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Article

Determination of Sn^{2+} in Lyophilized Radiopharmaceuticals by Voltammetry, Using Hydrochloric Acid as Electrolyte

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O objetivo do estudo foi desenvolver e validar um método de rotina para a determinação específica de Sn^{2+} em kits de radiofármacos 2-metóxi isobutil isonitrila (MIBI). Para a análise, foi utilizado o equipamento analisador voltamétrico. Experimentos de triagem mostraram que o eletrólito HCl 1 mol L^{-1} apresentou os melhores resultados entre todas as soluções testadas. Experimentos de estabilidade mostraram declínio gradual na corrente de Sn^{2+} no MIBI, e 23 dias depois da preparação da solução, a corrente desapareceu. Para confirmar a seletividade de técnica utilizando o HCl 1 mol L^{-1}, induzimos a oxidação do $SnCl_2$, resultando em um declínio proporcional da corrente no voltamograma. A confiabilidade do método foi observada com os valores de precisão e exatidão intra- e inter-ensaios, e com a robustez. Nós proporcionamos novos dados quanto a detecção seletiva de Sn^{2+} na presença de sua forma oxidada em kits de radiofármacos, utilizando HCl 1 mol L^{-1} como eletrólito.

This work aimed to develop and validate a routine method for the specific determination of Sn^{2+} 2-methoxy isobutyl isonitrile (MIBI) radiopharmaceutical kits. A voltammetric electrochemical technique was used for the analysis. Screening experiments revealed that 1 mol L^{-1} HCl electrolyte showed the best results, among all the tested solutions. Stability experiments showed a gradual decline in the current of MIBI, and 23 days after the preparation of the solution, the current corresponding to stannous ion disappeared. To confirm the selectivity of the technique using HCl, we have induced oxidation of $SnCl_2$ that resulted in a proportional decline of the current in the voltammogram. The reliability of the method was observed with the values of precision and accuracy intra- and inter-assay, and also its robustness. We provide novel evidence on the selective detection of Sn^{2+} in the presence of its oxidized form in radiopharmaceutical kits, by using 1 mol L^{-1} HCl as electrolyte.

Keywords: stannous ion, radiopharmaceutical kits, selective electroanalysis, electrolyte, voltammetry

Introduction

Radiopharmaceutical kits are used in more than 90% of all procedures in nuclear medicine diagnosis.[1-3] 2-Methoxy isobutyl isonitrile (MIBI) is extensively used in clinics, especially to evaluate myocardial function, besides the application in differential diagnosis of some cancer types.[4-7] Other isonitrile-based compounds have been used beforehand, but they presented low stability, having their application discontinued.[8] Subsequently, the radiopharmaceutical MIBI proved to be greatly efficacious, overcoming the limitations of previously developed compounds with the same diagnostic purposes.[9]

The stannous ion (Sn^{2+}), used mainly in the form of $SnCl_2$ salt, is added to lyophilized radiopharmaceutical kits to allow the complexation to the radioisotope. It is mainly employed in order to promote the reduction of pertechnetate ion $(TcO_4)^-$ for the preparation of ^{99m}Tc-radiopharmaceutical kits.[10,11] For that reason, quality control measurements, involving determination of Sn^{2+},

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are fundamental in the production of radiopharmaceutical kits. In fact, Sn^{2+} might be affected by several factors, such as oxygen and light exposure, generating its oxidized form stannic ion (Sn^{4+}). For instance, dental formulations containing SnF_2 are highly unstable in aqueous solutions, since Sn^{2+} can be easily oxidized to Sn^{4+}, compromising the physical and chemical properties of the product.[12]

The implementation of quality control procedures in radiopharmacy is extremely important to ensure that unsuitable products will not be used in patients. It is well known that either lacking or excess of Sn^{2+} in lyophilized formulations might affect the radiochemical purity, as well as the quality of images. Most analytical methods for the determination of tin, such as atomic absorption spectrometry, fluorimetry, spectrometry, or potentiometry do not allow distinguishing between Sn^{2+} and Sn^{4+} in solution.[13-17] At the present, there are a few techniques available for the selective determination of Sn^{2+}, including titrimetric analysis (redox-titration) and voltammetry. The low sensitivity of titrimetric methods for the concentrations of tin used in radiopharmaceutical kits impairs its precise and accurate measurement.[13] Thus, especially for radiopharmaceutical kits with low Sn^{2+} contents, the only reliable method to properly determine Sn^{2+} is voltammetry.[18]

The peaks obtained in the latter technique give qualitative information through the value of the potential peak E (V), while the quantitative information is provided by the current peak i (A), in the presence of the selected electrolyte.[19,20] The determination of Sn^{2+} by voltammetry has been performed before using electrolytes containing complex mixtures of salts, buffers, acids and bases, such as 4-(2-hydroxyethyl)-1-piperazineethanesulfonic acid (HEPES), piperazine-*N,N*'-bis(2-ethanesulfonic acid) (PIPES), hydrochloric acid (HCl), citric acid ($C_6H_8O_7$), potassium chloride (KCl) and sodium hydroxide (NaOH).[21,22]

The aim of this study was to validate a simple method for determination of Sn^{2+} in MIBI radiopharmaceutical kits to furnish a reliable routine method for quality control in radiopharmacy.

