06.80.15

HANDBOOK OF RADIOPHARMACEUTICAL CONTROLS

1980

COMMITTEE OF RADIOPHARMACY

Coordinator
Prof.Dr. Aldo E.A.Mitta

Members
Lic. María Noto
Lic.Amanda H.F. de Suárez

Cooperators

Prof. Dr. Mateo Chekherdemian	-	Member of the permanent committee Argentina Pharmacopeia.
Lic. Silvia G. de Castiglia	-	Radiopharmaceutist of the Nuclear Medicine Center San Martín Hospital.
Dra. Maela Viirsoo	-	Responsible Nuclear Control Sector Radioisotopes and Radiations : C.N.E.A.

Since 1962, at different occasions several essays have been made in order to prepare a Handbook of Radiopharmaceutical Controls.

At the III Congress of the Latinoamerican Association of Societies of Nuclear Biology and Medicine ALASBIMN in 1970 was presented a Handbook that served as basis for the next one. The Argentine National Atomic Energy Commission (C.N.E.A.), and the Nuclear Energy Council of Spain (J.E.N.) presented in cooperation in 1972 a Handbook of Radiopharmaceutical Controls.

The members of the Argentine Committee of Radiopharmacy of the Argentine Association of Nuclear Biology and Medicine decided the preparation of this Handbook, with the cooperation of other argentinean colleagues. The first part is a wider remake of the original Handbook of CNEA-JEN and further chapters review radionuclides and radiopharmaceuticals that are most widely used in nuclear medicine.

The president of ALASBIMN knowing our intention sponsored this work in order to carry by its distribution to all latinoamerican colleagues of ALASBIMN with the feeling of improvement and provision of new ideas.

This effort of ALASBIMN is equal to the activities of the Argentine CNEA in this field whose valuable help is aknowledged in the preparation of this Handbook that we hope will be useful to all our colleagues.

COMMITTEE OF RADIOPHARMACY

Argentine Association of Nuclear Biology and Medicine

RADIOCHEMICAL PURITY AND ITS DETERMINATION

Radiochemical purity is defined by Charlton as the fraction of a given radionuclide in a defined chemical form. An example will enlighten this definition: for a source of sodium pyrophosphate (^{32}P) containing 98,5 % ^{32}P as pyrophosphate and 1,5 % ^{32}P as orthophosphate, radiochemical purity will be 98,5%.

Radiochemical purity is influenced by a series of factors. First of all, preparation as well as purification methods of radiopharmaceuticals do not allow to reach 100% purity. On the other hand, stability depends on medium, radioactive concentration, storage time and conditions. Decomposition of the original labelled compound causes the apparition of radiochemical impurities.

Hence the importance of knowing all the factors that contribute to the stability of a compound as well as the methods for determinating radiochemical purity. We will try to point out briefly some ideas about storage and stability of radiopharmaceuticals and will describe methods and techniques used for purity determination.

Further on, details will be given about the analytical procedures to be used in each case.

Stability of radiopharmaceuticals

It is well known that all chemical compounds suffer alterations, due to the influence of temperature, pH, light, impurities, microorganisms, etc.

Obviously, radiopharmaceuticals are sensible to all the aforesaid factors. Apart from this, their stability may diminish by action of the radiation they emit.

Autoradiolysis may occur by differente mechanisms.

If in a molecule containing two or more radioactive atoms one of them desintegrates, recoil may cause the primitive molecule to split into several radioactive fractions. However, this procedures is not so important because the probability of finding two or more radioactive atoms in a single molecule is relatively small, except in labelled macromolecules or compounds containing

very short - lived radionuclides. Another mechanism, much more important in the case of sources of high specific activity, is radiolysis caused by the direct action of radiations emitted by one of the radioactive components on other labelled molecules. In order to minimize this phenomenon it is necessary to reduce the probability of interaction of radiations emitted by the radioactive atoms of a molecule with other labelled molecules, either by dilution with stable molecules of the same compound (in this case specific activity will also diminish) or by dilution in a convenient medium with a different inactive compound, compatible with the source and its uses, but above all stable in face of radiations.

This resource cannot always be used: usually a previous study is required.

Sometimes it may be convenient to distribute the source over the largest possible surface in a thin layer on a convenient backing.

However autoradiolysis of a source is mainly produced by action on the molecules of its medium: as a rule highly reactive species are produced by the action of ionizing radiations on chemical systems e.g. in the case of aquous solutions, radiolysis of water generates free radicals H* and OH*.

If one of free radicals reacts with labelled molecules of the medium, alterations are produced because new radioactive compounds appear and as a consequence the radiochemical purity of the source diminishes.

In order to reduce damages caused by the aforesaid secondary effects different precautions might be taken that are effective in most cases . However counterindications may exist, so that a previous study of optimum conditions is necessary.

Usual precautions may be:

- If possible, do not use water. If the compound can be reduced to solid state, dehydratation should be carried out very carefully. (i.e. by liofilization).
- Use solvent like benzene (because of its stability to radiations) to reduce radioactive concentration of the source when compatibily exists.
- Reduce to a minimum chemical impurities in the source: the action of radiations on impurities may produce highly active radiolysis products.
- Use when possible scavengers of free radicals, so as to prevent them from acting on labelled molecules. Simple primary alcohols in low concentration are recommendable. A careful previous study is necessary for choosing the scavenger.
- Keep radiopharmaceuticals at low temperature, near freezing point: in this way, radiolysis is reduced.

The influence of radiolysis on radiochemical purity of a

radiopharmaceutical is very important, but a series of other factors should also be kept in mind.

Special attention should be paid to careful cleaning of material and all the solutions should be kept in sterile conditions if possible. Proliferation of microorganisms in a solution may change radiochemical purity of a compound, specially if its concentration is low.

All light sensitive compounds should be stored in dark or in darkness.

Techniques for determination of radiochemical purity

Chromatography

Chromatography is a technique for separating mixtures of compounds by the different distances each of them may travel on a column or on layers of an absorbing material capable of producing different delays of migration rate by the action of a convenient solvent.

The absorbing material acts retaining on its surface a thin layer of molecules of gas, liquids or dissolved substances.

The procedures responsible for chromatographical separation can be divided into three groups:

- Absorption - Components are absorbed on the surface of the absorbent in different ways, depending on the chracteristics of each of them and on the absorption power of the material.
- Ionic interchange - The union of the components to be separated and the absorbing material is by ionic and/or polar links. The material interchanges with cations and anions of solution, producing enrichment of one of the components.
- Partition - The base material acts, not as absorbent or as interchanger, but as backing for a liquid layer representing the stationary phase. The mixture to be separated is dissolved in another solvent: the mobile phase. Separation is due to the different solubilities the components have in these two phases.

In most cases of chromatographic separation all the aforesaid

processes may occur simultaneously.

We will describe briefly the genral techniques used for chromatographic separations. The details of each procedure will be surveyed in the monography of each compound.

Ascending paper chromatography

Cut a 2 cm. wide and 25 cm. long strip of paper, make a horizontal line with graphite pencil about 3 cm. from the lower edge. In its center spot with a Hamilton syringe or a micropippete the solution of substances to be separated.

If necessary the spotted solution is dried after each drop with air or a jet of warm air. The diameter of the spot ought not to be more than 0.5 cm.

The mixture of solvents is placed in a chromatographic vessel till saturation with solvents vapours. The strip of paper is hung there, introducing its lower edge about 0.5 cm. in the solvent.

When the solvent has reached an adequate height the chromatogram is taken out, the solvent front is marked with a pencil and the chromatogram is dried with air or a jet of warm air.

The developing of different compounds and their eventual evaluation will be described in the respective sections.

Descending paper chromatography

Descending paper chromatography is carried out, like ascending paper chromatography, in a chromatographic vessel previously saturated with the solvents. The solution to be separated is spotted on the strip of paper about 3 cm. from its upper edge, the paper is introduced about 0.5 cm. in the

mobile phase and left hanging. The lenght of the strip might be extended if a definite separation is desired.

After some time the chromatogram is taken out, the solvent front is marked and evaluation is carried out following the general technique.

It is important to keep temperature constant, above all when using mixtures of volatile solvents.

Thin layer ascending chromatography

Thin layers for chromatography are commercially available (Mackerey & Nagel, Merck, Baker, etc.), or can be prepared according to the following technique:

Deposit on a flat glass plate 5 cm. wide and 20 cm. long a 250 µ high layer of an adsorbing material containing, or not, a binding agent.

Mix carefully a given quantity of adsorbing material with twice its volume of water or buffer in a beaker. Extend it on the glass plate as a homogeneous layer (using Stahl or similar equipment). Dry the plates for a few minutes, warm in a drying oven at 120°Cfor activation and place them in a dissecator.

For applying the sample take one or more drops of the solution with a Hamilton syringe or a capillary tube, letting them fall without touching the plate with the tip. Let the plate dry between drop and drop. Develope as ascending chromatography in a vessel previously saturated with solvents.

When the solvent has reached the front previously marked with a spatula, the plate is taken out, dried, impregnated with plastic material and covered with scotch tape.

The evaluation of different compounds will be described in the respective sections of this handbook.

Instantaneous thin layer chromatography

In this case glass microfiber sheets saturated with adsorbent material are used. Those saturated with silica gel are named ITLC-SC and those with silicic acid ITLC-SA. Their size can be either 1 cm x 6 cm or 2 cm x 14 cm. Make a pencil mark 1.5 cm from its lower edge and apply carefully a small drop of solution. Let it dry for 5 to 10 minutes, then introduce it in a beaker with solvent, covered or open.

When the solvent has reached the previously marked front, the glass is taken out and dried. Cut it into two pieces, so as to place one of them in a test tube for counting activity in a well type counter and cover the other with cellophane paper in order to pass it through a radio-chromatogram scanner.

