Selective Polarographic Determination of Stannous Ion in Technetium Radiopharmaceutical Cold Kits

Érika V. Almeida, Marcelo di M.V. Lugon, José L. da Silva, Neuza T.O. Fukumori, Nilda P.S. de Pereira, and Margareth M.N. Matsuda

Radiopharmacy Center, Nuclear Energy and Research Institute, São Paulo, Brazil

The aim of this work was to develop a selective method for quantification of Sn(II) and Sn(IV) in dimercaptosuccinic acid (DMSA), ethylcysteinate dimer (ECD), methylenediphosphonic acid (MDP), and pyrophosphate radiopharmaceutical cold kits by differential pulse polarography. **Methods:** A dripping mercury electrode 150 polarographic/stripping analyzer with a conventional 3-electrode configuration was used with 3 M H₂SO₄ and 3 M HCl supporting electrolytes for Sn(II) and Sn(IV), respectively. The polarographic analysis was performed using a 1-s drop time, 50-mV·s⁻¹ scan rate, -50-mV pulse amplitude, 40-ms pulse time, and 10-mV step amplitude. To quantify Sn(IV), oxidation of Sn(II) by H₂O₂ was performed. The calibration curves for Sn(II) and Sn(IV) were obtained in the range of 0–10 µg·mL⁻¹. **Results:** The analytic curves for Sn(II) in 3 M H₂SO₄ and Sn(IV) in 3 M HCl were represented by the following equations: $i (\mu A) = 0.098 [Sn(II)] + 0.018$ ($r^2 = 0.998$) and $i (\mu A) = 0.092 [Sn(IV)] + 0.016$ ($r^2 = 0.998$), respectively. The detection limits were 0.21 µg·mL⁻¹ for Sn(II) and 0.15 µg·mL⁻¹ for Sn(IV). In DMSA, ECD, MDP, and pyrophosphate, 90.0%, 64.9%, 93.2%, and 87.5%, respectively, of the tin was present as Sn(II). In this work, selective determination of Sn(II) and Sn(IV) was achieved using 2 supporting electrolytes (H₂SO₄ and HCl). In 3 M H₂SO₄, only Sn(II) produced a polarographic wave with the maximum current in -370 mV. Under the same conditions, no current could be determined for Sn(IV). In 3 M HCl, Sn(II) and Sn(IV) were electroactive and the maximum currents of the 2 waves appeared in -250 and -470 mV. No other components of the lyophilized reagents had any influence. **Conclusion:** The developed polarographic method was adequate to quantify Sn(II) and Sn(IV) in DMSA, ECD, MDP, and pyrophosphate cold kits.

Key Words: ^{99m}Tc-radiopharmaceuticals; polarography; Sn(II); Sn(IV)

J Nucl Med Technol 2011; 39:307–311

DOI: 10.2967/jnmt.111.087437

Radiopharmaceutical cold kits for labeling with ^{99m}Tc contain Sn(II) for reduction of technetium to lower oxidation states that are chemically reactive to specific ligands. Besides these ligands, the cold kits usually contain stannous chloride (SnCl₂) and different additives (complexing agents, antioxidants, and buffers). The amount of stannous ions varies (0.03–1.5 mg of SnCl₂), although a minimum concentration must be present to guarantee the lyophilized reagent shelf life and to allow efficient labeling with ^{99m}Tc (1).

Depending on the medium composition, Sn(II) ions in low-concentration solutions (<2.0·10⁻⁴ M) are oxidized, and the formation of basic complexes takes place above pH 2.00 (2,3). The quantitative determination of Sn(II) in radiopharmaceutical cold kits is an important aspect of quality control, and the analytic method must be accurate even in the presence of Sn(IV) ions (4).

Such techniques as colorimetry, titrimetry, spectrophotometry, voltammetry, and polarography have been described in the literature for Sn(II) determination in cold kits (5–12).

Zimmer et al. studied the formation of a red porphyrin complex in the presence of Sn(II) ions using a colorimetric method. The time of the color fading was proportional to the Sn(II) concentration in pyrophosphate, methylenediphosphonic acid (MDP), and diethylenetriaminepentaacetic acid (DTPA) (5). Chervu et al. have used a potentiometric titration of Sn(II) in HCl and potassium iodate as the oxidizing agent to analyze DTPA, glucoheptonate, hepatoiminodiacetic acid, MDP, and pyrophosphate (6). Muddukrishna et al. developed a method based on the oxidation of Sn(II) using a known excess of iodate or iodine, and the unreacted excess of the oxidizing agent was titrated with thiosulfate in glucoheptonate, hepatoiminodiacetic acid, MDP, DTPA, human serum albumin, albumin macroaggregate, and pyrophosphate. The procedure was used to overcome the need to perform experiments in an oxygen-free atmosphere as required by the direct iodometric titration. Reducing agents such as ascorbic acid and human serum albumin interfered with this method (7).