Materials and Methods

Apparatus and electrochemical technique

Equipment 757 VA Computrace (Metrohm) was used with a three electrode cell for differential pulse polarography technique: multimode mercury working electrode (MME), platinum auxiliary electrode (Pt) and electrode silver/silver chloride (Ag/AgCl) reference containing potassium chloride (3 mol L^{-1} KCl) electrolyte solution.

Reagents and solutions

Anhydrous stannous chloride ($SnCl_2$) (Sigma Aldrich, Switzerland); stannic chloride pentahydrate ($SnCl_4.5H_2O$) (Sigma-Aldrich, USA); MIBI radiopharmaceutical cold kit (tetrakis (2-methoxy isobutyl isonitrile) copper(I) tetrafluoroborate ($[Cu(MIBI)_4]BF_4$) (1 mg), anhydrous stannous chloride (0.084 mg), sodium citrate, L-cysteine hydrochloride monohydrate and mannitol (Radiopharmacus Group, Porto Alegre, Brazil); HEPES (Sigma-Aldrich, USA); nitric acid suprapur (HNO_3) (Merck, Germany); KCl (Merck); NaOH (Synth, Brazil); disodium ethylenediamine tetraacetic acid (EDTA-Na_2) (Quimex, Brazil); potassium nitrate (KNO_3) (Nuclear,Brazil); PIPES (Sigma Aldrich); sodium fluoride (NaF) (Merck); sodium nitrate ($NaNO_3$) (Dinâmica, Brazil); citric acid (Merck); HCl P. A. (Merck); hydrogen peroxide suprapur (H_2O_2) (Merck); and copper metal standard solution (Cu) (Fluka®).

General procedures

For initial screening of a series of electrolytes, we tested the current and reproducibility of standard solutions at the concentration of 50 mg L^{-1}. The sample used for analysis was the radiopharmaceutical MIBI containing approximately 0.052 mg of Sn^{2+}, corresponding to 17.53 mg L^{-1}, after suspension of lyophilized kit with 3 mL of distilled and deionized water (dd-water). The standard solution of $SnCl_2$ used for validation assays was prepared at the same concentration present in the radiopharmaceutical kit (17 mg L^{-1}), whilst the standard solution of $SnCl_4$ pentahydrate, due to the lower sensibility of the assay for Sn^{4+}, was prepared in a higher concentration (50 mg L^{-1}). The samples and the standards were dissolved in oxygen-free dd-water by nitrogen saturation to avoid oxidation. HEPES (1 mol L^{-1} HEPES, 1 mol L^{-1} NaF, 1 mol L^{-1} $NaNO_3$, and H_2O), 1 mol L^{-1} KCl, 1 mol L^{-1} NaOH, 0.1 mol L^{-1} EDTA, 0.1 mol L^{-1} KNO_3, PIPES (1 mol L^{-1} PIPES, 1 mol L^{-1} NaF, 1 mol L^{-1} $NaNO_3$, and H_2O), HCl plus citric acid (0.2 mol L^{-1}) and HCl (0.2 mol L^{-1} and 1 mol L^{-1}) electrolytes were tested. In the protocols to induce the oxidation of Sn^{2+}, 200 µL of 30% H_2O_2 were used.

The use of the electrolytes 1 mol L^{-1} PIPES, 1 mol L^{-1} NaF, 1 mol L^{-1} $NaNO_3$, and H_2O were prepared according to the newsletter of Metrohm (CH4-0381-042002), which was composed of 11 mL of deionized water, 7 mL of NaF, 1 mL of 1 mol L^{-1} $NaNO_3$, and 1 mL of 1 mol L^{-1} PIPES buffer. The electrolyte 1 mol L^{-1} HEPES was prepared according to the PIPES protocol, replacing PIPES by HEPES. The electrolyte HCl plus citric acid was made by mixing 5 mL of 0.4 mol L^{-1} HCl and 5 mL of 0.4 mol L^{-1}

citric acid in the vessel, with a final concentration of 0.2 mol L^{-1}. A volume of 10 mL of the electrolytes PIPES, HEPES, 1 mol L^{-1} KCl, 0.1 mol L^{-1} EDTA, 1 mol L^{-1} NaOH, 0.1 mol L^{-1} KNO_3, 0.2 mol L^{-1} HCl, and 1 mol L^{-1} HCl were added in the vessel during each analysis. The electrolytes were initially tested with a Sn^{2+} concentration of 50 mg L^{-1} for assessing the current and reproducibility. The analysis was performed in triplicate in order to determine the most suitable conditions concerning deposition time, concentration, and pH of the electrolyte. Those showing stable and reproducible currents were further tested with a Sn^{2+} concentration of 17 mg L^{-1}.

