R 2.1 Tin analysis

Tin is used for many technetium based radiopharmaceuticals and since this is the main radiopharmaceutical that is most widely used clinically the assessment of tin is essential. For an optimal radiopharmaceutical formulation milligram amounts are used and for some microgram amounts are used. The actual levels can affect the final radiochemical purity and alter the pharmacokinetics of the radiopharmaceutical. Well-established methods are identified and used as the standard methods of analysis for tin estimation. Analytical methods approved by the relevant regional or national authority for application to environmental samples may be suitable. Additionally, analytical methods are included that modify previously used methods to obtain lower detection limits and/or to improve accuracy and precision. The specific requirements are included in the relevant individual monographs.

R2.1.1 Tin estimation by gas chromatography or high performance liquid chromatography

Tin is usually determined as the total metal, but it may also be measured as specific organo-tin compounds. Flame atomic absorption analysis is the most widely used and straightforward method for determining tin; furnace atomic absorption analysis is used for very low analyte levels and inductively coupled plasma atomic emission analysis is used for multi-analyte analyses that include tin. The preferred separation technique for organo-tin compounds is gas chromatography (GC) due to its high resolution and detector versatility.

(HPLC) has also been used in the analysis of organo-tin compounds. The advantage of HPLC over GC is that no derivatization step is needed after extraction.

For determination of tin in biological samples, the sample is digested in an oxidizing acid mixture followed by atomic spectrometric determination. Determination of organo-tin compounds in biological materials will require extraction, derivatization, separation, and detection, as described. Whole blood samples are typically analysed by spectrophotometry and photometry.

R2.1.2 Tin estimation by polarography

Tin can be effectively analysed by polarography, which is also called polarographic analysis, or voltammetry method of analysing solutions of reducible or oxidizable substances. Polarography technique involves electric potential (or voltage) varied in a regular manner between two sets of electrodes (indicator and reference) while the current is monitored. The shape of a polarogram depends on the method of analysis selected, the type of indicator electrode used, and the potential ramp that is applied. The method is useful in detecting several substances simultaneously and is applicable to relatively small concentrations, e.g. 10^{-6} up to about 0.01 mole per litre, or approximately 1 to 1000 parts per million.

R2.1.3 Tin estimation by potentiometric titration with potassium iodate (for kits)

Potentiometric titration is based on the principle of measuring the change in redox potential when tin solution is titrated against potassium iodate solution. The redox potential is measured with redox-electrode couple. This method is ideal for estimating stannous (tin II) contents in radiopharmaceutical vials sealed in nitrogen or inert gases. Tin estimation by potentiometric titration is not possible in vials containing antioxidants such as ascorbic acid or gentisic acid. Since antioxidants are commonly found in radiopharmaceutical preparations this method is not suitable for such formulations.

Reagents

Prepare the following two reagents as described:

Potassium iodate stock solution VS Potassium iodate R, dissolved in water R, purged with nitrogen R for 5 minutes before use, to contain 0.357 g in 1000 mL (1.667×10^{-3} mol/l).

Method of standardization. Ascertain the exact concentration of the solution following the method described under potassium iodate (0.05 mol/l) VS.

Prepare a fresh solution every three months.

Potassium iodate working solution VS Dilute 10ml of Potassium iodate stock solution VS to 50ml with water R, purged with nitrogen R for 5 minutes before use (0.334×10^{-3} mol/l).

Method of standardization. Ascertain the exact concentration of the solution following the method described under potassium iodate (0.05 mol/l) VS.

Prepare a fresh solution each day.

Titration method

The apparatus consists of a suitable titration cell assembly with a redox-electrode operating in milli-volt mode. Pass a gentle stream of nitrogen R i through the assembly to mix the solution and provide an inert atmosphere. Reconstitute the stannous tin-containing test preparation with 4.0ml of sodium chloride (9g/l) TS and dispense 1.0ml of the resulting solution into the titration cell. Add 2.0ml of hydrochloric acid (1mol/l) VS and titrate immediately with either potassium iodate stock solution VS or potassium iodate working solution VS, as appropriate using a microburette until the end-point (a marked, persistent jump in

redox-electrode potential) is achieved. Record the volume of titrant in mL.

Titrate radiopharmaceutical kits containing high stannous (tin II) content (e.g. PYP and Phytate colloid kits) with potassium iodate stock solution VS which contains 594 microgram Sn(II) per mL solution. The volume of titrant required to achieve the projected end-point is indicated in the following table.

Type of kit	Theoretical Sn(II) content /mL	mL of titrant
Pyrophosphate (PYP)	2000	3.37
PHYTATE	532	0.90

Titrate radiopharmaceutical kits containing low stannous (tin II) content (e.g. DTPA, DISIDA kits) with potassium iodate working solution VS, which contains 119 microgram Sn(II) per mL. The volume of titrant required to achieve the projected end-point is indicated in the following table.

Type of kit	Theoretical Sn(II) content /mL	mL of titrant
Pentetate complex (DTPA)	313	2.61
Di-iso propyl imino deacetic acid (DISIDA)	313	2.61
Imidodiph-osphonate (IDP)	263	2.20
Stannous fluride SnF_2	488	4.11

Unless otherwise specified, the radiopharmaceutical kit being tested contains more than 85% of the theoretical content of tin (II).

R2.1.4 Tin estimation by UV absorption

Prepare the test and reference solutions as described in the monograph. To 1.0 mL of each solution add 0.05 mL of thioglycollic acid R, 0.1 mL of dithiol reagent R, 0.4 mL of a 20g/l solution of sodium laurilsulfate R and 3.0 mL of hydrochloric acid (0.2mol/l) VS. Mix each of the solutions thoroughly. Measure the absorbance (1.6) of of a 1-cm layer of each solution at 540 nm, against a solvent cell containing hydrochloric acid (0.2mol/l) VS. The absorbance of the test solution is not greater than that of the reference solution.