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POLAROGRAPHIC DETERMINATION OF Sn (II) AND TOTAL Sn IN PYRO AND MDP RADIOPHARMACEUTICAL KITS

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ABSTRACT

A sensitive, alternative method to atom absorption spectometry, fluorimetry or potentiometry for the evaluation of tin(II) ions (0.1- 10mg) and total tin in radiopharmaceutical kits was investigated. Differential pulse polarography was chosen. The supporting electrolyte was H_2SO_4 3 mol L^{-1} and HCl 3 mol L^{-1} solution. The potential was swept from –250 to –800 mV vs Ag/AgCl/saturated KCl, using a dropping mercury electrode with 1 s drop time, 50 mV s^{-1} scan rate, –50 mV pulse amplitude, 40 ms pulse time and 10 mV step aplitude. Pure nitrogen was used to deaerate the polarographic cell solution for 5 min, before and after each sample introduction. Oxidation of Sn(II) was made in the same sample vial by adding H_2O_2 (hydrogen peroxide) 10mol L^{-1}, at 37°C, in order to quantify the total Sn. The calibration curve for Sn(II) and Sn(IV) was obtained in the concentration range of 0-10 ppm from a 1000 ppm standard solution. The detection limit of Sn(II) is 0.5ppm and for Sn(IV) is 0.6ppm. Differential pulse polarography was performed in the pyrophosphate (PYRO) and methylenediphosphonic acid (MDP) radiopharmaceutical kits, containing 2 mg and 1 mg of $SnCl_2.2H_2O$ per vial, respectively. The described method for determination of stannous ion (Sn(II)), is selective, reproducible and adequate to be used in the quality control of lyophilized reagents and it shall be performed for other cold kits produced at IPEN.

1. INTRODUCTION

Stannous chloride is the major compound used for reduction of generator-derived ^{99m}Tc-pertechnetate in cold kits for on site preparation of ^{99m}Tc-radiopharmaceuticals. These cold kits usually contain a ligand, stannous chloride ($SnCl_2.2H_2O$), and different additives (complexing agents, antioxidants, buffers, etc.). The amount of stannous ions Sn(II) varies from kit to kit. In technetium labeling kits, where $SnCl_2.2H_2O$ is used for stabilizing the system, it is important to know the exact concentration of Sn(II) for ^{99m}Tc-pertechnetate reduction and the concentration of total Sn considering toxicological effects [1].

Various techniques were described for tin determination (atom absorption spectometry [2], titrimetric methods [3], spectrophotometry of tin complexes [4] or chromatography [5]), but they cannot distinguish between stannous (II) and stannic (IV) ions in solutions. Titrimetric methods, which are selective for Sn(II), are generally less sensitive. Nevertheless, with appropriate amounts of Sn(II) (0.1–10mg), the titration is not a time consuming method. Colorimetric methods are often associated with problems of specificity and stability of the formed tin complexes. The two methods described in literature for selective determination of Sn(II) are polarography and mass analysis (redox-titration). Polarography is a good selective method in the mg range as well as in the μg range for Sn(II) and Sn(IV) [6].

The basis of polarography is that a steadily increasing potential is applied on a hanging drop of Hg, and when a redox-process occurs, a current proportional to the amount of the species taking part in the electrochemical reaction can be measured [7].

The aim of this work is to develop an alternative, sensitive and selective method for the determination of tin (II) and total tin in the radiopharmaceutical cold kits as pyrophosphate acid (PYRO) and methylenediphosphonic acid (MDP) containing 2 mg and 1 mg of $SnCl_2.2H_2O$ per vial, respectively [8]. In order to quantify the total Sn, the oxidation of Sn(II) was made in the same sample vial by adding hydrogen peroxide.

2. EXPERIMENTAL

2.1- Apparatus

A MDE 150 polarographic/stripping analyzer (Radiometer Analytical), with a conventional three-electrode configuration consisting of a static mercury drop electrode, an AgCl/Ag (saturated KCl) reference electrode and a platinum wire auxiliary electrode were used in differential pulse polarography, with 1 s drop time, 50 mV s^{-1} scan rate, –50 mV pulse amplitude, 40 ms pulse time and 10 mV step amplitude.