The differential pulse voltammetric analysis was performed under the following conditions: –0.2 V deposition time, 90 s pulse time, 10 s equilibration time, –0.2 V starting potential, –0.55 V end potential, 0.004 voltage step, 0.050 V pulse amplitude, 0.04 s pulse time, and 0.1 s voltage step time. These values are defined by the manufacturer. To assess the possible interference of Cu^{2+}, we have used a potential range varying from 0 to –0.55 V. Initially, 10 mL of electrolyte were added to the polarographic vessel, and a flow of 1 kgf cm^{-2} of nitrogen gas was applied for 5 min. The method of manual standard addition for quantification was adopted. The calibration curve was made by blank determination (electrolyte) and five successive additions of 200 µL (10 mg L^{-1} of Sn^{2+}) standard solution into the vessel, in order to record the polarographic concentrations of 0, 10, 20, 30, 40 and 50 mg L^{-1}. For determination of Sn^{2+} in the MIBI kits, the samples were resuspended with 3 mL of dd-water and 200 µL of each sample were added into the vessel to obtain the initial voltammogram. Subsequently, two successive additions of 200 µL of standard (17.0 mg L^{-1}) were carried out. The analyses were performed in triplicate, and 3 separated samples of lyophilized compound were used. The results were expressed as mean ± standard deviation (SD).

Polarographic method validation

The polarographic method was quantitatively evaluated in terms of sensitivity, specificity, precision, accuracy, linearity, recovery and robustness.

Results

Electrolytes for determination of Sn^{2+}

The results for HEPES were not satisfactory, as the electrolyte caused interference in the baseline, and showed no peak in the voltammogram at the potential range corresponding to Sn^{2+}. For 1 mol L^{-1} KCl, the same potential was obtained for $SnCl_2$ and $SnCl_4$, according to assessment at 50 mg L^{-1}, following separate readings, clearly showing that is not possible to separate Sn^{2+} from Sn^{4+} (Figure 1).

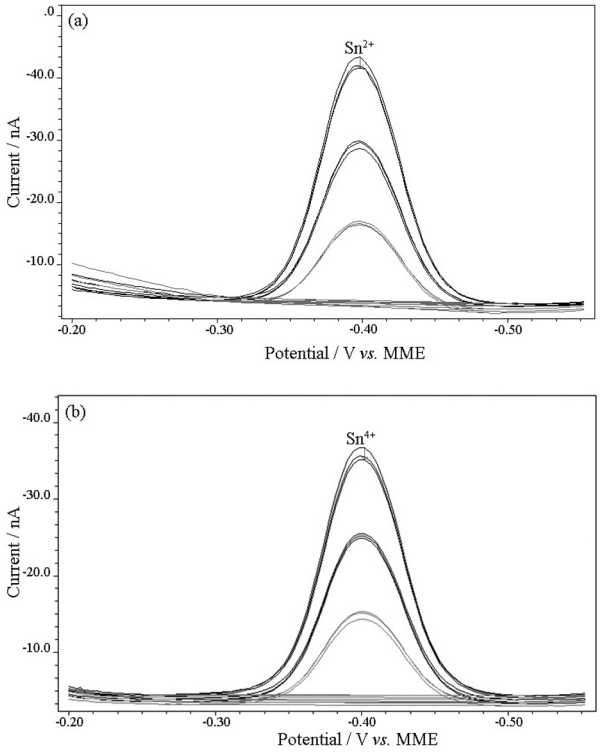

Figure 1. Voltammogram for Sn^{2+} and Sn^{4+} determination at 1 mol L^{-1} KCl: (a) Sn^{2+}; (b) Sn^{4+}. The concentration of the elements used in the polarographic cell in each analysis was 50 mg L^{-1}. The detection of Sn^{2+} and Sn^{4+} occurred at the same potential (–0.40 V).

The electrolytes 0.1 mol L^{-1} EDTA and 1 mol L^{-1} NaOH, using Sn^{2+} at 50 mg L^{-1}, generated erroneous results, due to the decay of the current between the standard additions, as it can be observed in Figures 2a and 2b, respectively.

The recovery with 0.1 mol L^{-1} KNO_3 and 50 mg L^{-1} Sn^{2+} was less than 50%, being also unsatisfactory (Figure 3).

For 1 mol L^{-1} PIPES and a concentration of 17 mg L^{-1} of Sn^{2+}, the obtained result was approximately 13 mg L^{-1}, giving a recovery of 76%. Similarly, the use of HCl with citric acid provided a reading of approximately 20 mg L^{-1}, for a standard Sn^{2+} solution of 17 mg L^{-1} (recovery of 118%). A decreased recovery was observed by employing 0.2 mol L^{-1} HCl as electrolyte, showing a reading of 12 mg L^{-1} (71%) (Figures 4a-c, respectively).

Considering that 1 mol L^{-1} HCl electrolyte showed the best reproducibility for determining Sn^{2+} when compared to the other solutions, according to assessment of either concentrations of 50 or 17 mg L^{-1} (Figure 5), this was chosen to proceed validation.