Mushtaq et al. have proposed a method in which the amount of Sn(II) in various cold kits was determined by a

Received Jan. 18, 2011; revision accepted May 31, 2011.

For correspondence or reprints contact: Margareth M.N. Matsuda, Nuclear Energy and Research Institute (IPEN-CNEN/SP), Radiopharmacy Center—DIRF, Av. Professor Lineu Prestes, 2242, 05508-000, São Paulo, Brazil.

E-mail: mmatsuda@ipen.br

Published online Oct. 3, 2011.

COPYRIGHT © 2011 by the Society of Nuclear Medicine, Inc.

spectrophotometric method using palladium chloride. This method was not applicable to dimercaptosuccinic acid (DMSA), DTPA, ethylcysteinyl dimer (ECD), or methoxyisobutyl isonitrile because of ligand or antioxidant interference (8). Boutakhrir et al. determined Sn(II) ions in DMSA by flow injection analysis with amperometric detection. Metal ions did not influence the signal of the Sn(II)-8-hydroxyquinoline complex and ascorbic acid, but medronic acid, 4-aminobenzoic acid, and pentetic acid increased or decreased the peak (9).

Polarographic analysis has been used as an alternative method in which the main advantage is the differentiation between Sn(II) and Sn(IV) ions. On a hanging drop of mercury, a redox process occurs, and a current proportional to the amount of the species taking part in the electrochemical reaction is measured (13,14).

Polarographic methods for selective determination of Sn (II) in radiopharmaceutical cold kits were reported by McBride et al., Decristoforo et al., Lejeune et al. and Ross et al. (10–12,15).

McBride et al. proposed a differential pulse polarography method for Sn(II) quantification in pyrophosphate and polyphosphate, in which 1 M H₂SO₄ was used as the supporting electrolyte. Sn(IV) interference in the Sn(II) signal was not evaluated in 0.12 M HCl (16).

The aim of this work was to develop a selective method for the determination of Sn(II) and Sn(IV) (total tin) in DMSA, ECD, MDP, and pyrophosphate radiopharmaceutical cold kits.

MATERIALS AND METHODS

Apparatus

The polarographic analysis was performed using a dripping mercury electrode 150 polarographic/stripping analyzer (Radiometer Analytic), with a conventional 3-electrode configuration consisting of a static mercury drop electrode, an AgCl/Ag (saturated KCl) reference electrode, and a platinum wire auxiliary electrode. The experimental conditions were a 1-s drop time, 50-mV·s⁻¹ scan rate, -50-mV pulse amplitude, 40-ms pulse time, and 10-mV step amplitude.

Reagents and Solutions

DMSA, ECD, MDP, and pyrophosphate radiopharmaceutical cold kits were from IPEN-CNEN/SP. The formulations were DMSA (1 mg) and SnCl₂·2H₂O (0.41 mg); ECD (1 mg), mannitol (24 mg), ethylenediamine tetraacetic acid (0.36 mg), and SnCl₂·2H₂O (0.125 mg); MDP (5 mg), ascorbic acid (0.10 mg), pyrophosphate (45 mg), and SnCl₂·2H₂O (1 mg); and pyrophosphate (10 mg) and SnCl₂·2H₂O (2 mg).

SnCl₂·2H₂O and a 1,000 µg·mL⁻¹ standard solution of Sn(IV) were *pro analysi* grade, and H₂O₂, H₂SO₄, and HCl were super-pure reagents from Merck. Purified water obtained from an Elix 10 system (Millipore) was used to prepare all the solutions. A stock solution of Sn(II) (1,000 µg·mL⁻¹) was prepared just before analysis by adding SnCl₂·2H₂O in nitrogen-deaerated 1.0 M HCl solution.

