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Ion-selective electrode for zinc determination in pharmaceutical analysis

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ABSTRACT

An optimal composition for liquid membrane chelating potential phase of a zinc function liquid electrode was established. Its basic analytical parameters, such as the slope of characteristics (29.5 mV pa $_{Zn}^{-1}$), the detection limit (7.3 x 10^{-6} mol L^{-1}), lifetime (50 days), response time (12 s), selectivity against some metal ions, as well as the dependence of the electrode potential on pH, were established. The electrode was used to determine the presence of zinc ions in pharmaceutical formulations. The results obtained were compared with the determination made by use of a voltammetric method.

KEYWORDS

A chelating complex;
Ion-selective electrode for zinc determination;
Drug analysis.

INTRODUCTION

Zinc is an essential element of nutrition and traces are present in a wide range of foods. It is a constituent of many enzyme systems and is present in all tissues. Features of zinc deficiency include growth retardation and defects of rapidly-dividing tissues such as the skin, the immune system, and the intestinal mucosa. Water-soluble zinc salts are used as supplements to correct zinc deficiency; for example, in malabsorption syndromes, during parenteral feeding, in conditions with increased body losses (trauma, burns, and protein-losing states), and in acrodermatitis enteropathica (a rare genetic disorder characterized by severe zinc deficiency). They have been tried in the treatment of a large number of conditions that may be related to zinc deficiency[1,2]. Doses of zinc salts are usually expressed in terms of elemental zinc, and the following salts contain about 50 mg of zinc, three times daily.

The new reagent N-undecyl-N'- (sodium *p*-aminobenzene-sulfonate)- thiourea (UPT) has not only very good sensitivity (ε300.4 nm = 2.39 x 10^5 l mol^{-1} cm^{-1}) but also good selectivity. Experimental data have indicated that these compounds have excellent analytical characteristics[3].

As a result of the search for new, sensitive and selective ways of metal ion determination in pharmaceutical formulations a number of compounds belonging to azo heterodiazo-lylazophenol dyes were synthesized. These compounds form stable chelate complexes with the numerous active metals, including zinc, copper iron, nickel, cobalt, aluminium and bismuth, and are used in spectrophotometric determination of elements[4-6].

Commonly, the analytical methods for the quantitation of zinc are neutron activation analysis (NAA), atomic absorption spectrometry (AAS) and inductively coupled plasma mass spectrometry (ICP-MS), which all base on expensive and sophisticated instruments[7]. Inductively coupled plasma atomic emission spectrometry (ICP-AES) is one of the most used

techniques for the determination of zinc. The most sensitive line for Zn is 213.856 nm. However, this line exhibits spectral interferences from elements like Fe, Ni, and Cu[8].

Zn(II) in biological material, food produce and pharmaceutical preparations was determined using fluorometric methods[9,10] and atomic absorption spectrophotometry (AAS)[11]. In pharmaceutical preparations, Zn(II) was determined by the azo-derivatives of 1,2,4-triazole[12] and benzimidazole[13], PAN[14,15], 1-(phenylo-2-pirydylo) car-bylideno-5-salicylidenotiocarbohydrazone[16]. Zn(II) occurring in conjunction with other elements in multivitamin pharmaceutical preparation—Vitrum^R was determined using Metrian derivatives[17-22].

N-undecyl-N'- (sodium *p*-aminobenzenesulfonate)- thio-urea (UPT)[23] which forms the relatively most stable complex with zinc. Therefore, we decided to examine its usefulness in the membrane phase preparation of a zinc-selective electrode.

EXPERIMENTAL

Reagents and Materials

Chlorides of zinc, nickel, cobalt, calcium, magnesium, cadmium and sodium, hydrogen peroxide, ammonia solution, sodium hydroxide, TEHP [tri-(2-ethylhexyl) phosphate] and PVC were obtained from Aldrich Chemical Company (Inc., Milwaukee, WI,USA). Sulfuric and hydrochloric acids and TBP(tributyl-phosphate) from Merck (Darmstad,Germany). The pharma-ceutical formulations containing zinc are Galzin tablets (Teva Tuteur, Argentina), Zincopan tablets (Gunther, Brazil) and both of (Biosanzink and Vitazink) tablets were from (Biocur, Germany).

Preparation of Solutions

Stock solutions of zinc, nickel, cobalt, cadmium, magnesium, calcium and sodium chlorides of 10^{-1} mol L^{-1} concentration were obtained by dissolving weighed amounts of corresponding salts in water. Solutions of 10^{-2}-10^{-6} mol L^{-1} concentration were obtained by diluting stock solutions.