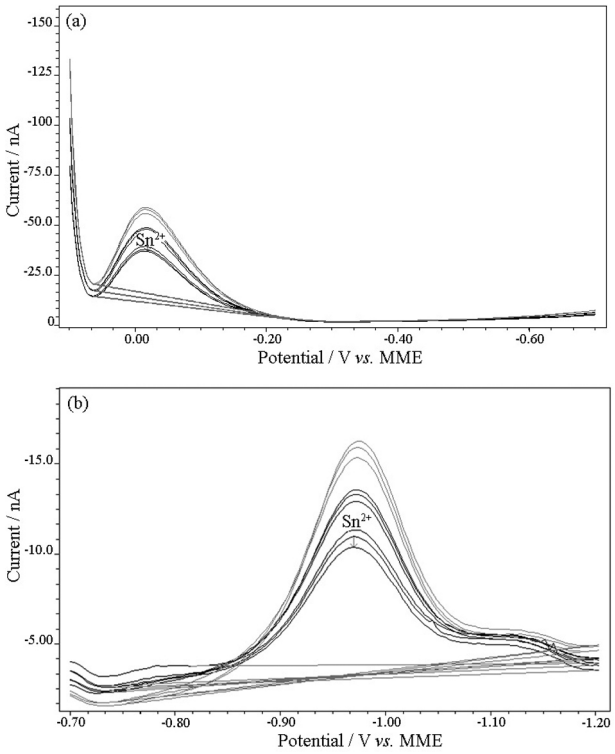

Figure 2. Voltammograms for Sn^{2+} determinations in EDTA and NaOH: (a) 0.1 mol L^{-1} EDTA; (b) 1 mol L^{-1} NaOH. The concentration for Sn^{2+} used in the polarographic cell in each analysis was 50 mg L^{-1}. Sn^{2+} standards were also added at 50 mg L^{-1}.

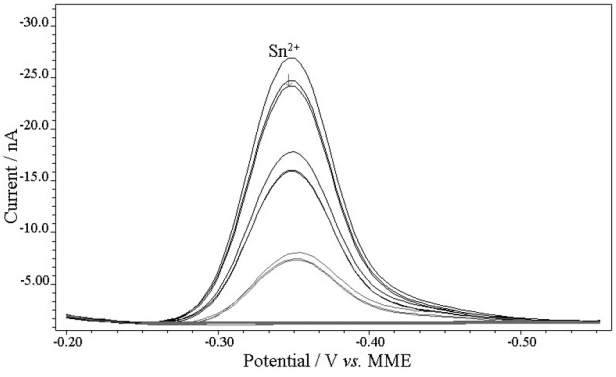

Figure 3. Voltammogram for Sn^{2+} determinations at 0.1 mol L^{-1} KNO_3. The concentration used in the polarographic cell was 50 mg L^{-1}.

Technique validation for determining Sn^{2+} for differential pulse polarography using 1 mol L^{-1} HCl as electrolyte

Stannous ion detection in the presence of stannic ion

The solutions were prepared from vials containing the lyophilized MIBI. The current measurement was performed during three weeks. There decrease of current was observed through this voltammetric technique few days after the preparation of the radiopharmaceutical solution, which was intentionally stored at room temperature and exposed to light (Table 1).

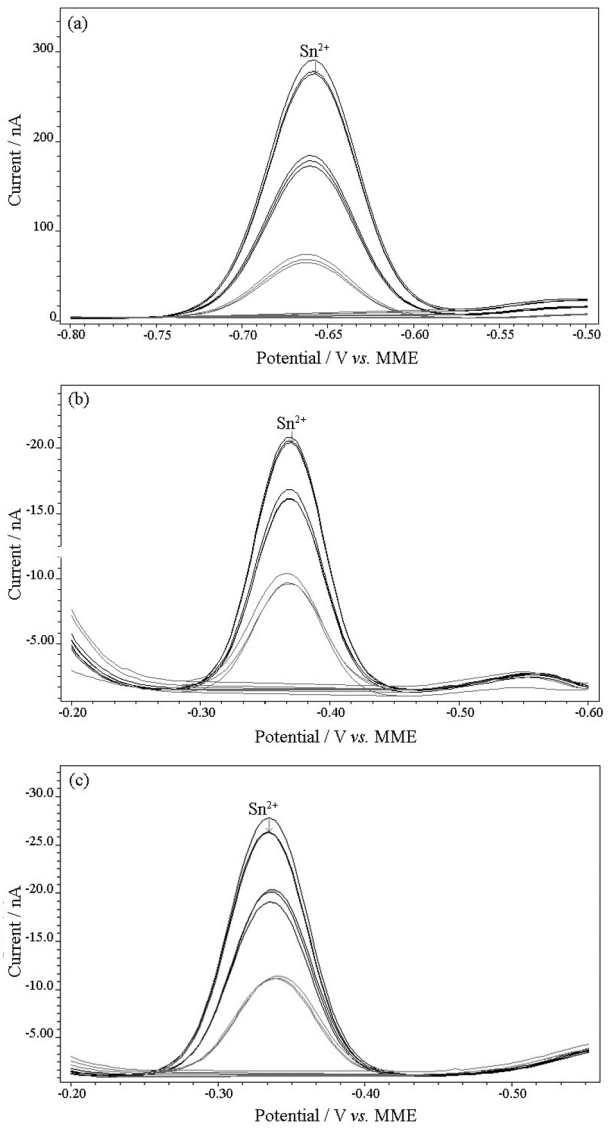

Figure 4. Voltammograms for Sn^{2+} determination in three different electrolytes: (a) 1 mol L^{-1} PIPES; (b) 0.2 mol L^{-1} HCl with citric acid; (c) 0.2 mol L^{-1} HCl. The concentration used in the polarographic cell in each analysis was 17 mg L^{-1}.