Procedure

A supporting electrolyte (10 mL) was initially added to the polarographic cell and deaerated with nitrogen gas for 5 min. The supporting electrolytes for Sn(II) and Sn(IV) determinations were 3 M H₂SO₄ and 3 M HCl, respectively. A differential pulse polarogram of the supporting electrolyte (blank) was obtained in the range -200 to -800 mV before 5 successive additions of 20 µL of 1,000 µg·mL⁻¹ Sn(II) or Sn(IV) standard solution into the cell, in order to record the polarographic waves of 0, 2.0, 4.0, 6.0, 8.0, and 10.0 µg·mL⁻¹ tin concentrations. The maximum current (µA) of the waves (peak height), measured from the baseline to the top, was used to obtain the analytic curve and quantify the Sn(II) and Sn(IV) concentrations in the cold kits. The analyses were performed in triplicate, and 3 vials of each lyophilized reagent were used. The results were expressed as mean ± SD.

The radiopharmaceutical cold kits were reconstituted by adding deaerated purified water (1.0 mL for DMSA, ECD, and pyrophosphate and 2.0 mL for MDP), and 100-, 320-, 80-, and 20-µL aliquots were separately added into the cell to determine Sn(II) or Sn(IV) in DMSA, ECD, MDP, and pyrophosphate, respectively. Sn(II) was oxidized to Sn(IV) by adding 20 µL of H₂O₂ to the reconstituted cold kit vial and letting it stand at 37°C for 5 min. Nitrogen was bubbled through the vial for 1 min before the aliquot was withdrawn for the Sn(IV) analysis. Sn(II) and Sn(IV) were quantified using the analytic curve.

The influence of increasing concentrations of each component of the cold kit formulation on the peak height of 2.0–6.0 µg·mL⁻¹ Sn(II) or Sn(IV) (20–60 µL of 1,000 µg·mL⁻¹ tin standard solution in the cell) was evaluated. The concentration range of each component was based on the tin-to-component ratio of the formulation.

Titrimetric determinations for Sn(II) in DMSA, ECD, MDP, and pyrophosphate were performed using 5.0 mM I₂ (17).

RESULTS

Figure 1 shows a typical differential pulse polarogram of Sn (II) and Sn(IV) in 3 M H₂SO₄ and 3 M HCl, respectively. The polarograms in H₂SO₄ were obtained separately from those in HCl. The tin concentration in the cell was 2.0 µg·mL⁻¹ (17.7 µM) for each 20-µL aliquot of 1,000 µg·mL⁻¹ tin standard solution, and after 5 successive additions the total tin concentration was 10.0 µg·mL⁻¹ (88.5 µM).

The analytic curves for Sn(II) in 3 M H₂SO₄ and Sn(IV) in 3 M HCl are represented by Equations 1 and 2, respectively.

$$i(\mu\text{A}) = 0.098[\text{Sn(II)}] + 0.018 \quad (r^2 = 0.998, n = 6) \quad \text{Eq. 1.}$$

$$i(\mu\text{A}) = 0.092[\text{Sn(IV)}] + 0.016 \quad (r^2 = 0.998, n = 6), \quad \text{Eq. 2}$$

where *i* (µA) is the current of the tin wave (peak height).

The detection limits for Sn(II) and Sn(IV) were 0.21 µg mL⁻¹ (18.6 µM) and 0.15 µg mL⁻¹ (13.3 µM), respectively.

FIGURE 1. Differential pulse polarograms for tin determination: Sn(II) in 3 M H_2SO_4 (a) and Sn(IV) in 3 M HCl (b). Tin concentration in polarographic cell was $2.0 \mu\text{g}\cdot\text{mL}^{-1}$ ($17.1 \mu\text{M}$) for each addition (5 aliquots). Experimental conditions: $10\text{-mV}\cdot\text{s}^{-1}$ scan rate, 40-ms pulse time, and -50-mV pulse amplitude.

The wave shapes, peak heights, and potentials of the maximum current for Sn(II) or Sn(IV) were compared in the absence and in the presence of increasing concentrations of each component of the formulation. Figure 2 shows the influence of MDP components (MDP, ascorbic acid, and pyrophosphate) on the peak height of $2.0\text{--}6.0 \mu\text{g}\cdot\text{mL}^{-1}$ ($0.2\text{--}0.6 \text{ mg}$) Sn(II) in 3 M H_2SO_4 and $2.0\text{--}4.0 \mu\text{g}\cdot\text{mL}^{-1}$ ($0.2\text{--}0.4 \text{ mg}$) Sn(IV) in 3 M HCl . The abscissa was represented in a logarithmic scale. Because the $\text{SnCl}_2\cdot 2\text{H}_2\text{O}$ content in MDP was 1 mg (i.e., 0.52 mg of Sn(II)), 1:10 to 1:50 dilution factors were used to calculate the mass range of the reagents and to perform the Sn(II) and Sn(IV) analyses using the analytic curve working range.