2.2- Reagents and solutions

Methylenediphosphonic acid was obtained from Plenum and pyrophosphate was from Aldrich. MDP and PYRO radiopharmaceutical cold kit samples were produced at IPEN/CNEN/SP. $SnCl_2.2H_2O$, Sn(IV) 1000 ppm standard solution, H_2O_2, H_2SO_4 and HCl were P.A. grade reagents from Merck. Purified water was obtained from Milli-RX 45 (Millipore) system and used to prepare all the solutions. MDP and PYRO kit formulations are described in the Table 1.

Table 1. MDP and PYRO radiopharmaceutical cold kit formulations.

MDP		PYRO	
Reagent	**mg/vial**	**Reagent**	**mg/vial**
Methylenediphosphonic acid	5.0	Pyrophosphate	10
$SnCl_2.2H_2O$	1.0	$SnCl_2.2H_2O$	2
Ascorbic acid	0.1		
Pyrophosphate	20		

The 1000 ppm stock solution of Sn(II) was prepared by adding $SnCl_2.2H_2O$ in acidified nitrogen deaerated water.

The supporting electrolytes (H_2SO_4 3 mol L^{-1} and HCl 3 mol L^{-1}) were deaerated during 20 min with 5.0 nitrogen gas prior the use.

2.3. Procedure

10 mL of supporting electrolyte was initially added to the polarographic cell and degassed with nitrogen for 5 min. A differential pulse voltamogram of the blank supporting electrolyte

was recorded in the range from –250 to –800 mV before sucessive addition of 20 µl of 1000 ppm Sn(II) or Sn(IV) standard solution in the cell. The supporting electrolytes for Sn(II) and Sn(IV) determinations were H_2SO_4 3 mol L^{-1} and HCl 3 mol L^{-1}, respectively. The current (µA) was measured at –370 mV and –470 mV potentials for Sn(II) and Sn(IV), respectively. The Sn(II) and Sn(IV) calibration curves were obtained in the range from 2 to 10 ppm.

The radiopharmaceutical cold kits were reconstituted by adding 1 mL of purified deaerated water and an aliquot was added in the polarographic cell in order to determine Sn(II). The oxidation of Sn(II) was carried out in the same vial, by adding H_2O_2 at 37°C, for 5 min to quantify Sn(IV).

3. RESULTS AND DISCUSSION

In this work, selective determination of Sn(II) and total Sn was carried out by using two different electrolyte solutions (H_2SO_4 and HCl). H_2SO_4 3 mol L^{-1} was chosen as the most appropriate medium for tin(II) determination because only Sn(II) produces a reduction peak in this electrolyte solution at the potential of -370 mV [9]. In HCl 3 mol L^{-1} supporting electrolyte, reduction waves for Sn(II) and Sn(IV) appear at the same potential, -470 mV.

Figure 1 shows typical Sn(II) in H_2SO_4 3 mol L^{-1} and Sn(IV) in HCl 3 mol L^{-1} polarograms. The tin concentration in the polarographic cell was 2 ppm for each added aliquot (number of aliquots (n) = 5; total tin concentration in the cell after the additions = 10 ppm).