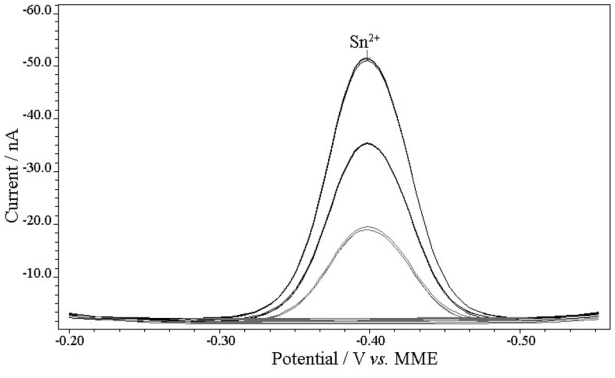

Figure 5. Voltammogram for Sn^{2+} at 1 mol L^{-1} HCl. The concentration used in the polarographic cell was 17 mg L^{-1}.

Table 1. Decay of the current of Sn^{2+} 1, 2, 13 and 23 days after preparation of solution for reading

time / day	Current (triplicate) / nA
1	–11.84
	–11.75
	–11.71
2	–9.71
	–9.61
	–9.59
13	–7.90
	–8.30
	–8.14
23	n.d.
	n.d.
	n.d.

n.d.: not determined.

To observe the selectivity of the electrolyte in the solution of $SnCl_2$, a reading using freshly prepared $SnCl_2$ standard was performed. The fast oxidation of Sn^{2+} was induced by adding H_2O_2, and incubating the solution in water bath at 37 °C for 5 min.[13] No current corresponding to Sn^{2+} was observed. However, despite the disappearance of the Sn^{2+} current, we observed an increase in the baseline current. This fact seems to be due to oxidation of the working electrode mercury drop by the action of H_2O_2 that could be hiding the Sn^{2+} current. To exclude this possibility, another Sn^{2+} standard was prepared and incubated for 24 h in water bath for 37 °C, without adding H_2O_2. Figures 6a-c, respectively, show the disappearance of the current of Sn^{2+} without any change of baseline current following this procedure.

These results show that oxidation of Sn^{2+} and the formation of Sn^{4+} do not affect the analysis, at the tested conditions.

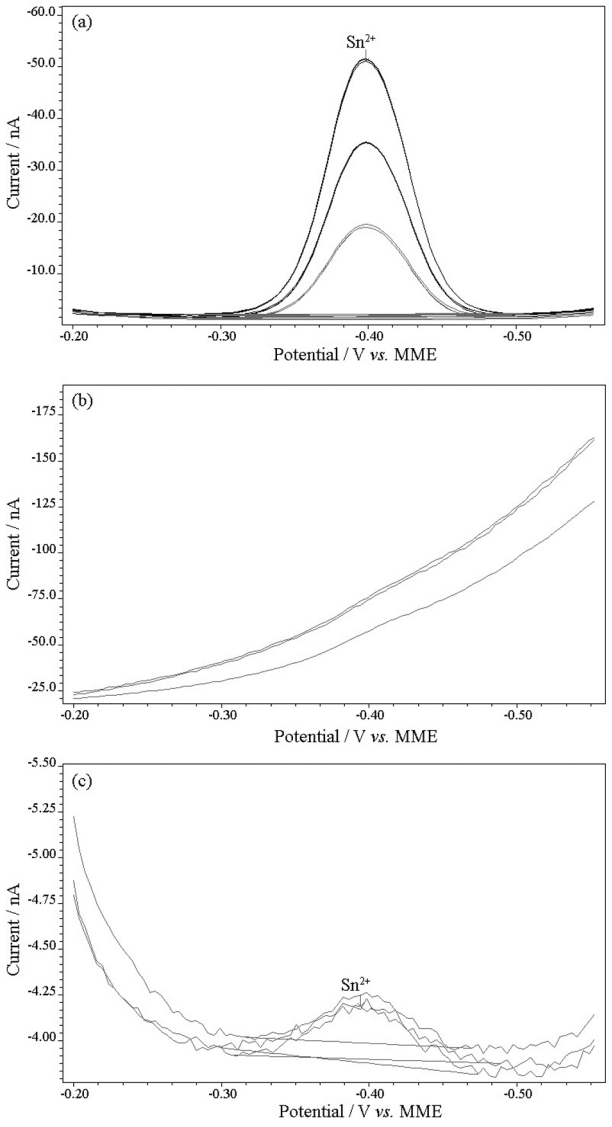

Figure 6. Voltammograms for Sn^{2+} at different conditions in 1 mol L^{-1} HCl: (a) 1 mol L^{-1} HCl; (b) Sn^{2+} oxidized with H_2O_2 addition and water bath in 1 mol L^{-1} HCl; (c) Sn^{2+} oxidized in water bath in 1 mol L^{-1} HCl. The concentration used in the polarographic cell was 17 mg L^{-1}.