Table 1 presents the Sn(II) and Sn(IV) concentrations in DMSA, ECD, MDP, and pyrophosphate considering the dilutions.

DISCUSSION

Differential pulse polarography was used for selective determination of Sn(II) and Sn(IV) in DMSA, ECD, MDP, and pyrophosphate. The $\text{SnCl}_2\cdot 2\text{H}_2\text{O}$ mass ranging from 0.125 to 2 mg covered most of the lyophilized reagent for labeling with $^{99\text{m}}\text{Tc}$ used in nuclear medicine.

For a specific and selective determination of Sn(II) and Sn(IV), 3 M H_2SO_4 was considered the most appropriate medium for Sn(II) because only Sn(II) produced a polarographic wave with the maximum current in -370 mV (Fig. 1A). Under the same conditions, no current could be determined for Sn(IV). In 3 M HCl , Sn(II) and Sn(IV) were electroactive and the potential of the 2 polarographic waves appeared in -250 and -470 mV (Fig. 1B).

Lingane et al. reported that Sn(IV) is an air-stable form and does not produce polarographic waves either in HNO_3 or H_2SO_4 because Sn(IV) ions are extensively hydrolyzed and precipitate as basic salts even in a highly acidic medium (4,18). On the other hand, HCl or bromide complexes can stabilize high-order halide complexes and produce 2 reduction waves for Sn(IV) (19).

An investigation of the polarographic behavior of Sn(IV) in fairly concentrated H_2SO_4 , HClO_4 , HNO_3 , or HF showed no wave in any of these media. After the addition of HCl ,

polarographic waves were observed for Sn(IV) and Sn(II) in a Sn(IV) solution, with an increase in the wave height without altering the half-wave potential (19).

The adequate establishment of the supporting electrolyte allows selective determination of the ion. The polarography study of tin in various supporting electrolytes was described by Lingane et al., and the Sn(II) waves in HCl , HNO_3 , and H_2SO_4 had a sigmoidal shape and were considered well defined for analytic use. The choice of the supporting electrolyte and the presence of stabilizing agents are the main factors that affect the reduction potential (18). In most media, Sn(II) ions produce 2 polarographic waves. In the cathodic wave, tin is reversibly reduced to Sn(amalgam), and in the anodic wave, Sn(II) is oxidized to Sn(IV), and the degree of reversibility and suitability for analytic application is dependent on the particular medium (19).

FIGURE 2. (A) Influence of MDP cold kit components on peak height of Sn(II) in 3 M H_2SO_4 : $2.0 \mu\text{g}\cdot\text{mL}^{-1}$ of Sn(II) and $0.4\text{--}2.0 \mu\text{g}\cdot\text{mL}^{-1}$ ($0.004\text{--}0.02 \text{ mg}$) of ascorbic acid (a), $6.0 \mu\text{g}\cdot\text{mL}^{-1}$ of Sn(II) and $20\text{--}100 \mu\text{g}\cdot\text{mL}^{-1}$ ($0.2\text{--}1.0 \text{ mg}$) of MDP (b), and $6.0 \mu\text{g}\cdot\text{mL}^{-1}$ of Sn(II) and $80\text{--}400 \mu\text{g}\cdot\text{mL}^{-1}$ ($0.8\text{--}4.0 \text{ mg}$) of pyrophosphate (c). (B) Influence of MDP cold kit components on peak height of Sn(IV) in 3 M HCl : $2.0 \mu\text{g}\cdot\text{mL}^{-1}$ of Sn(IV) and $0.4\text{--}2.0 \mu\text{g}\cdot\text{mL}^{-1}$ ($0.004\text{--}0.02 \text{ mg}$) of ascorbic acid (a), $2.0 \mu\text{g}\cdot\text{mL}^{-1}$ of Sn(IV) and $20\text{--}100 \mu\text{g}\cdot\text{mL}^{-1}$ ($0.2\text{--}1.0 \text{ mg}$) of MDP (b), and $4.0 \mu\text{g}\cdot\text{mL}^{-1}$ of Sn(IV) and $80\text{--}400 \mu\text{g}\cdot\text{mL}^{-1}$ ($0.8\text{--}4.0 \text{ mg}$) of pyrophosphate (c). Experimental conditions: 1-s drop time, $50\text{-mV}\cdot\text{s}^{-1}$ scan rate, -50-mV pulse amplitude, 40-ms pulse time, and 10-mV step amplitude.