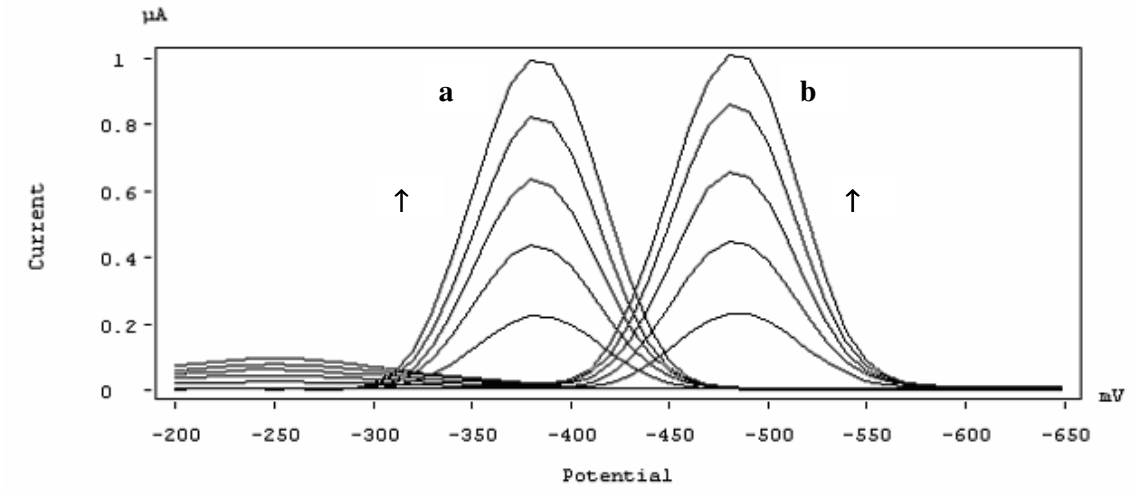

Fig 1. Differential pulse polarograms for tin determination: a) Sn(II) in H_2SO_4 3 mol L^{-1} b) Sn(IV) in HCl 3 mol L^{-1}. The tin concentration in the polarographic cell was 2 ppm for each addition (n = 5). Analysis conditions: 1 s drop time, 50 mV s^{-1} scan rate, –50 mV pulse amplitude, 40 ms pulse time and 10 mV step amplitude.

Figure 1 shows that the peak height, measured as current, increases proportionally to the tin concentration.

The calibration curves, which were linear in the range 0-10 ppm, have the following equations:

$i(\mu A) = 0.0978[Sn(II)] + 0.0181$ ($r = 0.9985$, $n = 6$)

$i(\mu A) = 0.0921[Sn(IV)] + 0.0164$ ($r = 0.9984$, $n = 6$).

The detection limit of Sn(II) and Sn(IV) was 0.5 ppm and 0.6 ppm, respectively.

According to the formulations, 0.12 mg of $SnCl_2.2H_2O$ is present with 0.6 mg of methylenediphosphonic acid or pyrophosphate.

The effect of pyrophosphate and methylenediphosphonic acid, that are the ligands used in technetium complexes for labeling bones, was verified.

Figures 2 and 3 show the influence of successive aliquots containing 0.2 mg of methylenediphosphonic acid or pyrophosphate solutions on the peak height of 0.06 mg of Sn(II).