Gel filtration chromatography

This method is mainly used for radiopharmaceuticals labelled with ^{99m}Tc. Sephadex column are used that permit fractination of teh compounds of a mixture according to the molecular weight and size.

Electrophoresis

This is a procedure for separating different substances, using the fact that molecules or charged particles dissolved or dispersed in a conducting solution will travel in different ways under the effect of an electric field. Electrophoresis can be carried out independently or using as backing filter paper, callulose, agar acetate, agar cellophane, starch gel, poliacryl amide gel, or ionic interchange resins.

The most widely used of all the backings is filter paper because is easy to handle, its low cost and many applications.

For a careful fractination e.g. proteins filter paper is replaced by starch gel or poliacryl amide gel that act as molecular filters. Inmune electrophoretic fractination can also be used.

Paper electrophoresis

Use 3 cm. wide and 35 cm. long stripes of paper. Mark with a graphite pencil the place where the solution will be spotted. Introduce the strip of paper in electrolytical solution.

Dry partially between two sheets of filter paper, place in an electrophoretic vessel, introducing its edges in an electrolytic solution and spot the sample with a micro-pippete or an aplicator.

Cover the vessel and apply continuos current from a power source, trying to keep constant voltage for each case.

After 30 to 120 minutes, interrupt the current, dry the paper and develop it by chemical, physical or radiochemical techniques.

Relation (Rf)

Rf is the relation between the distance:starting point-center of spot and the distance:starting point-solvent front.

$$Rf. = \frac{\text{distance travelled by the sample}}{\text{distance travelled by the solvent front}}$$

In order to have a value of Rf free of variations due to less controlable factors (temperature, saturation, etc.), carry out a chromatogram of a standard in the same conditions, and compare the distance travelled by the sample and the standard.

For sugars Rg (glucose relation) is

$$Rg = \frac{\text{distance travelled by the unknown sugar}}{\text{distance travelled by glucose}}$$

At certain working conditions Rf is constant for a given substance and a given solvent and serves to identify it.

In electrophoresis different compounds are identified by the mobility, when all other working conditions are constant.

This technique should always be checked by using a standard.

In electrophoresis migration relation is

$$Rm = \frac{\text{molecule mobility}}{\text{impurity mobility}}$$

Autoradiography

In electrophoresis or chromatography of coloured compounds (or in case of compounds that can be coloured "a posteriori" with adequate reagents) their position can be defined by inspection and radioactive substances can be located by their action on photographic solutions.

Place on a strip of paper or on the thin layer used for the separation, a photographic emulsion film (a X-ray film, hard type). Leave it for enough time (depending on activity, type of desintegration and energy) and make mark or reference so as to be able to know the correspondence of the photographic image and the position of the strip of paper. (e.g. a mark with scissors or ink labelled with ^{14}C).

Develop the film and identify spots, according to their Rf.

Data evaluation

When the radiopharmaceutical and inpurities have been separated by chromatography or electrophoresis, radiochemical purity is evaluated quantitatively by the following techniques:

a) Determination of radioactive distribution along the backing with a radiochromatogram scanner.

b) Determination of radioactive distribution counting different sectors.

a) Pass the strip of paper through a radiochromatogram scanner, using convenient range, time constant, collimation and speed. A curve corresponding to the detected activity will be registered on the chart paper of the recorder. The surface limited by the curve is proportional to the activity, so that by planimetric analysis or by weighing, radiochemical purity is obtained. Planimetry of inscribed peaks is carried out with a planimeter and data are expressed as follows:

Radiochemical purity of the radiopharmaceutical (%) =

$$= \frac{\text{Surface of the peak of the radiopharmaceutical}}{\text{Surface of radiopharmaceutical peak + Surface of impurity peak}} \times 100$$

In the chart paper is of constant thickness, cut out peaks and determine impurities by weighing.

Radiochemical purity (%) =

$$= \frac{\text{Weight of radiochemical "area"}}{\text{Weight of radiochemical "area" + Weight of impurity "area"}} \times 100$$

b) When a radiochromatogram scanner is not available, when activity is low or when radioisotopes are detected with low eficiency, the following technique is recomendable:

Divide the chromatogram in 0,5 cm. wide sectors perpendicularily to the strip, beginning 1 cm. before the spot and number them. Count each sector in an adequate detector. Make a histogram of data so as to locate Rf of radioactive spots.

In this case evaluation is carried out adding the activity of all sectors

corresponding to the compound and to its impurities.

$$\text{Radiochemical purity (\%)} = \frac{\text{Activity of radiopharmaceutical sectors}}{\text{Activity of radiopharmaceutical sectors + Activity of impurity sectors}} \times 100$$

TOXICITY TESTING

This test enables to exclude the possibility that the radiopharmaceutical might be toxic for the patient, due to an eventual chemical contamination with harmful substances introduced during the production process or any other reason.

For this test use 5 white mice, weighing 20 to 30 gram., injecting into the tail dorsal vein 0.1 to 0.2 ml of the sample, without dilution, in not more than 5 seconds. Wait for 6 hours, as minimum, before considering the substance as not toxic. The whole lot of animal must be alive. If one of them dies, repeat the test in order to confirm the experience with a new lot of 5 animals, who must survive 24 hours at least.

Take care of not introducing bubbles of air when injecting the sample; gaseous emboly would produce quick death.

The ratio of activity or injected volume per kilogram, must be considerably higher for mice than used for human beings. (100 to 500 times).

This test is adapted as a whole to the Argentine Pharmacopeia (VI Edition 1978) excepting injection dose and waiting time, owing to the same causes as for pyrogen and sterility testing. However in this case the disproportion of dose is not so important as the animals will be killed at the end of the experiment.

ISOTONICITY TESTING

A solution is isotonic with blood serum when it has the same osmotic concentration (osmolarity).

Isotonicity is essential in physiological research that require perfusion of isolated organs and cell culture, also in clinical studies requiring labelling of red blood cells and where all membranes must stay whole (e.g. volemia, red cell survival etc.). In case of subcutaneous or intramuscular injectables it is convenient to use isotonic solutions so that tisumes are not irritated.

For solutions to be injected intravenously, specially when volume is small, deviations from isotonicity may be tolerated, as dilution in blood is rapidly achieved. However, it is always convenient to keep isotonicity, as possibility of exudation exists.

Isotonicity tests are carried out by different methods, the most usual are by cryoscopic descent and by conductimetry.

STERILITY TESTING

All injectable material must be sterile, that is, not containing any kind of viable microorganisms.

Different methods of sterilization exist, according to the substance to be sterilized.

Radiopharmaceuticals that suffer alteration with temperature are sterilized passing them through filters of controlled pore (0,22 µ or 0,45 µ) like Milipore or similar. Filtration must be done in a sterile area. e.g. iodine albumin (^{131}I or ^{125}I).

Another method is sterilization by radiations with à 2,5 MRad dose of gamma rays in a Gammacell or similar equipment, e.g. chromic phosphate colloid (^{32}P).

This method can be used only when all physicochemical and toxicological essays show that during irradiation no decomposition or alteration occur, and no toxic compounds are originated.

After sterilization, it is necessary to confirm that it was effective, performing the following sterility test.

Add 2 or 3 drops of sample to three different culture media:
Culture media for aerobic microorganisms: simple broth.
Culture media for anaerobic microorganisms: broth with thioglicolate.
Culture media for fungis: Sabouraud media.

Incubate in a drying oven at 30°to 35°C, checking results after 24 hours and 48 hours. For fungi 20°to 22°C.

Keep tests for 14 days for a final check of results.

Owing to radioactive decay the distribution of radiopharmaceuticals is authorized when results are negative after 24 and 48 hours.

Culture media are dehydrated media prepared according to the indications of the manufacturer and controlled following the techniques of the Argentine Pharmacopeia.

Another method is radiometric sterility testing. Count $^{14}CO_2$ liberated by microorganisms in culture media labelled with ^{14}C, either with an ionization chamber or a liquid scintillation counter. Samples are counted after 24 hours.

PYROGEN TESTING

This test serves to study the presence of sustances that provoke, when injected in a homeothermal animal, variation of baseline temperature.

Follow the technique given by the Argentine Pharmacopiea, VI Edition 1978, page 1111. (Inoculated volume should be modified however).

Monitor rectal temperature of three rabbits weighing 2 to 4 kilogram, after 4 hours of fasting. Temperature must be 38,9 to 39,8 °C and must show only an increase of 0,2 °C after 20 minutes.

Inject 0,25 or 0,5 ml. of test sample, in the marginal ear vein, the volume depending on the radioactive concentration of the sample.

Do not follow the technique given in the Argentine Pharmacopiea concerning injected volume. This could mean that all the sample should be used and radiation dose would be excessive.

As a rule it is convenient to inject into animals doses (either activity or volume per kilograms of weight) that are 3 to 5 times greater than those used for human beings.

Monitor rectal temperature 60, 90 and 120 minutes after injection.

A tested substance is free of pyrogens if the sum of temperature variations for three rabbits is less than 1,4 °C.

Pyrogen testing can also be done "in vitro". Limulus amebosyte lysate reacts with minimum concentrations of endotoxin bacteria so that an assay mixture increases in viscocity and opacity until a firm gel is formed under apropriate conditions of temperature (37°C), pH (6-8) in one hour. The sensibility of this test is 10 times greater than for the test "in vivo".