TABLE 1

Determination of Sn(II) and Sn(IV) Concentrations in Radiopharmaceutical Cold Kits by Differential Pulse Polarography

Cold kit	mg total tin	i (μ A)		mg tin (% Sn(II) or Sn(IV)/total tin)	
		H ₂ SO ₄ , 3 M	HCl, 3 M	Sn(II)	Sn(IV)
DMSA	0.213	-0.202	-0.208	0.192 $\pm$ 0.003 (90.0)	0.211 $\pm$ 0.004 (98.9)
ECD	0.065	-0.152	-0.204	0.042 $\pm$ 0.001 (64.9)	0.625 $\pm$ 0.002 (96.6)
MDP	0.519	-0.201	-0.202	0.483 $\pm$ 0.013 (93.2)	0.499 $\pm$ 0.018 (96.1)
Pyrophosphate	1.038	-0.190	-0.203	0.908 $\pm$ 0.023 (87.5)	1.004 $\pm$ 0.032 (96.7)

$n = 9$ (triplicate of 3 vials). Data in parentheses are percentages.

Based on the results of Lingane et al. (18), some studies described the selection of a supporting electrolyte for selective determination of Sn(II) in radiopharmaceuticals. McBride et al. observed that in 1 M H₂SO₄, the reduction potential of Sn(II) in pyrophosphate and polyphosphate was -440 mV (16), but they did not evaluate either lyophilized reagent of lower SnCl₂ mass content or the presence of complexing reagents such as DMSA and ethylenediamine tetraacetic acid, which produce interference in some reported analytic methods (8,9). In our work, 3 M H₂SO₄ was used instead of 1 M to overcome any interference problem. Although Stefan et al. reported that only Sn(II) was electroactive in 0.1 M HClO₄ at -420 mV (2), Ross et al. observed waves for noncomplexed DMSA and tin complex in 0.1 mM perchlorate, pH 3.0, in the Sn(II) determination of DMSA (15). In our work, a DMSA wave was not observed at -200 to -800 mV potential range. In a more complex medium such as 0.7 M KF/1.8 M KNO₃, pH 7.7, or 0.7 M KF/0.1 M NaNO₃, pH 7.5, proposed by Lejeune et al., Sn(II) was not affected by Sn(IV) although it was necessary to use a buffered medium and another complexing reagent such as ZnCl₂ to suppress the MDP effect (12). Decristoforo et al. proposed a simpler medium composed of methanol in 35 mM HClO₄, and they focused their work on the evaluation of the stability of fractionated cold kits (11). The authors observed an overlapping between Sn(II) and ECD or DMSA waves. The potential range of the peak attributed to the reduction of stannous ions to tin metal was -350 and -400 mV, and the reduction potential of Sn(IV) to Sn(II) was between -150 and -190 mV.

Before the quantification of Sn(II), the tin redox reaction taking place in the mercury drop was assessed by the presence of the components of the cold kit formulation other than the tin species. No variation was observed in the peak height, shape, and reduction potential of Sn(II) and Sn(IV) in the concentration range studied (Figs. 2A and 2B). Because the conclusions for DMSA, ECD, and pyrophosphate were the same, only the MDP data were presented.

The analytic curves for Sn(II) and Sn(IV) (Eqs. 1 and 2) were linear in the concentration range of 0–10 μ g·mL⁻¹, and the correlation coefficients (r^2) were greater than 0.997.

The results presented in Table 1 show that in ECD, only 65% of the total tin is present as Sn(II), indicating oxidation

to Sn(IV) in the production process, which can yield a low ^{99m}Tc labeling and poor radiochemical purity. In DMSA, MDP, and pyrophosphate, more than 87% of the total tin is in the Sn(II) oxidation state.

Even using a millimolar titrant concentration to quantify Sn(II), by the titrimetric conventional method, the titrant volumes and the Sn(II) mass in the cold kits were 0.12, 1.12, and 1.75 mL, resulting in 0.060 $\pm$ 0.017, 0.607 $\pm$ 0.040, and 0.953 $\pm$ 0.025 mg in ECD, MDP, and pyrophosphate, respectively. Higher SD and mass results for Sn(II) by the titrimetric analysis than by the polarographic method (Table 1) can be attributed to the difficulty of visual detection of the endpoint.