Standard zinc chloride solutions used in zinc determination in pharmaceutical formulations were obtained by dissolving a corresponding amount of this salt in 0.05 mol L^{-1} of NaCl and diluting.

Pharmaceutical Formulations Mineralization

Solutions used in potentiometric measurements and the square wave voltammetry method were prepared in the following way: a tablet of pharmaceutical formulations (Galzin, Zincopan, Biosanzink and Vitazink) was placed in a conical flask, 10 ml of 30 % H_2O_2 were added and left until the solution dissolved. Then, 1 ml of concentrated H_2SO_4 was added and the solution heated until H_2O_2 decomposed. This activity was repeated five times. After the mineralisation was over, 15 ml of water and 5 ml of concentrated ammonia solution were added and left for 60 min. Then the solution was filtered quantitatively into 100 ml volumetric flask and diluted with water.

Electrode Construction

The electrode consists of a body and an exchangeable cylindrical teflon sensor containing a liquid-membrane phase with an internal Ag / Ag Cl reference electrode. The description of the electrode construction was presented as described before[24].

Active Substance of the Liquid-Membrane Phase

N-undecyl-N'- (sodium *p*-aminobenzenesulfonate)- thio-urea (UPT)[23] is the membrane phase active substance. This compound dissolved well in 10 % aqueous alkaline solutions. This substance appears in the form of white powder; it forms stable white chelate complex with zinc; its stability constant log K = 10.9.

Preparation of the Potential Creating Phase

A mixture of the optimal weight composition 0.01g active substance [Zn (UPT)$_3$], 0.35g TBP, 0.35g TEHP and 0.06g PVC constitute the electrode's membrane phase. The mixture was de-aerated; a teflon sensor with an Ag / Ag Cl electrode was filled with it and gelated at the temperature of 373 K for about 13 min. After the mixture had become colder, the electrode was conditioned for about 30 min in 10^{-3} mol L^{-1} Zn(II) solution.

Measurements of the Electromotive Force

The measurements of the electromotive force of the

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system consisting of a zinc electrode and a reference electrode Orion 90-02 was carried out at room temperature in a solution stirred with a mechanical stirrer by means of a Multifunctional Computer Meter CX 721 (Elmetron), which made measure-ments possible to an acZnracy of 0.1 mV. This device enables the recording of EMF changes with time. The stable bridge of the reference electrode was filled with Orion 90-00-01 solution containing 1.7 mol L^{-1} KNO_3, 0.64 mol L^{-1} KCl,0.06 mol L^{-1} NaCl and 1 ml of 37 % HCHO. The voltammetric measurements were made using the method of standard additions of the sample. Polarographic analyser Model 384B, EG & G Princeton Applied Research, was used. The measurements were made on a hanging mercury drop electrode; 0.01 mol L^{-1} NaCl was the base electrolyte.

RESULTS AND DISCUSSIONS

In order to estimate the analytical usefulness of the obtained zinc electrode its basic analytical parameters were established. The slope of characteristics, the detection limit, selectivity, response time and the dependence of the electrode's potential on the pH of the solution.

Calibration curves

The zinc electrode's calibration curves determined in Zn (II) solutions and in interfering ions solutions of concentration 10^{-1}-10^{-6} mol L^{-1} are given in Figure 1.

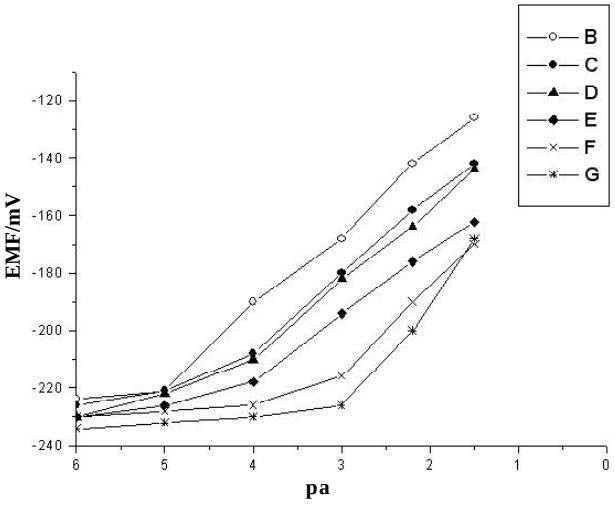

Figure 1 : Calibration Curves of zinc Electrodes; (B)Zn,(c)Cu,(D)Cd,(E)Ni,(F)Co and (G)Ca Cations

The zinc electrode's slope of characteristics is 29.5 mV pa_{Zn}^{-1}, the detection limit is 7.3 x 10^{-6} mol L^{-1} and the measuring range is 10^{-1} – 10^{-2} mol L^{-1}.