BIODISTRIBUTION

Biodistribution is carried out with laboratory animals, usually mice and rats. As a rule it is necessary to know what percentage of activity of an injected radiopharmaceutical is found in different organs at prefixed times.

a) For tests of biodistribution of labelled particles that will be localized on lung, use male rats, previously anaesthetized with urethan, injecting in the dorsal vein of the penis 0.1 to 0.2 ml. of the sample.
Sometimes breathing breaks may occur, but the animal will recover with energetic thorax massage.
Kill the animal 10 minutes after injection, anaesthetizing strongly with ether.
Open abdomen along the white line and extract blood from the abdominal aorta artery or from the heart.
Separate liver, lungs, spleen, etc., wash them, weigh extracted blood and count activity of the samples at constant conditions of geometry with a scintillation crystal and spectrometer.
To obtain percentages of total activity consider:
Act. liver + Act. spleen + Act. lungs + Act. total blood = 100%.
For calculations volemia should be about 7% of weight.
The obtained data serve as orientation for scintillography relating activity of liver, lungs, spleen and blood.
The compound is accepted when lung retention is more than 90% after 10 minutes.
This test must be carried out with all radiopharmaceuticals for lung scintillography e.g. ^{99m}Tc albumin macroaggregates, ^{99m}Tc microspheres, etc.

b) For biodistribution of almost all other radiopharmaceuticals mice are used.
Use adult animals, male or female, weighing 25-30 gram.
The radiopharmaceutical is injected into tails veins, keeping the animal completely motionless in an adequate device. Inject 0.1 to 0.3 ml. After a prefixed time anaesthetize with ether and cut off the head. Collect the freely flowing blood with a Pasteur pipette. (Blood may also be obtained by cardiac or ocular puncture). Place blood in a weighed test tube and weigh it.
Dissect the animal, separate organs, wash and place them in test tubes.
Count activity with a INa (TI) crystal and spectrometre, keeping geometrical conditions constant for all samples.

Count activity of blood, of different organs, of the body (after having cut off the tail) entire or in sections, making corrections for variations of geometry.
The value for total blood is obtained considering the volemia is about 7% of weight. From the activity corresponding to body, subtract the difference of measured blood and total blood.
Total Activity = Act.organs + Act. total blood + Act. body.
The percentage activity for each organ is refered to total value.
When the radiopharmaceutical has to be administered intracavitarily the test is carried out in the aponeurotic cavity of rears legs.

For beta emitters, preparation and counting conditions care should be specially careful.
Organs must be homogenized either mecanically or by chemical methods. If samples are to be counted in a G.M. counter certain conditions of sample thickness, surface, etc., should be constant.
It is advisable to count a standard under the same conditions.

c) For dynamic circulation studies use adult rats of 250 to 550 g Wistar stock. Anaesthetize them with an injection of urethane (1 g/kg weight).
The carotide artery is lengthened with a canula of poliethylene tubing treated with heparine, internal diameter 1 mm, of cephalic and cardiac ends.
The radiopharmaceutical is administered by a canula inserted in the yugular vein.
Activity is counted introducing the tubing in scintillation crystal coupled to a spectrometer with a ratemeter and a recorder.

DETERMINATION OF CHEMICAL CONCENTRATION BY SPECTROPHOTOMETRY

Sometimes is necessary to know the concentration of a solution e.g. albumin, Bengal Rose, etc.

As a rule spectrophotometric methods are used, basically by determination of the absorption produced when a ray of light is going through a solution.

The absorption of light follows for a given interval of concentration (at low concentrations), the Law of Lambert and Beer, that can be expressed mathematically as:

$$\log. \frac{Io}{Ic} = E\ c\ l$$

where $$\log. \frac{Io}{It} = A \text{ (absorbency)}$$

Io = intensity of incident light.
It = intensity of transmitted light after crossing the solution.
E = extinction coefficient (constant for each substance at given wawe lenght, expressed in the corresponding concentration unities).
c = concentration (g/l or mol/l).
l = thickness of liquid crossed by light (thickness of the cell of measurement in cm.)

If all measurements are carried out in the same cell, the previous formula is reduced to:

$$A = Ec$$

Make a graph with concentration values in abscissas and absorbency values in ordinates: a straight line for the interval of concentrations that follow the Law of Lambert and Beer at constant values of wave lenght.

In order to determine an unknown concentration it is necessary to obtain a calibration curve.

METHOD

1° Selection of convenient wavelenght

Make a graph of absorbency as function of wavelenght at given concentration. Check against blank.

Select as working conditions a wavelenght where maximum absorbency

is obtained. e.g. Bengal Rose mμ (pH 6,5).

2° Calibration curve

From a standard solution make dilutions of known concentration. Read absorbency, at the wavelenght that was previously determined, for each dilution. Check against blank.

Make a graph of absorbency versus concentration.

3° Determination of an unknown concentration

Determine absorbency and read concentration from the graph, provided that the concentration is within the limits where the Law of Lambert and Beer is valid.

If concentration is too high, the solution should be diluted, and the factor of dilution used in concentration calculations.

DETERMINATION OF RADIOACTIVE PURITY

Radioactive purity of a radiopharmaceutical is the proportion of the total activity of the source that is due to the specified radionuclide.

As a rule radioactive impurities appear during the production of radioisotopes, either due to inactive impurities in the target or due to secondary reactions produced on a pure target.

It is less probable, although no impossible, that an accidental contamination occurs after production of the radionuclide.

The determination of radioactive impurities is carried out analyzing the type and energy of the radiations emitted by the sample.

For analysis of beta radiations obtain an absorption curve in aluminium or some other light element and determine the range of the radiation. Deduce the energy of the emitted radiation and confirm whether some other beta emitter is present besides the specified one.

Another technique is beta spectrometry in a liquid scintillation counter. However if the probable impurity emitts also gamma radiations, it is advisable to use a scintillation crystal or a solid state detector.

In the case of an impurity emitting only beta radiation, within a source that is a pure beta emitter, the aforesaid method is not sufficiently reliable. Chemical separation is necessary so as to be able to isolate the different components. A typical case is ^{35}S within a source of ^{32}P: it is difficult to discover small quantities of ^{32}P by a simple analysis of emitted radiations. It is better to perform a chemical separation so as to be able to count sulphur independently (see "Radioactive purity of sodium phosphate").

The determination of an impurity emitting gamma rays is usually done by spectrometry with either a solid state detector or a scintillation crystal. Counting efficiency is lower for Ge (Li) detectors than for scintillation crystals, but their resolution is better, hence their use in studying the radioactive purity of radiopharmaceuticals. With both types of detectors a gamma ray spectrum is obtained using a multichannel pulse height analyzer. The spectrum is compared with that of a standard of a pure radionuclide determined under the same conditions. If an impurity is present this analysis will reveal the appearance of gamma peaks that do not exist in the standard and it is necessary to identify the impurity and determine its activity. This is carried out evaluating the area of one or several peaks of the impurity: knowing the desintegration schema, the abundance of gamma rays and the eficiency of the detector, calculate the activity of the impurity.

The quantitative determination of a radioactive impurity by gamma ray spectrometry is a delicate task that may require different measurement techniques according to the source and the impurities to be analysed. We advise to consult the existant bibliography for each particular case.

DETERMINATION OF ACTIVITY

The determination of activity of radiopharmaceuticals that emit gamma rays is mostly done by measurement in an ionization chamber.

The total activity of each source or solution is given with 95% precision. The ionization chamber is calibrated with standard solutions of known activity of the same way as the radiopharmaceutical.

The stability of the measuring device is controlled daily with a standard of ^{226}Ra or some other radionuclide of long half-life.

For variation of activity due to geometry (different measured volumes) make a table with the percentage of measured activity of the standard versus

volume.

Radioactive concentration is the ratio of total activity and measured volume or the weight of the sample.(For activity per unity of volume, consider density of solution). For a given activity indicate day and time of measurement.

For beta emitters use special types of counters:either liquid scintillation counting for low energy or Bremsstrahlung for high energy beta radiation.

This material might be replaced by a thin window GM counter. Compare activity of the sample with that of a standard of the same radionuclide of known absolute activity, prepared at the same conditions so as to reduce problems of geometry, self absorption and backs cattering.

BIBLIOGRAPHY

1- Farmacopea Nacional Argentina.
VI Edición 1978.

2- The United States Pharmacopeia.
XX Edición 1980.

3- NOTO, M.; MITTA, A.E.A.
Control de Calidad de los Radiofármacos.
Acta Bioq.Clí.Latin. XIII, 69, 1979.

4- VIVIAN, A.; ICE, R.D.; SHEN, V. and HETZEL, R.
Radiochemical Purity of Radiopharmaceutical Using Gelman Seprachrom (ITLC) Chromatography.
Techinical Bulletin 32, 1977.

5- CASTIGLIA, S.G.; SUAREZ, A.H.F. de; MITTA, A.E.A.
Control de Calidad de Radiofármacos Utilizados en Medicina Nuclear.
Rev. de Biol. y Med.Nuclear (en prensa 1980).

6- COOPER, J.F.
Pyrogen Test.
Quality Control In Nuclear Medicine.
Ed. B.A.RHODES.Mosby St.Louis 1977.

7- HETZEL K.R. and ICE, R.D.
Sterilization and Sterility Testing.

Quality Control In Nuclear Medicine.
Ed. B.A.Rhodes Mosby St.Louis 1977.

8- COOPER J.F. and Avis, K.E.
Control and Detection of Microbial Contamination in Short-Lived Radiopharmaceuticals.
Radiopharmaceuticals.
Ed. G.Subramaniam, et al (Society of Nuclear Medicine New York, 1975).

9- SERVIAN, J.L.
Report of an Inetrnational Atomic Energy Agency Meeting on Quality Control of Radiopharmaceuticals.
Int.J.of Appl.Rad. and Isot. 28, 653, 1977.

10- RHODES, B.A.
Radiometric Sterility Testing.
Quality Control In Nuclear Medicine.
Ed. Rhodes. Mosby, St.Louis, 1977.

11- HANSER, W. and CAVALLO, L.
Measurement and Quality Assurance of the amount of administered tracer.
Quality Control In Nuclear Medicine.
Ed.B.A.Rhodes, Mosby, St.Louis, 1977.

