanol and ethanol after a few hours, while in the other solvent systems show a deviation of slopes in their calibration studies in comparison with the aqueous systems. The response of the electrode in 50% methanol and ethanol-water systems is steady up to 30 h, after which the potential deviates (Table-2).

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Table 1: Composition and response characteristics of PVC-based Ionophore I membranes selective for Al^{3+} ions

		1	2	3	4	5	6	7	8	9	10
Response time (s)		15	12	10	25	10	10	12	10	15	13
Slope (mV/decade of activity)		18.6	25.8	25.0	27.9	21.5	26.6	25.2	19.58	18.20	19.20
Working conc. range (M)		7.9×10^{-6}–1.0×10^{-1}	3.2×10^{-4}–1.0×10^{-1}	9.8×10^{-5}–1.0×10^{-1}	4.0×10^{-5}–1.0×10^{-1}	1.0×10^{-5}–1.0×10^{-1}	1.2×10^{-5}–1.0×10^{-1}	9.2×10^{-5}–1.0×10^{-1}	4.0×10^{-8}–1.0×10^{-1}	6.2×10^{-6}–1.0×10^{-1}	7.1×10^{-7}–1.0×10^{-1}
% w/v composition of each membrane	PVC	97	64	65	64	65	64	64	60	64	60
	NaTPB	–	–	–	1	1	1	1	–	–	–
	Ionophore	3	3	3	2	2	2	2	2	3	2
	OA	–	–	–	–	–	–	–	5	–	6
	NPOE	–	–	–	–	–	–	–	–	33	32
	BA	–	–	–	–	–	–	–	33	–	–
	DOP	–	–	–	–	–	33	–	–	–	–
	BES	–	–	–	–	32	–	–	–	–	–
	TEHP	–	–	–	33	–	–	–	–	–	–
	DBBP	–	–	32	–	–	–	–	–	–	–
	DBP	–	33	–	–	–	–	–	–	–	–
Electrode no.		1	2	3	4	5	6	7	8	9	10

Response and lifetime of the electrode

The average time required for the Al^{3+} sensor to reach a potential within ± 1 mV of the final equilibrium value after successive immersion in a series of Al^{3+} solutions, each having a 10-fold difference in concentration, was measured. The dynamic response time thus obtained was less than 10 s in the whole concentration ranges. The potentials remained constant for more than 6 min, after which only a very slow divergence was recorded (± 2.5 mV). Lifetime of the proposed sensor was evaluated by the measuring the slope of the three sensors during ten weeks. Each sensor was used for one hour per day (after using, it was washed and dried). After nine weeks, the slopes of Al^{3+} ion-selective membrane sensors reduces gradually from 19.58 ± 0.3 to 16.2 ± 0.5 mV/decade.

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Table 2: Electrode response time and electrode response slopes in 50% (v/v) Non-aqueous solvents media of PVC based Al^{3+} selective electrode

Time (s)	Al(III) Response Time (mV decade^{-1})				Al(III) response slopes (mV decade^{-1})	
	Dioxane (50%)	Acetone (50%)	Ethanol (50%)	Methanol (50%)	Solvent	Slope
00	20	23	28	28	Methanol	20.0
05	35	33	28	28	Ethanol	19.5
10	50	45	28	28	Acetone	25.0
15	70	65	28	28	Dioxane	14.0
20	100	90	37	25		
25	120	100	38	20		
30	140	70	37	22		
35	140	80	27	17		
40	156	97	16	10		
45	156	125	–	–		
50	160	190	–	–		

pH effect

Effect of pH on the response of the sensor was studied over two different concentrations (10^{-3} M and 10^{-2} M) of Al^{3+} ions. Studies were carried out over a pH range of 1-12. Addition of HCl or NaOH drop wise adjusted the pH. The potential difference is independent of pH in the range 3-11 (figure 3). Therefore, this can be taken as the working pH range for the proposed electrode system. Since, at pH value lower than 4, a decrease in potential is observed, probably the electrode start responding to H^+ ions. At pH greater than 12, the deviation can be assigned to the formation of $Al(OH)_3$ precipitates.
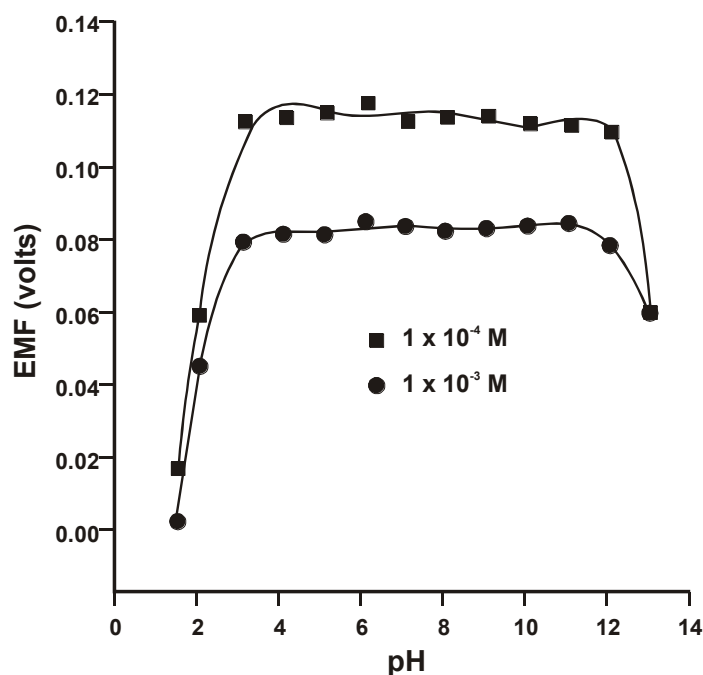

Figure 3: Effect of pH of test

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Selectivity coefficients

In addition to the Nernstian behaviour, linear range and detection limit, the selectivity of the membrane sensor for Al^{3+} ions over the other metal cations is also of fundamental importance. Thus, the selectivity of the membrane electrode was tested by its potential response measurement in the presence of a wide variety of cations including alkaline earth, transition and heavy metal ions. The selectivity coefficients K_{Al}^{Pot}, were evaluated graphically by the mixed solution method [19]. Here, the fixed concentration of interfering ions (1×10^{-5} M) was used against the varying concentration of the primary ions.