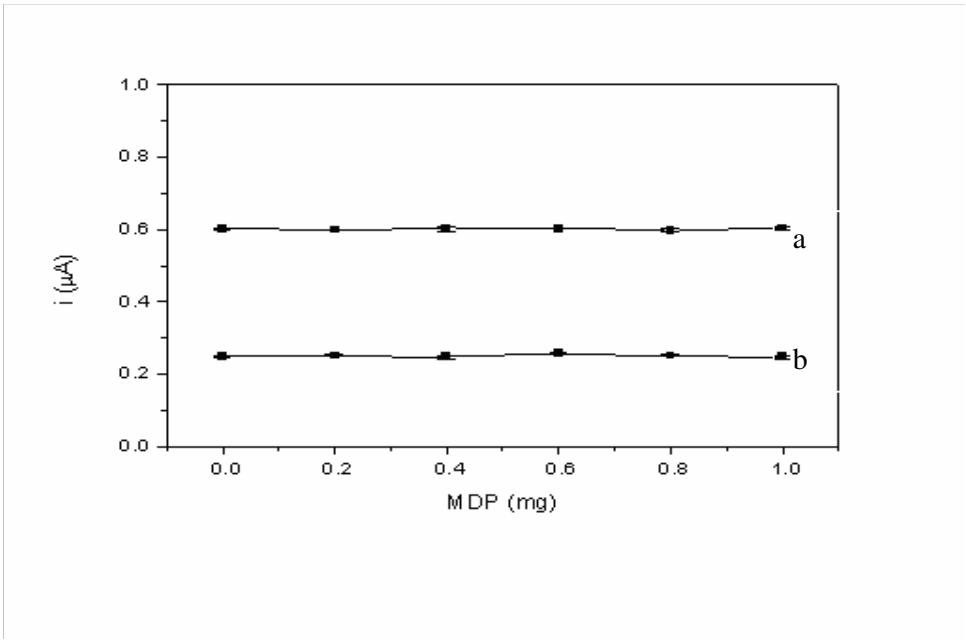

Fig. 2. Effect of methylenediphosphonic acid concentration on tin species in two supporting electrolytes: (a) 0.06 mg of Sn(II) in H_2SO_4 3 mol L^{-1}; (b) 0.02 mg of Sn(IV) in HCl 3mol L^{-1}. Analysis conditions: 1 s drop time, 50 mV s^{-1} scan rate, –50 mV pulse amplitude, 40 ms pulse time and 10 mV step amplitude.

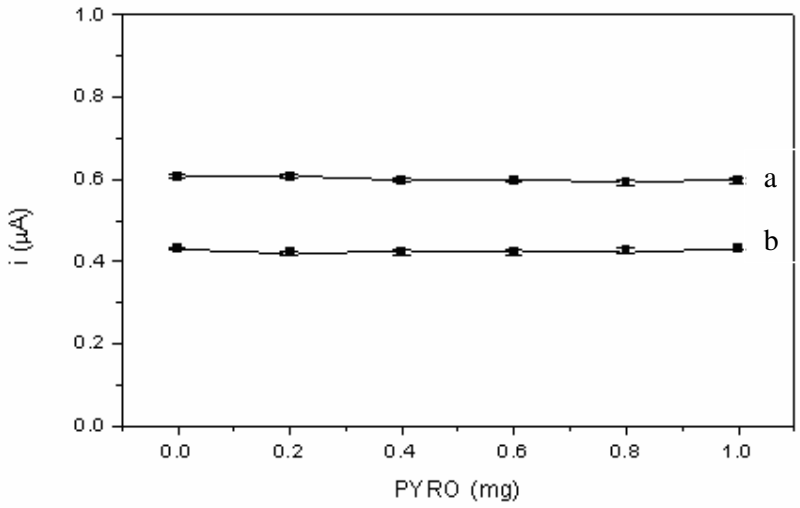

Fig. 3. Effect of pyrophosphate concentration on tin species in two supporting electrolytes: (a) 0.06 mg of Sn(II) in H_2SO_4 3 mol L^{-1}; (b) 0.04 mg of Sn(IV) in HCl 3 mol L^{-1}. Analysis conditions: 1 s drop time, 50 mV s^{-1} scan rate, –50 mV pulse amplitude, 40 ms pulse time and 10 mV step amplitude.

It was observed that the signals of Sn(II) and Sn(IV) standard solutions were not influenced by methylenediphosphonic acid and pyrophosphate in the range of 0.2-1.0 mg.

MDP and PYRO (3 samples of each one) radiopharmaceutical cold kits were analyzed and the concentrations of Sn(II) and $SnCl_2.2H_2O$, determined as Sn(IV) after oxidation of Sn(II), were calculated (Table 2).

Table 2. Determination of Sn(II) and total tin concentrations in MDP and PYRO radiopharmaceutical cold kits.

Sample	i (μA)		(%)	
	H_2SO_4 3 mol L^{-1}	HCl 3 mol L^{-1}	Sn(II)	$SnCl_2.2H_2O$
MDP	0.201	0.202	92.5 ± 2.6	100.0 ± 0.0
PYRO	0.190	0.203	87.5 ± 2.3	100.0 ± 0.0

4. CONCLUSION

The developed polarographic method was selective to determine Sn(II) in the presence of Sn(IV) and can be used to quantify the tin content in MDP and PYRO technetium cold kits.

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