12- KRISTENSEN, K.
Preparation and Control of Radiopharmaceuticals in Hospitals Techmical Reports Series N°194.
Intern. Atomic Energy Agency-Viena, 1979.

13- TUBIS, M. and WOLF, W.
Radiopharmacy.
John Wiley & Sons, Inc. 1976.

14- BALABAN, A.T.; GALATEANU, I.; GEORGESCU, G.; SIMIONESCU, L.
Compusi Marcati Si Radiofarmaceutici Cu Aplicati In Medicina Nucleara.
Editura Academici Republicu Socialiste Romania - Bucarest - 1979.

15- RHODES, B.A. and CROFT, B.Y.
Basics of Radiopharmacy.
The C.V. Mosby Co., St.Louis, 1978.

16- TRAN P.T. and WASNICH R.
Practical Nuclear Pharmacy
Banyan Enterprises - Honolulu - 1979.

17- COHEN, I. and BESNARD, M.
Analtycal Methods of Radiopharmaceutical.
Quality Control.
Radiopharmaceuticals.
Ed. G.Subramaniam et. al. (Society of Nuclear Medicine, New York, 1975.

18- STEGBAHN, K.
Alpha, Beta and Gamma Ray Spectrometry.
North - Holland Publishing Company Amsterdam (1966).

19- HEATH, R.L.
Scintillation Spectrometry. Scintillation Gamma-Ray.
Spectrum Catalogue - USAEC Rep. TID 4500 31 Ed., (1964).

20- DAVIS, R.; ADAMS, F.
Gamma Ray Energies of Radionucleidos Formed by Neutron Capture Determined by Ge(Li) Spectrometry.
Radiochem. Acta 10 (1968).

21- CASTAGNINO, J.M.
Electroforesis.
Eudeba, Buenos Aires, 1968.

22- ROCHA, A.F.G.da y HARBERT, J.C.
Medicina Nuclear Bases.
Guanabara - Koogan S.A. 1979 -

23- CRESPI, M.B.A.
Introducción a la Radioquímica.
Comisión Ecuatoriana de Energía Atómica.
Quito - Ecuador 1979 -

24- RODRIGUEZ PASQUES, R.H.
Introducción a la Tecnología Nuclear.
Eudeba, Buenos Aires, 1978.

25- CARO, R.A.; CISCATO, V.A. y PICCINI, Z.F.de
La Metodología de Radioisótopos en el Laboratorio Moderno.
Ed.Medica Panamericana, Buenos Aires 1974.

26- CHASE, G.D. and RABINOWITZ, J.L.
Principles of Radioisotope Methodology.
Burgess Publ. Co. Minneapolis, Minn. 55415 U.S.A. 1968.

27- Physician's Desk Reference.
For Radiology and Nuclear Medicine.
Ed. Freedman L.M. and Blaufox M.D. 1976/77.

^{113}Sn ^{113m}In Generators

1 - Ionic ^{113m}In.

2 - Colloid ^{113m}In.

3 - Macroaggregated Albumin ^{113m}In.

4 - Diethylenetriaminepentacetic ^{113m}In.

5 - Ethylenediaminetetramethylenphosphoric ^{113m}In.

^{113m}Indium. (Half-life 1,7 hours. Gamma energy 390 KeV).

^{113m}In is obtained as $^{113m}In\ Cl_3$ eluting a ^{113}Sn-^{113m}In generator with hydrochloric acid 0,05 N.

Tin is absorbed on hydrated zirconium oxide or silicium dioxide in a glass column. Column size depends on activity.

^{113m}In is produced by K-capture of ^{113}Sn and equilibrium is reached after 18 hours.

Elution can be repeated after 1,7 hours with 50% yield.

The life of the generator depends on the half-life of ^{113}Sn (116 days) and the half-life of ^{113m}In (1,7 hours).

Radioactive purity

Determination of ^{113}Sn. The eluate is counted in aionization chamber, and recounted 24 hours later. Under these conditions (equilibrium ^{113}Sn-^{113m}In) ^{113}Sn should be less than 0,1%.

Another method is by coloration with hematoxyline; deposit two drops of eluate, on a white touch plate, add one drop of reactive (10 mg hematoxylene in 10 ml ethanol + HCl 0,2 N 1:1). Ten minutes later red-violet colour appears indicating 0,1 ppm tin. Dark red colour would indicate a significant loss of tin.

Chemical purity

Determine zirconium as follows: Moisten a strip of Whatman N°1 paper in p-dimethilaminephenilazo-benzene arsenic acid 0,1%. Let it dry under a hood.

Deposit a drop of eluate (do not neutralize) and one drop of each standard solution (2,5 and 10 mg/ml).

When drops are dry, wash the paper with 3 portions of 50 ml each of hydrochloric acid. Heat till 50-60°C.

Red colour will vanish and brown spots appear where the drops were.

Evaluation is by comparison with the colour of the standards.

Concentration of zirconium in the eluate is normally less than 2 mg/ml.

After some use of the generator these values may increase, but not to more than 5 mg/ml.

Determination of SiO_2: Take one drop of eluate and one drop of ammonium molybdate (5 g in 100 g water + 35 ml NO_3H 1:2). Heat in porcelain crucible. When cold one drop benzidine (0,05 g benzidine in 10 ml concentrated acetic acid and water till 100 ml). The apperance of blue colour indicates the existence of silicium. Compare colour with standard solution.

Another method for SiO_2: deposit 0,3 ml of eluate in a test tube, add 0,4 ml tartaric acid 10% and a speck of ascorbic acid. Add water till 10 ml and measure in a spectrophotometer at 540 mμ. Compare blue color of silicium molybdene complex with a standard curve.

Determination of heavy metals: Take 0,5 ml eluate in a test tube, add 0,25 ml ammonium acetate solution 10% and a drop of sodium sulphur 20%.

Compare colour with that of a similary prepared solution of 10 ppm Pb, which is considered as limit concentration.

CALIBRATION TABLE

T 1/2 ^{113}Sn = 116 days. T 1/2 ^{113m}In = 99,4 min. (1,65 hours).

^{113}Sn decay in generator		^{113m} Ingeneration after first elution		^{113m}In decay	
Decay time	Remaining mCi	Hours	^{113m}In (*) (mCi)	Minutes	Factor
2 days	0,988	0,25	0,099	3,0	0,98
		0,50	0,188	5,0	0,97
4 days	0,977	0,75	0,270	7,0	0,95
		1,00	0,340	9,0	0,94
1 week	0,960	1,25	0,408	10,0	0,93
		1,50	0,464	15,0	0,90
2 weeks	0,920	1,75	0,520	20,0	0,87
		2,00	0,564	25,0	0,84
3 weeks	0,884	2,25	0,610	30,0	0,81
		2,50	0,649	35,0	0,78
4 weeks	0,849	2,75	0,684	40,0	0,76
		3,00	0,716	45,0	0,73
5 weeks	0,814	3,50	0,768	50,0	0,71
		4,00	0,813	55,0	0,68
6 weeks	0,781	4,50	0,849	60,0	0,66
		5,00	0,877	65,0	0,64
7 weeks	0,750	5,50	0,901	70,0	0,61
		6,00	0,916	75,0	0,59
8 weeks	0,720	6,50	0,935	80,0	0,57
		7,00	0,947	85,0	0,55
9 weeks	0,691	7,50	0,957	90,0	0,53
		8,00	0,965	95,0	0,52
10 weeks	0,666	8,50	0,972	100,0	0,50
		9,00	0,978	105,0	0,48
11 weeks	0,637	9,50	0,982	110,0	0,46
		10,00	0,985	115,0	0,45
12 weeks	0,612	10,50	0,988	120,0	0,43
		11,00	0,991	125,0	0,42
13 weeks	0,587	11,50	0,993	130,0	0,40
		12,00	0,994	135,0	0,39
14 weeks	0,563	12,50	0,995	140,0	0,38
		13,50	0,997	145,0	0,35
15 weeks	0,540	15,00	0,984	150,0	0,35
		17,00	0,995	155,0	0,34
16 weeks	0,518	18,00	0,995	160,0	0,33
		19,00	0,995	165,0	0,32
116 days	0,500				

(*) Multiply by 100 = Recovery percentage

Ionic ^{113m} In

^{113m} In Cl_3

Hydrochloric solution 0,05 N, sterile, pyrogen-free, pH 1,5 containing $^{113m}In\ Cl_3$ (Indium trichloride).

Radiochemical purity

Backing: ITLC Gelman S.G.
Solvent: Methanol 85%.
Time: 5 minutes.
Rf.: ^{113m} In Cl_3: 1.0

Activity

Count in an ionization chamber. Error: 5%.

Biological controls

Test sterility, pyrogens and toxicity according to general method.

Use and dose

Use for determination of blood pool and placentary scanning. Inject by intravenously way 1-3 mCi.

^{113m}In Colloid

Colloidal suspension of sodium bicarbonate and polyvinyl-pyrrolidone or phosphate-manitol labelled with ^{113m}In, sterile, pyrogene-free, pH 6,5.

Particle size: less than 1 μ.

Radiochemical purity

Backing: ITLC Gelman S.G.
Solvent: Methanol 85%.
Time: 5 minutes.
Rf.: ^{113m}In Cl_3: 1.0
Rf.: ^{113m}In colloid: 0.0

Biological controls

Test sterility, pyrogens, and toxicity according to general methods.

Control of biological affinity

Administer intravenously to mice and study disrtibution 30 minutes after injection. 90% of activity should be found in liver.

Activity

Count in an ionization chamber.

Use and dose

Use for liver and spleen scanning. Inject intravenously 800 uCi - 1 mCi.

^{113m}In macroaggregated albumin

Suspension of macroaggregated albumin, sterile, pyrogene-free, pH 6.0 7.0, particle size: 20-50 μ.