The fixed interference method is based on the semi-empirical Nikolsky-Eisenman equation (1).

$$E_{ISE} = E^o \pm \frac{RT}{Z_A F} \ln \left[a_A + \sum K^{pot}_{A,B} (a_B)^{ZA/ZB} \right] \qquad (1)$$

It is quite well known that the above equation works well in modeling the non-specific response of a membrane when the ions under investigation have the same charge, *i.e.*, $Z_A = Z_B$, but the same is not well suited for ions having different charges i.e., $Z_A \neq Z_B$. Coefficients are either deceptively large or small depending on whether the ion of higher charge is considered as primary or interfering species. However, it is seen that Pb^{2+}, which is a serious interference with other aluminum sensors [20-22] does not cause any interference at all with the present one, meanwhile, the proposed electrode is also working smoothly even in the presence of Ba^{2+} & Hg^{2+}, which do cause interference to some extent to the previously reported electrode prepared in this laboratory [23] (table 3).

Table-3: Selectivity coefficients (K_{ij}) Values of PVC-based Ionophore I membranes selective for Al^{3+} ions for different cations

Metal Ions	Selectivity coefficients values (K_{ij})	Metal Ions	Selectivity coefficients values (K_{ij})
Mg^{2+}	0.40×10^{-4}	Co^{2+}	0.47×10^{-3}
Ca^{2+}	0.28×10^{-4}	Ni^{2+}	0.44×10^{-3}
Sr^{2+}	0.27×10^{-4}	Mn^{2+}	0.22×10^{-3}
Ba^{2+}	0.37×10^{-4}	Pb^{2+}	0.67×10^{-3}
Cd^{2+}	0.05×10^{-4}	Fe^{3+}	0.08×10^{-3}
Hg^{2+}	0.76×10^{-4}	Bi^{3+}	0.85×10^{-3}
Zn^{2+}	0.21×10^{-3}	Th^{4+}	0.69×10^{-4}
Cu^{2+}	0.29×10^{-3}	UO_2^{2+}	0.54×10^{-4}

The proposed aluminum ion-selective electrode is found to work well under laboratory conditions. This electrode can be used as an indicator electrode in the titration of Al^{3+} with EDTA, and the resulting titration curve is shown in (Fig. 3). As shown, the amount of Al^{3+} ions in solution can be determined with this electrode.

Applications

The proposed electrode is also used for the indirect determination of aluminum in biological fluids. Under the optimum range of the experimental conditions (pH 8.75, 1×10^{-2} M Al^{3+} and 0.03 M NH_4OAc-$NH_3 \cdot H_2O$ buffer solution), the linear range $4.75 \times 10^{-8} – 3.25 \times 10^{-7}$ M has the detection limit of aluminum of 1.0×10^{-8} M and the relative standard deviation for 4×10^{-6} M Al^{3+} is 3.1 % (N = 7).
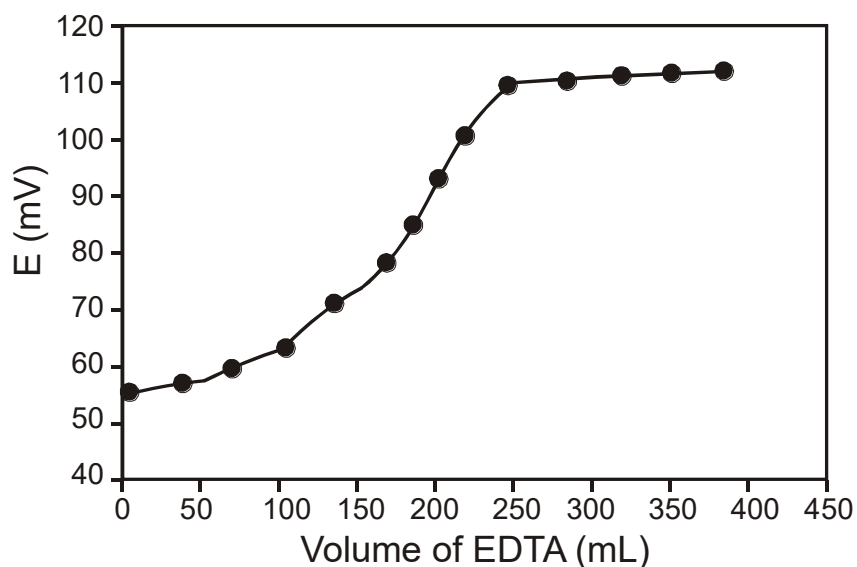
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Figure 4: Potentiometric titration curve of 20.0 mL of 1.0×10^{-3} M Al^{3+} with 1.0×10^{-2} M EDTA using the proposed membrane electrode as an indicator electrode

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