The analytical parameters of the zinc electrode are presented in TABLE 1.

TABLE 1 : Analytical parameters of the zinc electrode

Characteristics slope / mV pa_{Zn}^{-1}	29.5 + 0.1
Intercept / mV	*-79.8 + 0.5*
Detection limit / mol dm^{-3}, μg cm^{-3}	7.3 x 10^{-6},0.38
Measuring range / mol dm^{-3}, mg cm^{-3}	10^{-1}-7.3 x 10^{-3}, 6.73-0.00038
Response time / s	*12*
Lifetime / d	50
Range of pH	4.5 – 7.5

Selectivity of the Electrode

The selectivity of the electrode under examination was measured by establishing its selectivity coefficients with reference to interfering ions. The selectivity coefficients were determined by the separate solution method or by the MPM (matched potential method) proposed by Christian and Gadzekpo[25] using the following equations:

$$\log k_{ij}^{pot} = \frac{E_2 - E_1}{S} - \left(\frac{z_i}{z_j} - 1\right)\log a_i \quad , \quad K_{Zn/M}^{pot} = \frac{a_i}{a_j^{zi/zj}}$$

In the separate solution method, with the EMF value at the zinc (II) concentration 10^{-3} mol L^{-1} and the activity value at the potential –160 mV. For the MPM method, the equatio is the following:

$$K_{Zn/M}^{pot} = \frac{a_i}{a_j^{zi/zj}}$$

The results obtained are presented in TABLE 2.

TABLE 2 : Selectivity coefficients of the zinc electrode

$K_{Zn/M}^{pot}$	Separate solution method		
	$E_i = E_j$	$a_i = a_j$	MPM
$CuCl_2$	0.312 + 0.011	0.382 + 0.02	0.321 + 0.02
$CdCl_2$	0.265 + 0.009	0.315 + 0.01	0.270 + 0.010
$NiCl_2$	0.252 + 0.007	0.303 + 0.01	0.252 + 0.010
$CoCl_2$	0.086 + 0.004	0.132 + 0.003	0.073 + 0.005
$CaCl_2$	0.012 + 0.0005	0.035 + 0.001	0.011 + 0.0006
$MgCl_2$	0.010 + 0.0006	0.021 + 0.001	0.004 + 0.0002

Response Time

The response time of the examined electrode was established by injecting concentrated standard solution into intensively stirred Zn(II) solution. Simultaneously, changes of the SEM system zinc electrode-reference

electrode were recorded. After injecting concentrated standard, the solution was diluted with water (1:1). Solutions used to establish the response time of the examined electrode conformed to the following conditions: $c_1 : c_2 = 1:100$, $v_1 : v_2 = 1: 20$ Where c_1 is the concentration of the sample, c_2, the concentration of the standard, v_1 the volume of the sample and v_2 the volume of the standard. The obtained results are presented in Figure 2.

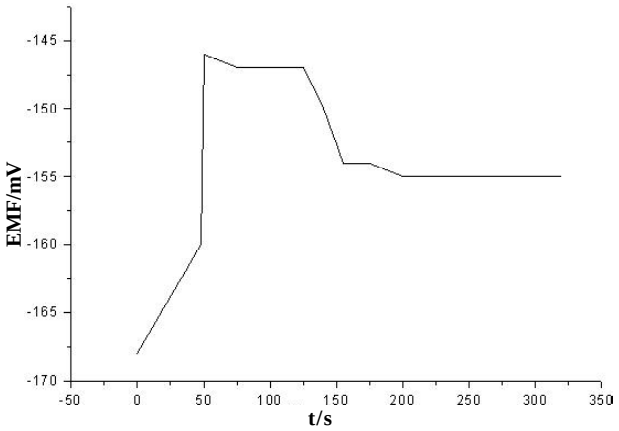

Figure 2 : Response Time of Zinc Electrode

Dependence of EMF on pH

Because of the chemical character of zinc salts the dependence of the electrode's potential on pH was established. To achieve this aim, HCl or NaOH drops were added to the examined Zn(II) sample of concentration 10^{-3} mol L^{-1}. After each addition of the acid or base, the solution's pH was measured and then, after the electrode's response stabilised, the ratio of the EMF of the system examined zinc electrode / reference electrode was read.