Radiochemical purity

Backing: ITLC Gelman S.G.
Solvent: Methanol 85%.
Time: 5 minutes.
Rf.: ^{113m}In Cl_3: 1.0.
Rf.: ^{113m}In MAA: 0.0.

Biological controls

Test sterility, pyrogenicity and toxicity according to general methods.

Control of biological affinity

Administer intravenously to rats and study distribution 30 minutes after injection.

Percentage of activity in lungs should be 88%.

Physical control

Determination of particle size and number is done with an optical microscope with ocular micrometer and a cell counting chamber. No particle should be of more than 100 μ.

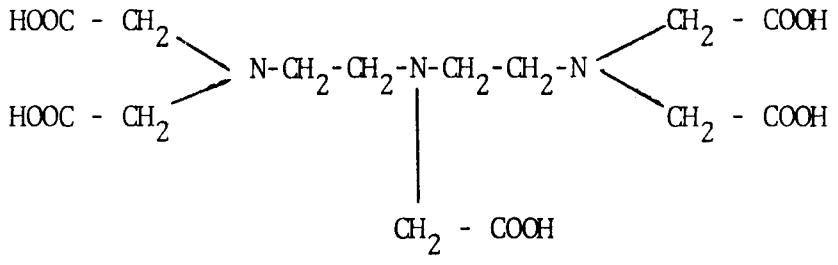
Activity

Count in an ionization chamber.

Use and dose

Use for lung scanning. Inject intravenously 1-3 mCi.

^{113m} In (diethylene triaminepenta acetic)



Solution of DTPA in buffer phosphate labelled with ^{113m} In. Sterile, pyrogene-free, pH 6.

Radiochemical purity

Backing: ITLC Gelman S.G.
Solvent: ClNa 0,9 % or $HONH_4$: 0,1 N.
Time: 5 minutes.
Rf.: $^{113m}In\ Cl_3$: 0.
Rf.: ^{113m}In DTPA: 1.0.

Whatman Paper N°1 o TLC can also be used with the same solvents.
Time: 15-30 minutes.

Biological controls

Test sterility, pyrogens and toxicity according to general methods.

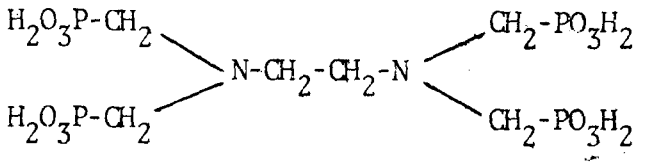
Activity

Count in an ionization chamber.

Use and dose

Use for brain and kidney scanning. Inject intravenously 6-12 mCi for brain and 2-10 mCi for kidney studies.

^{113m} In E.D.T.M.P. (Ethylenediaminetetramethylenphosphoric)



Solution of E.D.T.M.P. in sodium bicarbonate 0,5 M labelled with ^{113m} In. Sterile, pyrogen-free, pH 8.

Radiochemical purity

Backing: ITLC Gelman S.G.
Solvent: (OH) NH_4 0.1 N or ClNa 0.9%.
Time: 5 minutes.
Rf.: ^{113m} In E.D.T.M.P.: 1.0.
Rf.: ^{113m} In: 0.0.

Whatman paper N°1 or TLC can be used with the same solvents.

Biological controls

Test sterility, pyrogens and toxicity according to general methods.

Control of biological affinity

Administer intravenously to mice. Count activity in different organs 2 hours after injection. 30% of activity should be found in bones and the rest in urine.

Activity

Count in an ionization chamber.

Use and dose

Use for bone scanning. Inject intravenously 10-15 mCi.

BIBLIOGRAPHY

1 - Desarrollo e Instalación en Celda de Generadores de $^{113m}Sn/^{113m}$ en la C.N.E.A. de La R.Argentina.
SALAS, G.N.B. de; ARCIPRETE, J.A. y MITTA, A.E.A.
Inf. C.N.E.A. N° 444 (1978).

2 - Control de Calidad de Radiofármacos Usados en Medicina Nuclear.
CASTIGLIA, S.G. de; SUAREZ, A.H.F. de y MITTA, A.E.A.
Acta Bioq.Clín.Lat. (en prensa) (1980).

3 - El ^{113m} In E.D.T.M.P. Un Nuevo Radiofármaco para Centellografía Osea.
NOWOTY, G.; SUAREZ, A.H.F. y MITTA, A.E.A.
Revista de Biología y Medicina Nuclear 9 66 (1977).

4 - Cromatografía en Capa Delgada de Diversos Radiofármacos.
ALVAREZ, J.; SALAS, G.N.B. de; y MITTA, A.E.A.
Inf. C.N.E.A. N°285 (1970).

5 - Dosimetría en manos durante el manipuleo de ^{113m} In.
GARRETA, A.C. de; FELD, D.; CASTIGLIA, S.G. de; y MITTA, A.E.A.
Inf. C.N.E.A. N°329 (1973).

6 - The United States Pharmacopeia. Ed. XX 1980.

^{99}Mo - ^{99m}Tc Generator

1 - ^{99m}Tc Sodium pertecnetate.

2 - ^{99m}Tc DTPA.

3 - ^{99m}Tc Calcium glucoheptonate.

4 - ^{99m}Tc Calcium gluconate.

5 - ^{99m}Tc Colloidal sulfur.

6 - ^{99m}Tc Sodium phytate.

7 - ^{99m}Tc Macroaggregated albumin.

8 - ^{99m}Tc Methylenediphosphonate.

9 - ^{99m}Tc H.E.D.S.P. Hydroxiethylidendisodiumphosphonate.

10 - ^{99m}Tc Pyrophosphate.

11 - ^{99m}Tc H.I.D.A. (dimethyl-IDA, diethyl-IDA, diisopropyl IDA, p-butil IDA).

12 - ^{99m}Tc D.M.S. (dimercaptosuccinic).

13 - ^{99m}Tc I.D.P. (imidodiphosphonate).

14 - ^{99m}Tc P.G. (pyridoxylidenglutanate).

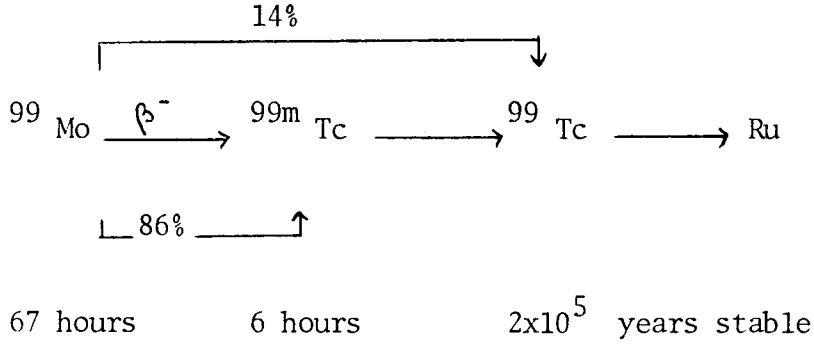
15 - ^{99m}Tc Albumin.

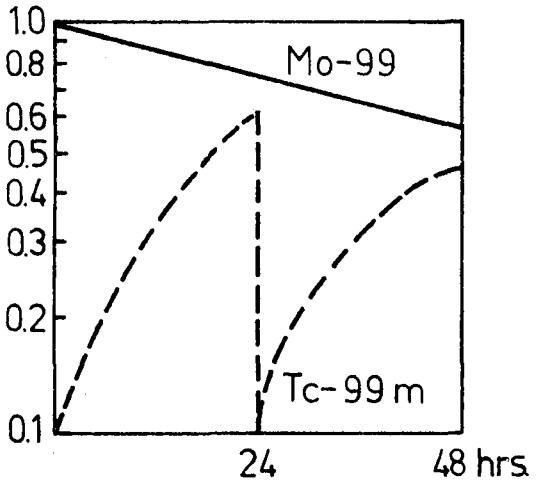
16 - ^{99m}Tc Antimony sulfide.

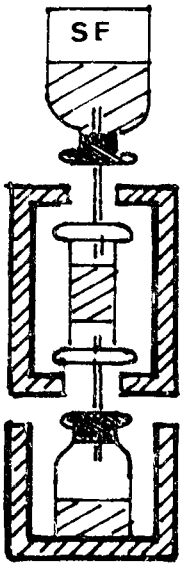
Technetium 99m (^{99m}Tc) (half-life 6,0 hours-Gamma energy 140 KeV).

Obtain as sodium pertechnetate ($^{99m}TcO_4Na$) by elution with physiological solution from a ^{99}Mo - ^{99m}Tc generator.

^{99}Molybden is obtained by irradiation of molybden 98 with neutrons or as fission product of uranium 235. In the generator it is absorbed on aluminium oxide. β^- decay of molybdene 99 produces ^{99m}Tc. Equilibrium is reached after 23 hours. Elution can be made dayly. Another method of obtaining sodium perchnetate is by solvent extraction or sublimation of oxides.







Decay of ^{99}Mo (T 1/2 67 hours)

Days	0	1	2	3	4	5	6	7
% remaining ^{99}Mo	100	78	61	48	37	29	23	18
Days	8	9	10	11	12	13	14	15
% remaining ^{99}Mo	14	11	8.4	6.5	5.1	4	3.1	2.4

^{99m}Tc yield is proportional to ^{99}Mo and time since last elution.

Hours after last elution	1	2	3	4	5	6	7
% ^{99}Tc	9.4	18	26	33	39	40	50
Hours after last elution	8	9	10	11	12	18	24
% ^{99}Tc	54	59	62	66	69	80	87

Decay of ^{99m}Tc (T 1/2 6 hours).

