Polymeric membrane ion-selective electrode for determination of bismuth (III) in pharmaceutical substances

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Abstract

A PVC-based membrane of tridecylmethylammonium chloride reveals a Nernstian potentiometric response (with slope of 55 mV/decade and a correlation coefficient of 0.99) for complex of bismuth (III) with ethylenediaminetetraacetate-anion $[Bi(EDTA)]^-$ over a wide concentration range (1×10^{-1} to 3×10^{-5} mol/l). The potential of this electrode is independent of pH in the range of 4.0–11.0. It has a fast response time of about 30 s and was used for a period of 3 months with good reproducibility. The detection limit of this membrane electrode was 1×10^{-5} M. This sensor exhibits a very good selectivity for [Bi(EDTA)] over a wide variety of complex metal ions with ethylenediaminetetraacetic acid. The proposed electrode has been used in the direct potentiometric monitoring of bismuth (III) in stomach anti-acids. © 2002 Elsevier Science B.V. All rights reserved.

1. Introduction

Clinical/medical interest in bismuth dates back about 70 years, when the element was first introduced in a pharmaceutical used in the treatment of syphilis [1]. Since then, its pharmaceutical uses have expanded to anti-acids, peptic ulcer treatments, and topical dermatological creams. Therefore, there is a necessity for methods to determine bismuth contents in pharmaceutical substances [2].

A variety of techniques have been described for the determination of bismuth with adequate detection limits (≤ 1 μg/l) and specificity for clinical studies. Recent methods such as inductively-coupled plasma atomic-emission spectrometry (ICP-AES) [3], hydride generation (HG)-ICP-AES [4], ICP-mass spectrometry (MS) [5,6], X-ray fluorescence spectrometry [7], electrothermal atomic absorption spectrometry (ETAAS) [8], HG-ETAAS with in situ preconcentration [9] are now widely used for the determination of bismuth in biological and pharmaceutical materials. However, most of these methods suffer from either widespread availability of instrumentation, prohibitive cost, or technical. Because of these considerations, potentiometry with ion-selective electrodes (ISEs) seems attractive for the determination of bismuth in pharmaceutical substances.

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Potentiometric sensors or so-called ISEs have been the subject of continuous research efforts. This group of chemical sensors is characterized as simple in preparation, robust in operation and moderately selective in analytical performance. Some kinds of ISEs become routine devices in analytical laboratories, though one still tries to further improve their performance. Most research works focus on the search for new sensor materials, in particular new carriers with optimized potentiometric response to different chemical species [10–15]. The great development, during latter years, in the field of ISEs [16–22] has evidenced their multiple possibilities for analysis of organic and metalloorganic molecules of biological, clinical, and pharmaceutical interest [23,24]. Research in this direction presents interesting aspects.

Few articles describing bismuth (III)-selective electrodes with liquid membranes have been published. Liquid membrane electrode based on the ion-associate complex trioctylmethylammonium with tetraiodobismuthate incorporated onto a poly(vinyl chloride) matrix was offered [25]. The investigation of a coated copper-sensitive electrode to bismuth (III) based on the chlorobismuthate salt of tricaprylmethylammonium has been proposed by [26]. The substitution of the trioctylmethylammonium by trinonyloctylammonium cation in the preparation of the active material with tetraiodobismuthate (III) was reported by [27]. A liquid membrane ISE, sensitive to bismuth (III) cation on the basis of complex with bismuthiol III, was described by [28]. Liquid membrane electrode based on the ion-associate complex [Bi(EDTA)]$^-$ with tricaprylylmethylammonium cation incorporated onto a coated graphite-epoxy electrode was described recently [29]. However, results, received in work [29], have appeared non-reproducible. Therefore, earlier we carried out all-round researches of similar electrodes [30]. In this work [30] the mechanism of selectivity of electrodes also was offered.

This article describes the preparation and characterization of ion-selective membrane electrode based on tridecylmethylammonium chloride (TDMACl)and sensitive to complex of bismuth (III) with ethylenediaminetetraacetate-anion [Bi(EDTA)]$^-$. These electrodes are useful for direct potentiometric monitoring of bismuth (III) in stomach anti-acids. The advantages of the developed ISE are its simplicity, low cost, fast response, wide pH range and applicability to turbid and coloured solutions.

2. Experimental

2.1. Equipment

Potentiometric measurements at 20 ± 1 °C were made with an I-135 high-impedance pX-meter (Tbilisi, Georgia) using membrane sensor in conjunction with an Radelkis OP-0820P Ag–AgCl double junction reference electrode containing 1 M KNO$_3$ solution in the outer compartment. Adjustment of pH was made with a combination glass electrode. A Perkin Elmer atomic absorption spectrophotometer was used for the determination of bismuth in the samples.