Sensibility, specificity and selectivity

The limit of detection was determined by adding concentrations of 1 mg L^{-1} of the Sn^{2+} standard. The detection limit of this method was 3 mg L^{-1}. The limit of quantification was the lowest analyzed amount, which can be measured with defined precision and accuracy and reproducible with a coefficient of variation (CV) up to 20% and accuracy of 80-120%. The limit of quantification values was 4.57 ± 0.49 mg L^{-1}, with CV of 1.06 % and accuracy of 114.21%.

For determination of specificity, the excipient of MIBI was tested to assess the interference with voltammetric method. The ability of the method to detect Sn^{2+}, without interference of excipients in its potential, is depicted in Figure 7.

To assess the interference of copper in the potential of Sn^{2+}, we obtained voltammograms with (*i*) Cu^{2+} standard, (*ii*) Cu^{2+} standard with Sn^{2+} standard and (*iii*) radiopharmaceutical MIBI kit under normal conditions, as demonstrated in Figures 8a-c, respectively.

The obtained peaks of copper were detected at a different potential than Sn^{2+} (–0.13 V), and all assay tests were free of interference from this element during determination of Sn^{2+}.

Precision and accuracy (recovery) intra- and inter-assay

The intra- and inter-day precision and accuracy data are shown in Table 2. Precision was expressed as the percentage of coefficient of variation (CV), and

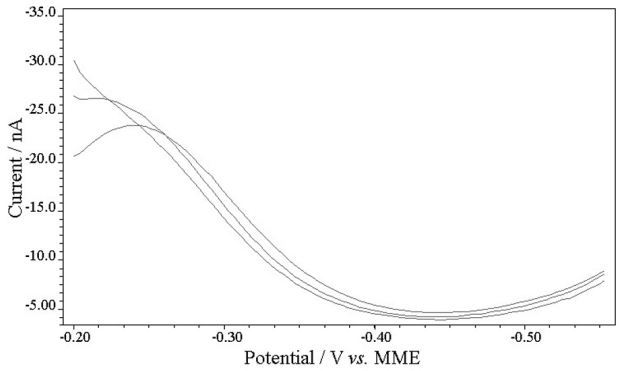

Figure 7. Voltammogram showing the specificity of the analysis for Sn^{2+} at 1 mol L^{-1} HCl. For this parameter, MIBI radiopharmaceutical kits and excipients without Sn^{2+} were analyzed.

accuracy was expressed as the percentage of the added concentration.

Robustness

As shown in Table 3, intentional variations were performed in the concentration of electrolyte, deposition time, use of water without nitrogen, and different operators.

The results indicate that the method is robust in relation to the possible variations that may occur during the execution of the technique, including the small variations in the electrolyte concentration and the execution by different operators. However, some specific parameters, such as the deposition time of 90 seconds, and water nitrogenation must be strictly respected.

Linearity

At least three calibration curves were carried out in the range of 10-50 mg L^{-1} of Sn^{2+} (Figure 9).

This experimental set presented a correlation coefficient of 0.9993, revealing the linearity of the method.

Discussion

The determination of Sn^{2+} concentrations represents a very important step in the quality control procedures