Hours	-4	-3	-2	-1	0
% remaining ^{99m}Tc	159	141	126	112	100

Hours	1	2	3	4	5
% remaining ^{99m}Tc	89	80	71	63	56

Hours	6	7	8	9	10
% remaining ^{99m}Tc	50	44	40	36	32

Determination of aluminium

A simple test is using the aluminium Ion Kit of New England Nuclear. On a humid paper deposit a drop of elution. If existing aluminium is more than 10 ug/ml the observed color will be deeper than a for standard solution.

Sodium pertechnetate - $^{99m}TcO_4Na$

Sodium pertechnetate and sodium chloride in isotonic solution. Sterile, pyrogen-free. Other chemical forms of ^{99m}Tc should not exceed 5% of total activity.

pH: 4.5.

Radiochemical purity

a) Backing: Whatman N°1 (ascending).
Solvent: Methanol 85%.
Time: 20 minutes.
Rf.: TcO_4: 1.0

At least 95% should be sodium pertechnetate ^{99m}Tc.

b) Backing: ITLC S.G.
Solvent: Methanol 85%.
Time: 5 minutes.
Rf.: Tc VII : 1.0.
Rf.: Tc V : 0.3.
Rf.: Tc IV : 0.0.

At least 95% must be sodium pertechnetate ^{99m}Tc.

Radionuclidic purity

Loss of ^{99}Mo in eluate can be determined with a solid state detector and multichannel analyser. Another method is counting a calibrated sample of ^{99}Mo in a lead container (5 mm thick walls, cover and bottom) and without it. The ratio of both measurements is the attenuation factor (R) for ^{99}Mo.

Then the sample of ^{99m}Tc is counted in the container and without it. This last value is ^{99}Mo in the sample: multiply it by attenuation factor.

Biological controls

Test sterility, pyrogens and toxicity according to general methods.

Activity

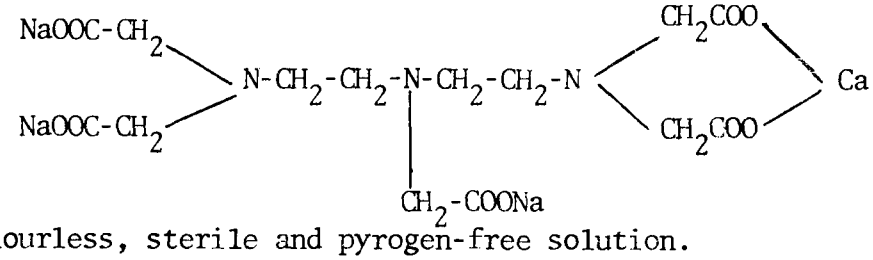
Count in an ionization chamber.

Use and dose

Brain scanning:	2-10 mCi.
Thyroid scanning:	1-2 mCi.
Salivary gland scanning:	0.1-3 mCi.
Stomach scanning:	0.5-1 mCi.
Heart scanning:	3-5 mCi.
Brain flux studies:	10-20 mCi.

For brain and brain flux studies administer previously 300-500 mg potasium perchlorate in order to blockade thyroid.

^{99m}Tc D.T.P.A. (trisodium and monocalcium salt of diethylentriaminepentaaceticacid)



Limpid, colourless, sterile and pyrogen-free solution.

pH: 4.0-4.2.

Radiochemical purity

Backing: ITLC S.G.	ITLC S.G.
Solvent: Acetone.	Physiological solution.
Time: 5 minutes	5 minutes.
Rf.: $^{99m}TcO_4^-$: 1.0.	Rf.: $^{99m}TcO_4$ } 0.6 - 1.0. ^{99m}Tc DTPA }
Rf.: col. ^{99m}Tc DTPA : 0.0.	Rf.: col. : 0.0.

Biological controls

Test sterility, pyrogens and toxicity according to general methods.

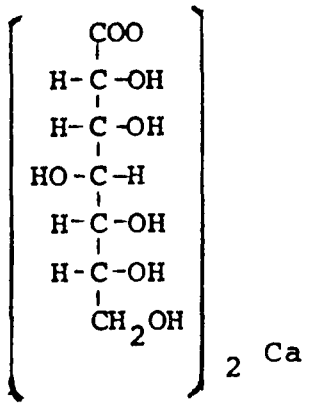
Activity

Count in an ionization chamber.

Use and dose

Brain and kidney scanning. Inject intravenously 10-20 mCi for brain and 3-5 mCi for kidney studies.

^{99m}Tc Calcium glucoheptonate



Limpid, colourless, sterile and pyrogen-free solution.
pH: 6.0

Radiochemical purity

Backing: ITLC S.G.
Solvent: Acetone.
Time: 5 minutes
Rf.: $^{99m}TcO_4$: 1.0.

Rf. $^{99m}TcGH$ / $^{99m}TcO_2$ } 0.0

ITLC S.G.
Physiological solution.
5 minutes.
Rf.: $^{99m}TcO_4^-$ / $^{99m}TcGH$ } 0.0

Rf.: $^{99m}TcO_2$: 0.0

Biological controls

Test sterility, pyrogens and toxicity according to general methods.

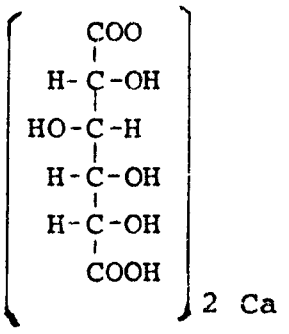
Activity

Count in an ionization chamber.

Use and dose

Use for kidney and brain scanning. Inject intravenously 5 mCi and 15 mCi.

^{99m}Tc - Calcium gluconate



Limpid, colourless, sterile and pyrogen-free solution.
pH: 6.0.

Radiochemical purity

Backing: ITLC S.G.
Solvent: Acetone.
Time: 5 minutes.
Rf.: $^{99m}TcO_4^-$: 1.0.

Rf.: ^{99m}Tc Gluc, $^{99m}TcO_2$ } 0.0.

ITLC S.G.
Physiological solution
5 minutes.
Rf.: $^{99m}TcO_4^-$, ^{99m}Tc Gluc. } 1.0.
Rf.: $^{99m}TcO_2$: 0.0.

Biological controls

Test sterility, pyrogens and toxicity according to general methods.

Biological affinity

33% of activity will be found in kidney 1-2 hours after injection rats.

Activity

Count in an ionization chamber.

Use and dose

Use for kidney scanning. Inject intravenously 5 mCi.

^{99m}Tc injectable Sulfur Colloid

$^{99m}Tc_2S_7$

Colloidal dispersion, slightly white and opalescent; pyrogen-free and sterile.
pH: 4.0 - 7.0

Radiochemical purity

Backing: ITLC S.G.
Solvent: Methanol 85%.
Time: 5-6 minutes.
Rf.: $^{99m}TcO_4^-$: 1.0.
Rf.: Sulfide, $^{99}TcO_2$: 0.0.
Whatman paper N°1 can be used.
Time: 20-30 minutes.

Biological controls

Test sterility, pyrogens and toxicity according to general methods.

Biological affinity

Administer intravenously to mice and study distribution 10-30 minutes after injection.

80% of activity should be found in liver.

Activity

Count in an ionization chamber.

Use and dose

Use for liver, spleen and bone marrow scanning. Inject intravenously 1-6 mCi.

^{99m}Tc Sodium phytate

$C_4 H_{10} O_{24} P_6 Na_8$

Clear, colourless, pyrogen-free and sterile solution.
pH: 6.0 - 6.5

Radiochemical purity

Backing: ITLC S.G.	ITLC S.G.
Solvent: Acetone or MEC	ClH 0.3N.
Time: 5 minutes.	5 minutes.
Rf.: $^{99m}TcO_4^-$: 1.0.	Rf.: $^{99m}TcO_4^-$, phytate } 1.0.
Rf.: phytate, colloid } 0.0.	Rf.: colloid 0.0.

Biological controls

Same as for ^{99m}Tc sulfur colloid.

Biological affinity

Same as for sulfur colloid.

Activity

Same as for sulfur colloid.

Use and dose

Use for liver scanning. Inject intravenously 1-6 mCi.

^{99m}Tc M.A.A. (macroaggregated albumin)

Suspension of macroaggregated albumin. Sterile, pyrogen-free.
pH : 5.5 - 6.0.
Particle size: 30-80 μ.

Radiochemical purity

Backing: ITLC S.G.
Solvent: Methanol 85%.
Time: 5-6 minutes.

Rf.: ^{99m}Tc M.A.A.	0.0.
$^{99m}TcO_2$	
Rf.: $^{99m}TcO_4^-$	1.0.

Biological controls

Test sterility, pyrogens and toxicity according to general methods.

Biological affinity

Administer intravenously to rats and study distribution 30 minutes after injection. Activity in lungs should not be less than 80% and in liver not more than 5%.

Physical controls

Particle size and number is determined by optical microscopy with ocular micrometer and a cell counting chamber. No particles should be more than 100 μ.

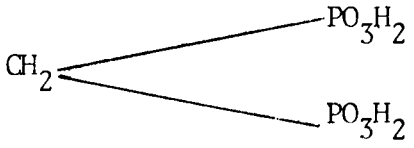
Activity

Count in an ionization chamber.

Use and dose

Use for lung scanning. Inject intravenously 1-4 mCi.

^{99m}Tc M.D.P. (methylenediphosphonate)



Limpid, colourless, sterile and pyrogen-free solution.
pH: 6 - 6.5

Radiochemical purity

Backing: ITLC S.G.			ITLC S.G.		
Solvent: MEC or Acetone.			Physiological solution.		
Time: 5 minutes.			5 minutes.		
Rf.: ^{99m}Tc M.D.P.	}	0.0.	Rf.: $^{99m}TcO_4^-$	}	1.0.
$^{99m}TcO_2^-$			^{99m}Tc M.D.P.		
Rf.: $^{99m}TcO_4^-$:		1.0.	Rf.: $^{99m}TcO_2$:		0.0.