CONCLUSION

The developed polarographic method was selective and adequate to determine Sn(II) even in the presence of Sn(IV) and can be used as a quality control to quantify Sn(II) and Sn(IV) in DMSA, ECD, MDP, and pyrophosphate radiopharmaceutical cold kits.

ACKNOWLEDGMENTS

We thank IPEN-CNEN/SP for providing the materials and samples for the experiments and the quality control facilities for the execution of the tests. No potential conflict of interest relevant to this article was reported.

REFERENCES

1. Ilse Z. *Technetium-99m Pharmaceuticals: Preparation and Quality Control in Nuclear Medicine*. Berlin, Germany: Springer; 2007:61–63.
2. Stefan G, Zenon K. Polarographic investigation of the stability of tin(II) solutions in the presence of some stabilizing agents. *Anal Chim Acta*. 1981;130:133–140.
3. Pettine M, Frank M, Macchi G. Hydrolysis of tin(II) in aqueous solutions. *Anal Chem*. 1981;53:1039–1043.
4. McBride MHD, George RE, Kessler WV, Shaw SW. Stannous-ion quantitation in pyrophosphate and polyphosphate radiopharmaceutical kits using differential pulse polarography. *J Pharm Sci*. 1977;66:870–871.
5. Zimmer AM, Spies SM. The paper spot test: a rapid method for quantitating stannous concentrations in radiopharmaceutical kits. *J Nucl Med*. 1981;22:465–467.
6. Chervu LR, Vallabhajosyula B, Mani J, Chun SB, Blaufox MD. Stannous ion quantitation in ^{99m}Tc-radiopharmaceutical kits. *Eur J Nucl Med*. 1982;7:291–293.
7. Muddukrishna SN, Chen A, Sykes TR, Noujaim AA. Indirect iodometric procedure for quantitation of Sn(II) in radiopharmaceutical kits. *Appl Radiat Isot*. 1994;45:293–299.

8. Mushtaq A, Haider I. Spectrophotometric determination of Sn(II) using palladium chloride in kits for ^{99m}Tc radiopharmaceuticals. *Appl Radiat Isot.* 1999;50:649–653.
9. Boutakhrif K, Yang ZP, Kauffmann JM. Inorganic tin(II) determination by FIA with amperometric detection of its oxinate complex. *Talanta.* 1995;42:1883–1890.
10. McBride MH, Shaw SM, Kessler WV. Deterioration of stannous ion in radiopharmaceutical kits during storage. *Am J Hosp Pharm.* 1979;36:1370–1372.
11. Decristoforo C, Obendorf D, Reichart E, Riccabona G. Determination of Sn(II) in technetium cold kits by voltammetry at the hanging mercury drop electrode (HMDE) and relevant radiopharmaceutical applications. *Nucl Med Biol.* 1998;25:675–683.
12. Lejeune R, Thunus J, Thunus L. Polarographic determination of Sn(II) in samples containing Sn(IV) such as in ^{99m}Tc -technetium radiopharmaceuticals kits. *Anal Chim Acta.* 1996;332:67–71.
13. Breda EJ, Meites L, Reddy TB, West PW. Half-wave potentials of metal ions in organic hydroxyacid supporting electrolytes. *Anal Chim Acta.* 1956;14:390–399.
14. Meites L. *Polarographic Techniques.* New York, NY: Interscience Publishers; 1965.
15. Ross AJ, Moore HA, Ritter CO, Moros SA. Differential pulse polarographic determination of 2,3 dimercaptosuccinic acid and tin(II) in radiopharmaceuticals. *J Pharm Sci.* 1979;68:657–658.
16. McBride MHD, George R, Kessler W, Shaw S. Stannous-ion quantitation in pyrophosphate and polyphosphate radiopharmaceutical kits using differential pulse polarography. *J Pharm Sci.* 1977;66:870–871.
17. Ohlweiler OA. *Química Analítica Quantitativa.* Vols. 1 and 2. Rio de Janeiro, Brazil: Editora Livros Técnicos Científicos S.A.; 1986.
18. Lingane JJ. Systematic polarographic metal analysis characteristics of arsenic, antimony, bismuth, tin, lead, cadmium, zinc, and copper, in various supporting electrolytes. *Ind Eng Chem Anal Ed.* 1943;15:583–590.
19. Bond AM. Direct current, alternating current, rapid, and inverse polarographic methods for determination of tin(IV). *Anal Chem.* 1970;42:1165–1168.