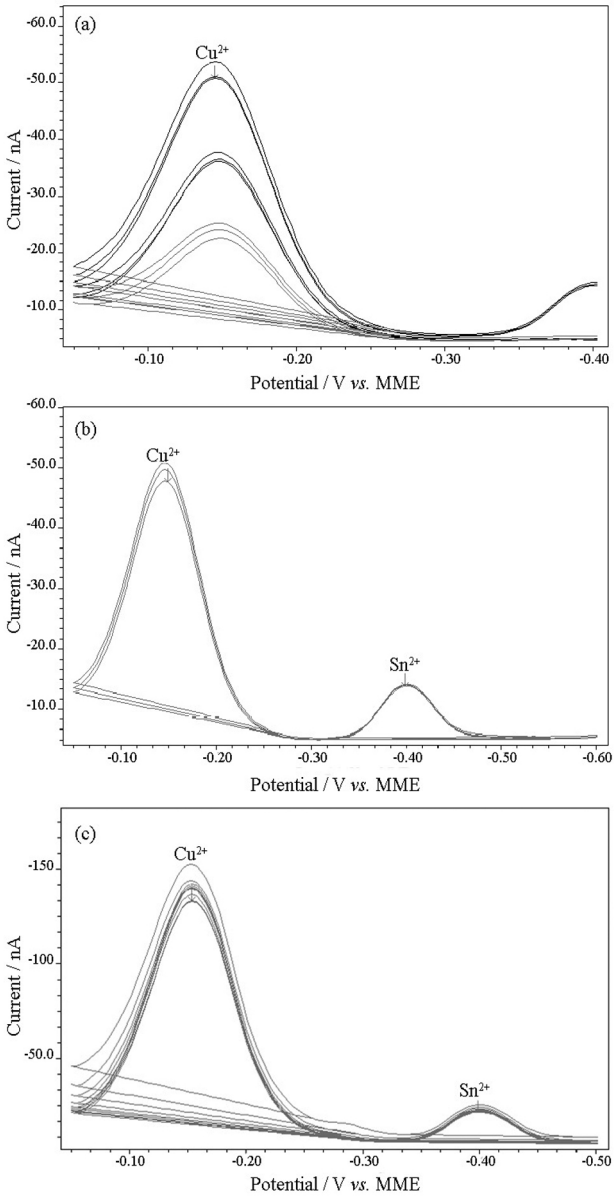

Figure 8. Voltammograms for Cu^{2+}, Sn^{2+} and MIBI radiopharmaceutical at 1 mol L^{-1} HCl. (a) Cu^{2+}; (b) Cu^{2+} and Sn^{2+}; (c) MIBI radiopharmaceutical. The concentration used in the polarographic cell was 5 mg for Cu^{2+} and 17 mg for Sn^{2+}. The potential readings were initiated at 0.0 V to permit observing the peak for Cu^{2+}.

Table 2. Intra and inter-assay accuracy and precision of the method

	Sn^{2+} added / (mg L^{-1})	Sn^{2+} found (mean ± SD) / (mg L^{-1})	Precision CV / %	Accuracy / %
Intra-assay (n = 5)	10	10.54 ± 0.39	3.71	105.44
	15	15.84 ± 0.78	4.91	105.59
	20	21.20 ± 0.61	2.90	105.98
	50	50.20 ± 2.83	2.80	100.01
Inter-assay (n = 5)	10	10.42 ± 0.26	2.48	104.15
	15	15.67 ± 0.49	3.16	104.50
	20	21.58 ± 0.78	3.64	107.92
	50	50.52 ± 0.52	1.03	101.04

Table 3. Robustness evaluation of the method

Test (n = 5)		Sn^{2+} added / (mg L^{-1})	Sn^{2+} found (mean ± SD) / (mg L^{-1})	Precision CV / %	Accuracy / %
Electrolyte concentration	0.9 mol L^{-1} HCl (pH 0.130)	15	15.98 ± 0.75	4.71	106.53
	1.1 mol L^{-1} HCl (pH 0.010)	15	15.76 ± 1.51	9.61	105.03
Water not nitrogenated		15	18.04 ± 2.42	13.42	120.29
Deposition time	30 s	15	9.46 ± 1.73	18.29	63.09
	60 s	15	13.83 ± 2.45	17.74	92.18
Different operators	First operator	15	15.82 ± 1.51	9.61	105.03
	Second operator	15	15.84 ± 0.77	4.91	105.59

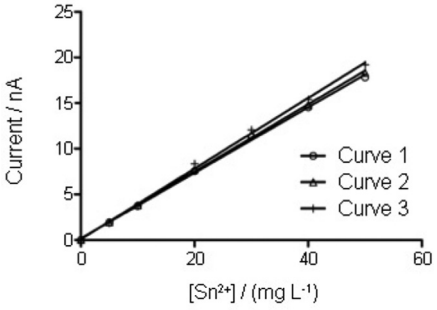

Figure 9. Linearity test of the method represented by three calibration curves.

in radiopharmacy, guaranteeing safety and allowing the correct diagnosis.[13] In the case of MIBI radiopharmaceutical kits, the exact concentration of Sn^{2+} is essential for efficient cardiac perfusion and adequate scintigraphy.[13]

Previous studies published methods for tin determination using technologies such as inductive coupled plasma-mass spectrometry (ICP-MS)[14] and gas chromatography coupled with mass spectrometry (GC/MS).[23,24] However, these techniques do not allow selective determination of tin species, considering that Sn^{2+} concentrations are calculated on the basis of total tin concentrations. Tin can also be determined by atomic absorption spectroscopy (AAS), but this technique requires complex extraction procedures.[24,25] Currently, voltammetry represents a low-cost technique able to precisely detect small concentrations of this ion, both quantitatively and qualitatively. Nevertheless, there are only few studies for this purpose using the MIBI radiopharmaceutical kit, especially when considering the appropriate electrolyte to be used in the selective analysis of Sn^{2+}. Thus, we developed and validated a simple voltammetric method for speciation of Sn^{2+} in the MIBI radiopharmaceutical, using 1 mol L^{-1} HCl.