Biological controls

Test sterility, pyrogens and toxicity according to general methods.

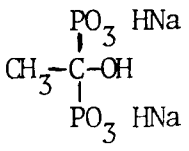
Activity

Count in an ionization chamber.

Use and dose

Use for bone scanning. Inject intravenously 10-20 mCi.

^{99m}Tc H.E.D.S.P. (hydroxiethylidendisodiumdiphosphonate)



Limpid, sterile, pyrogen-free solution.

pH : 6.0 - 6.5

Radiochemical purity

Backing: ITLC S.G.
Solvent: Acetone.
Time: 5 minutes
Rf.: $^{99m}TcO_4^-$: 1.0.

Rf.: ^{99m}Tc H.E.D.S.P. / $^{99m}TcO_2$ } 0.0.

ITLC S.G.
Physiological solution.
5 minutes.
Rf.: $^{99m}TcO_4$ / ^{99m}Tc H.E.D.S.P. } 1.0.
Rf.: $^{99m}TcO_2$: 0.0.

Biological controls

Test sterility, pyrogens and toxicity according to general methods.

Activity

Count in an ionization chamber.

Use and dose

Use for bone scanning. Inject intravenously 10-15 mCi.

^{99m}Tc Pyrophosphate

$P_2 O_7 Na_4 . 10 H_2O$

Limpid, colourless, pyrogen-free sterile solution.
pH : 6.

Radiochemical purity

Backing: ITLC S.G.
Solvent: Acetone.
Time: 5 minutes
Rf.: $^{99m}TcO_4^-$: 1.0.

Rf.: ^{99m}Pyrof. / $^{99m}TcO_2$ } 0.0.

ITLC S.G.
Physiological solution.
5 minutes.
Rf.: $^{99m}TcO_4^-$ / ^{99m}Pyrof. } 1.0
Rf.: $^{99m}TcO_2$: 0.0.

Biological controls

Test sterility, pyrogens and toxicity according to general methods.

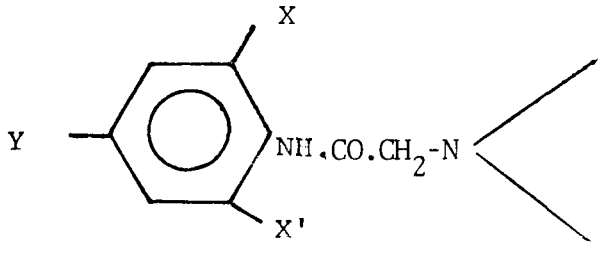
Activity

Count in an ionization chamber.

Use and dose

Use for bone scanning, myocardium infarct and blood pool studies. Inject intravenously 15-20 mCi.

^{99m}Tc. H.I.D.A.



X=X' -CH_3 - C_2H_5 - C_3H_7

Y= -C_4H_9

Limpid, colourless, sterile, pyrogen-free solution containing dimethyl-IDA or diethyl-IDA or diisopropyl-IDA or p-butil-IDA.

pH : 5.5 - 6.0.

Radiochemical purity

Backing: Whatman N°1.
Solvent: Acetone.
Time: 25 minutes.
Rf.: $^{99m}TcO_4^-$: 1.0.

Rf.: ^{99m}Tc H.I.D.A. / $^{99m}TcO_2$ } 0.0.

Whatman N°1.
CO_3HNa 1.6%.
25 minutes.
Rf.: $^{99m}TcO_4^-$ / ^{99m}Tc H.I.D.A. } 1.0.
Rf.: $^{99m}TcO_2$ 0.0.

Electroforesis can also be used. Phosphate buffer solution 0.05 N, Whatman N°1, 300 volt, 120 minutes.

Biological controls

Test sterility, pyrogens and toxicity according to general methods.

Activity

Count in an ionization chamber.

Use and dose

Use for gallbladder and biliary conduct scanning. Inject intravenously 5 - 10 mCi.

^{99m}Tc D.M.S. (dimercapto succinic)

Limpid, colourlesss, sterile, pyrogen-free solution.
pH : 2 - 3.

Radiochemical purity

Backing: ITLC S.G.
Solvent: Acetone.
Time: 5 minutes.
Rf.: $^{99m}TcO_4^-$: 1.0.
Rf.: ^{99m}Tc D.M.S, $^{99m}TcO_2$ } 0.0.

Biological controls

Test sterility, pyrogens and toxicity according to general methods.

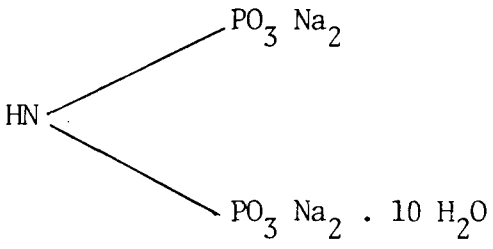
Activity

Count in an ionization chamber.

Use and dose

Use for kidney scanning. Inject intravenously 3 - 5 mCi.

^{99m}Tc I.D.P. (Imidodiphosphonate)



Limpid, colourless, pyrogen-free, sterile solution.
pH : 6.0.

Radiochemical purity

Backing: I.T.L.C. S.G.	I.T.L.C. S.G.
Solvent: Acetone.	Physiological solution.
Time: 5 minutes	5 minutes
Rf.: $^{99m}TcO_4^-$: 1.0.	Rf.: $^{99m}TcO_4^-$ / ^{99m}Tc I.D.P. } 1.0.
Rf.: $^{99m}TcO_2$ / ^{99m}Tc I.D.P. } 0.0.	Rf.: $^{99m}TcO_2$ 0.0.

Biological controls

Test sterility, pyrogens and toxicity according to general methods.

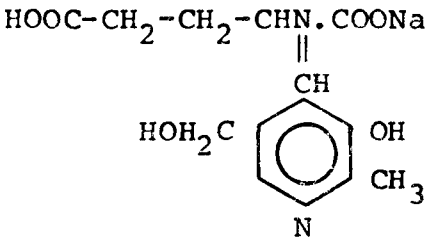
Activity

Count in an ionization chamber.

Use and dose

Use for bone scanning and myocardium infarct studies. Inject intravenously 15 - 20 mCi.

^{99m}Tc P.G. (Pyridoxyliden glutamate)



Clear brown, sterile, pyrogen-free solution.
pH : 8.5 - 9.0.

Radiochemical purity

Backing: ITLC S.G.
Solvent: Propanol 70%.
Time: 20 minutes.
Rf.: $^{99m}TcO_4^-$: 1.0.
Rf.: ^{99m}TcPG : 0.5.
Rf.: ^{99m}TcP : 0.3.

Biological controls

Test sterility, pyrogens and toxicity according to general methods.

Activity

Count in an ionization chamber.

Use and dose

Use for gallbladded and biliary conduct scanning. Inject intravenously 5 - 10 mCi.

^{99m}Tc Albumin

Clear, slightly yellow, sterile, pyrogen-free solution.
pH : 2.5 - 3.0

Radiochemical purity

Backing: I.T.L.C. S.G.
Solvent: Methanol 85%.
Time: 5 minutes.
Rf.: $^{99m}TcO_4^-$: 1.0.
Rf.: ^{99m}Tc Alb: 0.0.

Biological controls

Test sterility, pyrogens and toxicity according to general methods.

Biological affinity

Administer intravenously to rats. Activity in blood is more than 50% after 1 hour.

Activity

Count in an ionization chamber.

Use and dose

Use for blood pool. Inject intravenously 3 - 5 mCi.

^{99m}Tc Antimony Sulfide

S_3 Sb_2

Orange, slightly opalescent, pyrogen-free, sterile colloidal dispersion.
pH : 6.0.

Radiochemical purity

1)
Backing: ITLC S.G.
Solvent: Acetone.
Time: 5 minutes.
Rf.: $^{99m}TcO_4^-$: 1.0.
Rf.: Colloid : 0.0.

2) Determine by dialysis against distilled water.

Biological controls

Test sterility, pyrogens and toxicity according to general methods.

Biological affinity

Same as for colloidal sulfur.

Activity

Count in an ionization chamber.

Use and dose

Use for liver-spleen scanning. Inject intravenously 1 - 5 mCi.

BIBLIOGRAPHY

1 - The United States Pharmacopeia.
XX Edición - 1980.

2 - Farmacopea Argentina.
VI Edición 1978.

3 - MURPHY, Consuelo A. de
El Tecnecio.
Sociedad Mexicana de Medicina Nuclear 1977.

4 - HEINDEL, N.D.; BURNS, H.D.; HONDA, T. and BRADY, L.W.
The Chemistry of Radiopharmaceuticals.
Masson Publishing U.S.A. Inc. 1977.

5 - A.A.P.M. Monograph N°1.
Biophysicals Aspects of the Medical Use of Technetium - 99m.
Kereickes J.G. and Corey K.R.
(American Association of Physicists in Medicine).
Committee of Nuclear Medicine 1976.

6 - GARCIA, E.J. y MITTA, A.E.A.
Guía de Trabajos Prácticos de Agentes para Radiodiagnóstico.
F.C.E.N. (U.B.A.) y I.B. (U.F.R.G.S.) 1978.

7 - CIFKA, J.
Production and Control of Mass Produced Radiopharmaceuticals.
Praga (Checoslovaquia) 1971.

8 - International Atomic Energy Agency's.
Consultant's Meeting on:
Chemistry and Biochemistry of Radiopharmaceuticals. Viena (Austria). 1975.

9 - SUAREZ, A.F. de; CASTIGLIA, S.G. de; CAMPOS, A. y MITTA, A.E.A.
Normas para la preparación y control de radiofármacos marcados con Tecnecio 99m.
VII Congreso ALASBIMN, Punta del Este, Uruguay 1979.

10 - Comisión Nacional de Energía Atómica (R.Argentina) y Junta de Energía Nuclear (España) 1972.
Manual de Controles Radiofarmacéuticos.