2.2. Reagents and preparation of solutions

All solutions were prepared with deionized water. Dibutyl phthalate (DBP), poly(vinylchloride) (PVC) of relative high molecular mass, tetrahydrofuran (THF), bismuth, dissodic EDTA (Na$_2$C$_{10}$H$_{14}$N$_2$O$_8$·2H$_2$O), NaOH and TDMACl were of analytical reagent grade.

The Na$_4$EDTA solution was prepared by dissolving 372.28 g of Na$_2$C$_{10}$H$_{14}$N$_2$O$_8$·2H$_2$O and 80.00 g NaOH in 1000 ml of water. The Na$_4$EDTA solution was used in the preparation of the Na[Bi(EDTA)] solution.

The bismuth (III) solution was prepared by dissolving 2.0898 g of bismuth with concentrated nitric acid on a hot plate. After dissolution and cooling, this solution was transferred to 100 ml volumetric flask. After that, reference solution of bismuth (III) in EDTA medium was obtained by suitable dilution of the stock solution, with the appropriate amount of EDTA at several pH values.

Metallic cation solution at concentration of 0.01 mol/l in 0.25 mol/l Na$_4$EDTA was used in the potentiometric selectivity coefficients determinations.

2.3. Procedures

2.3.1. Membrane material

The quaternary ammonium cation, tridecylmethylammonium, is a well-known ion-pairing extracting agent and was used to obtain the ion-pair association complex with $[Bi(EDTA)]^-$ anion in membrane phase. TDMACl was embedded in a PVC matrix containing DBP as plasticizer. The membrane composition was 5.0% (w/w) electroactive material (TDMACl), 65.0% (w/w) DBP and 30.0% (w/w) PVC.

2.3.2. Sensor assembly and calibration

The basic principle of the electrode construction is described elsewhere [31,32]. The electroactive material, TDMACl (50 mg), was well mixed with 650 mg of the plasticizer and later with 300 mg of PVC powder dissolved in 10 ml THF. The clear liquids were poured into a 28 mm glass ring on a glass plate. A pad of filter paper placed on the top of the ring was kept in place by a heavy metallic weight, and each assembly was left for 72 h to allow evaporation of the solvent. A disc (9 mm diameter) was cut out from the membrane and fixed to the end of a 10 mm PVC tube using a PVC–THF solution as adhesive. The other end of the PVC tube was fitted onto a glass tube to form the electrode body. A silver–silver chloride wire was inserted and the electrode was filled with an inner filling solution containing 0.01 M Na[Bi(EDTA)] and 0.01 M KCl. The sensor was conditioned by soaking in 1×10^{-2} M aqueous Na[Bi(EDTA)] solution for 24 h and stored in the same solution when not in use.

The membrane sensors were calibrated by immersion in 1×10^{-1} to 1×10^{-6} M Na[Bi(EDTA)] solutions on a background of 0.25 M Na$_4$EDTA and allowed to equilibrate with constant stirring in conjunction with an AgCl–Ag reference electrode. The sensors were stored in bidistilled deionized water between measurements. The electrode potential was recorded as a function of $[Bi(EDTA)]^-$ concentration. The calibration plot obtained was used for subsequent measurements of unknown Na[Bi(EDTA)] concentrations.

2.3.3. Direct potentiometric determination of bismuth in pharmaceutical substances

About 0.5 g of the stomach anti-acids powder was initially dissolved in 5 ml of concentrated nitric acid by heating to decolouration of a solution. The cooled solution was transferred to 100 ml volumetric flask and diluted with bidistilled deionized water. After that, the sample (10 ml) was dissolved in 25 ml of Na$_4$EDTA solution and was transferred to a 100 ml volumetric flask, and this volume was completed with the bidistilled deionized water. The percentage of mass content of bismuth in this sample was determined by the standard addition method and by official volumetric procedure [33].

In this work samples of stomach anti-acids (Russian formula) of the following structure were analysed:

Sample	Drug	Amount of drug
1	Bismuth oxonitrate (BiONO$_3$)	0.25
	Kaolin	0.25
2	Bismuth oxonitrate (BiONO$_3$)	0.35
	Magnesium carbonate (MgCO$_3$)	0.40
	Sodium bicarbonate (NaHCO$_3$)	0.20
	Rutin (C$_{27}$H$_{30}$O$_{16}$)	0.01
3	Bismuth oxonitrate (BiONO$_3$)	0.35
	Magnesium carbonate (MgCO$_3$)	0.40
	Sodium bicarbonate (NaHCO$_3$)	0.20
	Vegetative extract	0.05

3. Results and discussion

3.1. Electrode response and system suitability

Typical calibration graphs for the [Bi(EDTA)]⁻-membrane sensor performed with solutions in the range 10^{-1} to 10^{-6} mol/l show that a linear response is observed in the range 1.0×10^{-1} to 3.2×10^{-5} mol/l for the sensor, in 0.25 M Na_4EDTA solution (pH 8.0), as shown in Fig. 1.