Hubert *et al.* developed a simple and rapid method for the separation and determination of Sn^{2+} and Sn^{4+} in tin octoate, a catalyst used in the synthesis of polydimethylsiloxane (PDMS).[24] The detection of Sn^{2+} at the same potential of Sn^{4+} is a problem for nuclear medicine, since Sn^{4+} represents an impurity in lyophilized radiopharmaceutical kits. Several electrolytes have been described for the determination of Sn^{2+}, but there are differences in the specificities reported. Therefore, many methods used are effective in determining the sum of Sn^{2+} and Sn^{4+}, but they fail to provide a selective identification of Sn^{2+}. Decristoforo *et al.* described a polarographic method for determination of Sn^{2+} in technetium cold kits using a mixture of water, methanol and perchloric acid as electrolyte.[10] In addition, Almeida *et al.*[13] described the selective detection of Sn^{2+} (–0.350 to –0.400 V) by using 3 mol L^{-1} H_2SO_4 in pyrophosphate (PYRO) and methylene diphosphonate (MDP) radiopharmaceutical kits, although the authors have not investigated the effects of Sn^{2+} oxidation in their study. Herein, we tested several electrolytes, demonstrating that a series of complicating factors, such as determination of Sn^{4+} at the same potential of Sn^{2+}, decrease in current after standard addition, or disproportionate growth of the currents, excluded the use of most options. In our study, among all the electrolytes tested for determining Sn^{2+}, the only one showing good reproducibility and specificity was 1 mol L^{-1} HCl. Moreover, this electrolyte is easily prepared and presented a good stability. The best result obtained among the other electrolytes was achieved with HCl plus citric acid, but this solution presented some problems in the recovery (more than 115%) and linearity. These problems were detected in both determination of standard of Sn^{2+} in the excipient and lyophilized radiopharmaceutical kit. This appears to represent a good option for other samples, as described by Pérez-Herranz *et al.* for tin octoate, although it does not seem to be reliable for MIBI kits.[18]

To gain further insight on the applicability of 1 mol L^{-1} HCl, we initially prepared a solution of $SnCl_2$ for reading, followed by forced oxidation of Sn^{2+} with H_2O_2. The hydrogen peroxide acts as an oxidizing agent in acid aqueous solution.[26] After the reading, we observed a decrease of the current, which was accompanied by an increased

baseline. To rule out the possibility that baseline would hide the Sn^{2+} peak, we carried out separate experiments without adding H_2O_2, which would be responsible for the increase in baseline, using water bath at 37 °C to oxidize Sn^{2+}. Additionally, a decrease of Sn^{2+} currents was observed throughout the three weeks of exposition to room temperature and light. Studies show that the temperature is directly related to the oxidation of Sn^{2+}.[10,13] In this case, Sn^{4+} formed even at high concentrations of Sn^{2+}, was not enough to interfere with the analysis and recovery of the analyte. According to this analysis, we might affirm that our method using 1 mol L^{-1} HCl was selective for Sn^{2+} quantification. However, when we performed a reading of Sn^{4+} using $SnCl_4$ salt in 1 mol L^{-1} HCl we observed a peak at the same potential of Sn^{2+}. The same does not occur when we performed the readings using $SnCl_2$, because the results obtained by us showed that after the oxidation of Sn^{2+} to Sn^{4+} in solution, the current disappears in the potential where Sn^{2+} is detected (–0.40 V), indicating the selectivity of the method for Sn^{2+}. We suppose that this occurs because the Sn^{2+} oxidized by oxygen in solution (reaction that is favored by the presence of 1 mol L^{-1} HCl)[27,28] generates complex species of Sn^{4+} which cannot be detected at the potential of –0.40 V. The formation of Cl^-/Sn complex can display several electrochemical profiles[29] and the formed complex can be responsible for the non-detection of oxidized Sn^{2+} in solution. This hypothesis is strengthened by the fact that Sn^{4+} complexes display completely different properties in relation to Sn^{2+} complexes.[30,31] Therefore, these conditions related to the oxidation of Sn^{2+} were confirmed by our study because the Sn^{2+} oxidized was not detected in the voltammetric analysis.

During the Sn^{2+} analysis with 1 mol L^{-1} HCl, considering all steps to guarantee the quality of $SnCl_2$ (preparation at the time of use, correct manipulation, ideal storage, and protection against light), it is possible to presume that the read current of Sn^{2+} corresponds to the amount weighed for analysis. Altogether, intra- and inter-assay tests on robustness, accuracy and precision, revealed the method presented by us as a simple, quick, and inexpensive voltammetric approach to selectively determine Sn^{2+} in lyophilized MIBI kits. However, to maintain satisfactory robustness, accuracy, and precision, it is imperative to maintain the methodological parameters, as well as qualified operators.

Conclusion

Validation results provided by us indicated that the method presented herein shows high specificity for Sn^{2+} determination, without interference by Sn^{4+}, excipients from formulation of MIBI or copper. The method presented high sensitivity, and might as well be considered a reliable parameter for the selective determination of Sn^{2+} in radiopharmaceutical MIBI solutions, without interference of degradation products of Sn^{2+} using 1 mol L^{-1} HCl electrolyte. In summary, the method has advantages, such as the easy and quick preparation of the electrolyte, rapid analyses, reproducibility, and can be applied in a routine laboratory.

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