The dependence of the EMF on pH is presented in Figure 3. The decrease in potentials above and below

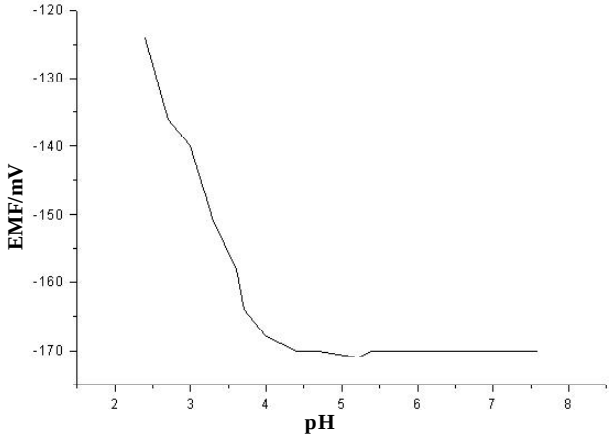

Figure 3 : Effect of pH on Response of Electrode to Zinc

these pH values(4.0 – 8.0) may be due to non-complete complex formation or the hydrolysis of zinc ion.

Lifetime of the Electrode

The prepared electrode's analytical usefulness time was tested by measuring slopes of characteristics of the electrodes kept in air. The measurements were made systematically, usually every 10 days, in freshly prepared Zn(II) solutions. On the basis of the obtained results it was noticed that the electrode's lifetime is about 7 weeks.

Zinc Determination in Pharmaceutical Formulations

In order to test the analytical usefulness of the electrode, zinc determination in pharmaceutical formulations was conducted by using it. The method of standard additions of the sample and the calibration Curve method were used. The results obtained were compared with those obtained by the square wave voltammetry method. The determination's results and their statistical evaluation are presented in TABLE 3.

TABLE 3 : Results of zinc determination in the pharmaceutical formulations

Determination method	Samples	Producer's data	Zn^{+2} found/ mg	Relative error (%)	V (%)[a]
Calibration curve	Galzin tablets[(1)]	20.0	20.54	2.70	1.30
	Zincopan tablets [(2)]	15.0	15.06	0.40	1.22
	Biosanzink tablets [(3)]	15.0	15.12	0.80	1.12
	Vitazink tablets [(4)]	10.0	10.08	0.53	1.06
Standard addition in the sample with dilution	Galzin tablets[(1)]	20.0	21.52	7.60	1.14
	Zincopan tablets [(2)]	15.0	15.02	0.13	1.05
	Biosanzink tablets [(3)]	15.0	15.24	1.60	1.11
	Vitazink tablets [(4)]	10.0	10.18	1.80	1.13
Voltammetry	Galzin tablets[(1)]	20.0	20.78	3.90	1.16
	Zincopan Biosan zink[(3)] Vitazink[(4)]	10.0			
	Zincopan tablets [(2)]	15.0	15.14	0.93	1.13
	Biosanzink tablets [(3)]	15.0	15.10	0.66	1.09
	Vitazink tablets [(4)]	10.0	10.24	2.04	1.16

[a] $V = \frac{\delta n - 1}{x} \times 100\ \%$.

(1) Teva Tuteur, Argentina.
(2) Gunther, Brazil.
(3) Biocur, Germany.

CONCLUSION

In the course of the research, an optimal composition of the potential creating phase of the zinc function electrode was described. This electrode is character-

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ized by good analytical parameters: for the Nernst slope of the characteristics, short response time and relatively long lifetime. The examined electrode's analytical parameters are presented in TABLES 1 and 2.

In comparison with the zinc function electrodes described earlier, the electrode described in this paper is characterized by the shortest response time and low detection limit. These parameters, to a large extent, account for the electrode's analytical usefulness.

The electrode was used for the determination of zinc ions in four different, commonly used pharmaceutical formulations. Two different methods were employed: the calibration curve method and the standard additions method. An analysis of the results of zinc determination in pharmaceutical formulations samples shows that the standard additions method is slightly less reliable: this could results from the essential part of this method, double EMF measurement. Therefore, the calibration curve method is recommended in zinc determination. After repeating this method for several times, the error is no bigger than 3 %. The results obtained were compared with those presented by the producers of the pharmaceutical formulations and those obtained with the voltammetric method. In all cases the quality of results was satisfactory, which confirms the analytical usefulness of the electrode described.

The zinc function electrode is characterized by good analytical parameters: it can be used both in pharmaceutical industry laboratories and in research laboratories. Its use shortens the time required for analyses with no effect on the results' precision reliability.

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