To ascertain the resolution and reproducibility of the potentiometric method, system suitability tests were carried out using working standard solutions of Na[Bi(EDTA)]. This solution was spotted five times, and parameters such as intercept, linear range, slope, limit of detection (LOD) and response time were studied. Their average values, along with relative standard deviation (RSD) values, are presented in Table 1. RSD of limit of quantification for [Bi(EDTA)]⁻ ISE was 8.5%. These values are considered to be good enough for a reasonable accuracy in most of the laboratories worldwide.

Table 1
System suitability and detection/quantification limits in Bi determination with ISE ($n = 5$)

Parameters	[Bi(EDTA)]⁻-ISE
Intercept	−33.7
RSD (%)	2.4
Linear range (M)	1.0×10^{-1} to 3.2×10^{-5}
Slope (mV/pC)	55.4
RSD (%)	2.3
LOD (μg Bi/ml)	2.0
RSD (%)	10.1
Response time (min)	2.5
RSD (%)	30.3

3.2. Linearity

The plot of potential ISE versus the respective concentration of Na[Bi(EDTA)] was found to be linear in the concentration range 1.0×10^{-1} to 3.2×10^{-5} mol/l ($20.9 – 6.7 \times 10^{-3}$ mg Bi/ml). It was represented by the linear regression equation $E = 55.36 \times pC - 37.7$.

The correlation coefficient (r) was 0.99991. The r-value was found to be close to 1. The r^2 statistic indicates that model as fitted explains 99.98% of the variability in potential.

3.3. Effect of pH

The effect of pH on the potential of the sensor was checked by recording the emf of a standard cell and varying the acidity by the addition of small volumes of hydrochloric acid and/or potassium hydroxide solution (2.0 mol/l each). The graph presented in Fig. 2 shows the linearity in the range 4–11 of the potential E (mV) versus pH function. For pH values less than 4 there is a decrease in the potential of the electrode due to the protonation of the $[EDTA]^{4-}$ anion. In the pH range of 4–11, [Bi(EDTA)]-complex does not suffer influence of the medium, which demonstrates that the Bi(III) complex with Na_4EDTA is sufficiently stable ($K_f = 6.3 \times 10^{27}$). At pH values higher than 11–12 the potentials changed quickly because of the interference of the hydroxide anion (because of destruction of a complex).
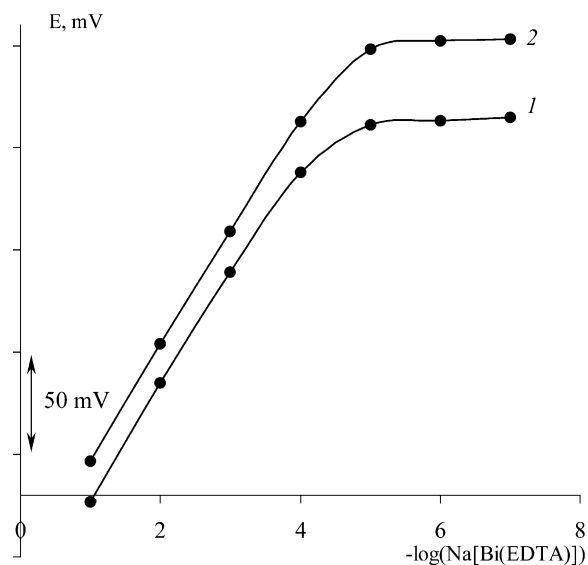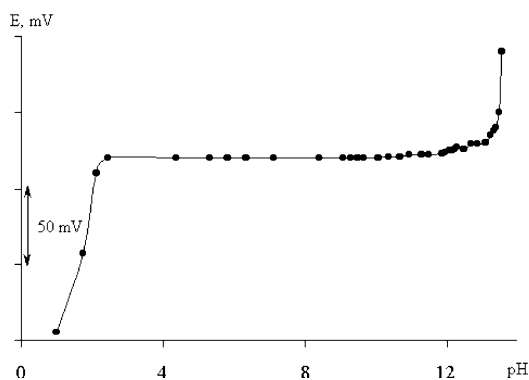

Fig. 1. The electrode response of the bismuth (III) ISE on a background of 0.25 M Na_4EDTA solution: (1) electrode without preliminary conditioning; (2) electrode after 4 weeks of conditioning in 0.01 mol/l Na[Bi(EDTA)] solution.

Fig. 2. Effect of pH on the response of [Bi(EDTA)]⁻-selective electrode.

3.4. Selectivity of the electrode

Potentiometric selectivity coefficients were evaluated by the mixed solution method [34] over a wide variety of complex metal ions with ethylenediaminetetraacetic acid. The data are presented in Fig. 3. Strong interfering influence render of lipophilic anions—$ClO_4^- > SCN^- > I^- > NO_3^-$

—and also complexes of Tl^{3+}, In^{3+}, Hg^{2+} with EDTA. There was no response of the sensor to a number of potentially interfering ionic excipients (kaolin, talc, organic acids, amino-acids, glucose or starch) usually used in the manufacturing of the stomach anti-acids.

3.5. Pharmaceutical preparation assay, and accuracy and precision evaluation

The electrode proved useful for the assay of the bismuth (III) content in stomach anti-acids by using the standard addition method. Table 2 shows the results obtained for bismuth (III) determination in stomach anti-acid powder sample using potentiometric and atomic absorption spectroscopy methods and by official volumetric procedure [33]. The results are in good agreement and are within an acceptable range of error, indicating that electrode can be utilized for a determination of this species in various samples. To confirm the accuracy of the proposed method, recovery experiments were carried out by stan-
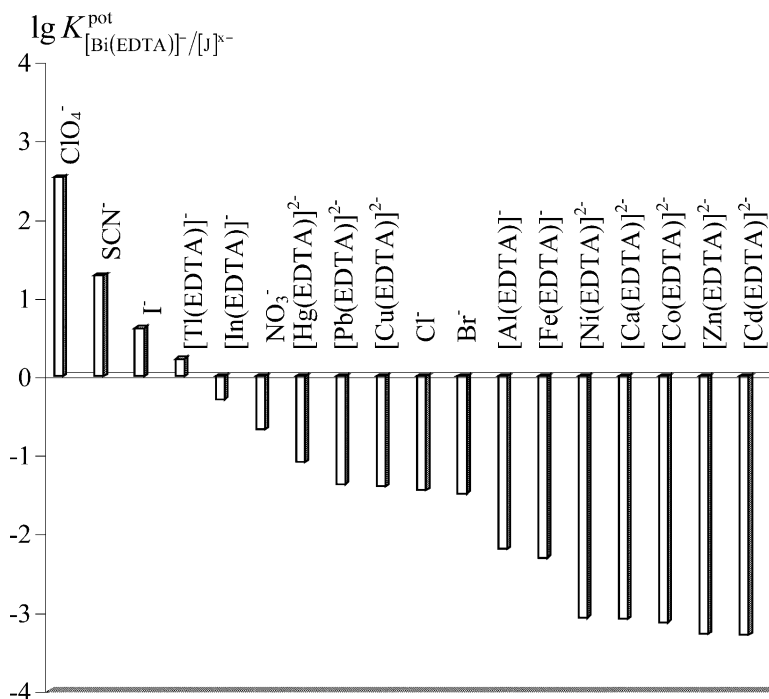

Fig. 3. Potentiometric selectivity coefficient values for the bismuth (III) ISE ($\log K^{pot}_{[Bi(EDTA)]^{-1}/[J]^{x-}}$) in 0.25 M Na₄EDTA solution.

Table 2
Comparison of mean values of potentiometric method, atomic absorption spectrophotometry method and official volumetric procedure for the assay of bismuth (III) in stomach anti-acids

Sample	Potentiometric method		Atomic absorption spectrophotometry method [8]		Pharmaceutical method [33]	
	Recovery[a]	RSD (%)	Recovery[a]	RSD (%)	Recovery[a]	RSD (%)
1	98.12	1.03	99.44	0.77	98.85	1.12
2	98.53	0.99	99.13	0.65	98.45	0.89
3	99.48	1.12	98.43	0.96	97.96	1.10

[a] % of nominal value. All values were the average of five determinations.

dard addition technique by adding a known amount of standard at four different levels to the pre-analysed sample. Each level was repeated five times ($n = 5$).

Usually, the potentiometric determination could be performed within 15 min, in contrast to the longer times required for assay by the official standard method [33]. The proposed potentiometric method presented a better linearity at low concentrations than the official volumetric one. The proposed potentiometric method proved to be reproducible, sensitive and more convenient for routine analysis of the numerous samples generated during in vitro dissolution procedures compared with the official volumetric method and also for the assay of bismuth (III) compounds' pure form and pharmaceutical formulations containing excipient. In comparison with conventional analyses [1–3,8,9,35], this assay is much faster, especially for large number of assays and is extremely economical. This assay is safe and does not cause environmental contamination.

4. Conclusion

The bismuth (III) ISE was prepared, characterized, compared and used for rapid and accurate selective determination of this metallic cation in stomach anti-acids. The advantages of the developed ISE are its simplicity, low cost, fast response, best reproducibility and sensitivity and applicability to turbid and coloured solutions. The developed electrode has a superwide range of pH of functioning in comparison with the de-scribed electrodes. The detection limit obtained in this study was comparable to the literature values [1–3,8,9,35].

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