11 - LEVIT, N.B.; JORDAN, W.and RHODES, B.
Laboratory Manual For Nuclear Medicine Technologists.
University of New México. College of Pharmacy 1980.

12 - SUBRAMANIAN, G.
Preparation and Quality Control of Radiopharmaceuticals.
Division of Nuclear medicine. Dept. of Radiology Upstate Medical Center.

Syracuse. N.Y. 13210. 1978.

13 - CLOUTIER, R.J.; COFFEY, J.L.; SNYDER, W.S. and WATSON, E.E.
Radiopharmaceuticals Dosimetry Symposium.
Proceedings of a Conference Held at Oak-Ridge 1978.

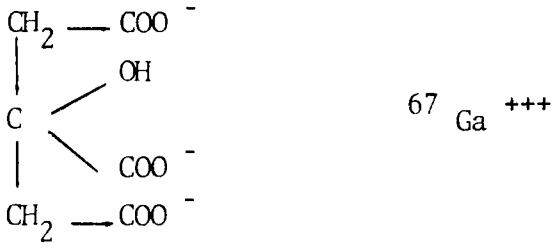
^{67}Ga - ^{111}In - ^{201}Tl

1 - ^{67}Ga citrate.

2 - ^{111}In D.T.P.A. (diethylentriaminepentaacetic salt of calcium).

3 - ^{201}Tl Chloride.

^{67}Ga citrate



Limpid, clear, pyrogen-free, sterile solution.
pH : 4.5 - 7.5.

Radiochemical purity

Backing: ITLC S.G.
Solvent: Cl_3 CH: acetic acid (9:1).
Time: 6 minutes.
Rf.: ^{67}Ga: 0.1.

Biological controls

Test sterility, pyrogens and toxicity following the general methods.

Activity

Count in an ionization chamber.

Use and dose

Use to prove the presence and extension of hodgkin disease, lymphoma and bronchogenic carcinoma. Inject intravenously 2 - 5 mCi.

^{111}In D.T.P.A.

Sterile, pyrogen-free, limpid, isotonic solution.
pH : 6.0 - 8.0.

Radiochemical purity

Backing: ITLC S.G.
Solvent: Methanol 85%
Time: 5 minutes.
Rf.: $^{111}In^{+++}$: 0.0.
Rf.: ^{111}In D.T.P.A. : 1.0.

Biological controls

Test sterility, pyrogens and toxicity according to general methods.

Activity

Count in an ionization chamber.

Use and dose

Use for cisternography and brain scanning. Inject by intrathecal, rachidic or intravenous way 0.5 mCi.

^{201}Tl Thallium chloride

Limpid, colourless, pyrogen-free, sterile, isotonic solution.
pH : 4.5 - 6.0.

Radiochemical purity

Backing: ITLC S.G.
Solvent: Acetone.
Time: 5 minutes.
Rf.: $^{201}Tl^{+}$: 0.0.
Rf.: $^{201}Tl^{++}$: 1.0.

Biological controls

Test sterility, pyrogens and toxicity according to general methods.

Activity

Count in an ionization chamber.

Use and dose

Use for myocardium scanning, visualization of isquemic and necrotic area of myocardium infarct (cold area). Inject intravenously 1.5 - 2.5 mCi.

BIBLIOGRAPHY

1 - SILVESTER, J.D. and WATERS, S.L.
Radionuclide Production.
2 nd. International Symposium on Radiopharmaceuticals.
March 19-22, 1979; Seattle, Washington, U.S.A.

2 - Medical Research Council.
Cyclotion Unit.
Annual Research and Development.
Report 1978.
Hammersmith Hospital London W 12 and Western General Hospital Edinburgh.

3 - Radiochemistry - Vol. 3 -
A Review of the Literature Published during 1974 and 1975.
G.W.NEWTON.
The Chemical Society.
Burlington House, London WIV o BN 1976.

4 - THAKUR, M.L.
Gallium 67 and Indium 111 Radiopharmaceuticals.
Int.J.Appl. Radiation & Isotopes 28, 183, 1977.

5 - TRAN, P.T. and WASNICH, R.
Practical Nuclear Pharmacy.
Banyan Enterprises - P.O.Box 27825 - Honolulu H 196827.

6 - VIVIAN, A.; ICE, R.D.; SHEN, V.; and HETZEL, K.R.
Radiochemical Purity of Radiopharmaceuticals.
Using gelman Seprachrom (ITLC) Chromatography.
Techemical Bulletin 32 - June 1977 -

7 - SERVIAN, J.L.
Production of Radionuclides and Labelled Compounds from Accelerator.
Int. J. Appl. Radiation & Isotopes 26, 763, 1975.

8 - WOLF, A.P.; CHRISTMAN, D.R.; FOWLER, J.S. and LAMBRECHT, R.M.
Synthesis of Radiopharmaceuticals and Labelled.
Compounds Using Short-Lived Isotopes.
Chemistry Department - Brookhaven National Laboratory Upton N.Y. U.S.A.

IODINE 123 - 125 - 131

1 - ^{131} I Sodium iodide (solution).

2 - ^{131} I Sodium iodide (injectable).

3 - ^{131} I or ^{125} I Albumin.

4 - ^{131} I Fibrinogen.

5 - ^{131} I M.A.A. (macroaggregated albumin).

6 - ^{131} I Bromosulfophthalein.

7 - ^{131} I Rose - Bengal.

8 - ^{131} I Sodium ortho-iodohipurate.

9 - ^{131} I Sodium iodotalamate.

10 - ^{131} I 19 Iodo cholesterol.

11 - ^{131} I 6 β Iodo methyl-19 norcholesterol (NP 59).

IODINE 123

Half - life: 13 hours.
Energy : (MeV)

Beta	Gamma
--	0,159 - (97%)

IODINE 125

Half - life: 60,2 days.
Energy : (MeV)

Beta	Gamma	X-Rays
--	0,0355 (7%)	0,027

IODINE 131

Half - life: 8,05 days.
Energy : (MeV)

Beta	Gamma
0,61 (87,2%)	0,36 (79%)
0,33 (9,3 %)	0,64 (9.5%)

^{131}I Sodium iodide (solution)

^{131}I Na

Aqueous solution, not injectable.

pH : 7.5 - 9.0.

Radiochemical purity

Backing: Whatman N°1	ITLC S.G.
Solvent: Methanol: H_2O (3:1)	Methanol 85%
Time: 4 hours.	5 minutes.
Rf.: $^{131}I^-$: 0.85.	Rf.: $^{131}I^-$: 0.9.
Rf.: $^{131}IO_3^-$: 0.46.	Rf.: $^{131}IO_3^-$: 0.2

Use iodide carrier. See Argentine Pharmacopeia. VI Edition 1978.

Biological controls

Test toxicity according to general methods.

Chemical purity

Limit test for tellurium: in a small reaction tube with cover placed in a container, deposit 0,5 ml $Na^{131}I$ solution. Add 1 drop SNa_2 20%, then 1 drop SO_4H_2 4N. Cover inmediately and compare brown colour with that of a Te solution 10 ppm treated similarly. A white precipitate of S might appear, but the solution of Na ^{131}I will not be black. Work under a hood.

Activity

Count in an ionization chamber.

Use and dose

Use for iodine uptake, thyroid scanning. Administer bucally 20-500 UCi. For thyroid carcinome 100 UCi also bucally.

^{131} I Sodium - iodide (injectable)

^{131} INa

Aqueous solution injectable, sterile, isotonic, pyrogen-free.
pH : 7.5 - 9.0.

Radiochemical purity

Same as for ^{131} INa not injectable.

Biological controls

Test isotonicity, pyrogens, sterility and toxicity according to general methods.

Activity

Count in an ionization chamber.

Use and dose

Use for thyroid scanning, administer bucally or inject intravenously 50 - 100 µCi.

^{125}I or ^{131}I Albumin

Aqueous solution, isotonic, sterile, pyrogen-free.
pH : 7.0 - 8.5.

Radiochemical purity

Backing: ITLC S.G.
Solvent: Methanol 85%.
Time: 5 minutes.
Rf.: ^{131}IAlb. : 0.0.
Rf.: $^{131}I^-$: 1.0.

Whatman N°1 (ascendent, work in darkness)
Methanol 70%.
4 hours.
Rf.: ^{131}IAlb. : 0.0.
Rf.: $^{131}I^-$: 0.8 - 0.85.
Rf.: $^{131}IO_3^-$: 0.5 - 0.55.

Biological controls

Test isotonicity, pyrogens, sterility and toxicity according to general rules.

Activity

Count in an ionization chamber.

Use and dose

Use for determination of blood volume and intrathecal scanning 5 UCi and 50 - 100 µCi, respectively.

^{131}I Fibrinogen

Aqueous solution, isotonic, sterile, pyrogen-free.
pH : 7.0 - 8.5.

Radiochemical purity

Backing: Whatman N°1.
Solvent: Methanol 70%.
Time: 4 hours.
Rf.: ^{131}IFib. : 0.0.
Rf.: $^{131}I^-$: 0.8 - 0.85.

Biological controls

Test pyrogens, sterility and toxicity according to general methods.

Biological affinity

Determine in rabbit blood, the percentage of activity bound to tromb after 1 hour of incubation at 38°C.

Activity

Count in an ionization chamber.

Use and dose

Use for venous trombosis scanning. Inject intravenously 100 µCi.

^{131}I M.A.A. (macroaggregated albumin)

Aqueous suspension, sterile, pyrogen-free. Particle size 20-70 µ.
pH : 5.0 - 6.0.

Radiochemical purity

Backing: Whatman N°1.
Solvent: Methanol H_2O (7:3).
Time: 3 hours.
Rf.: ^{131}I M.A.A. : 0.0.
Rf.: $^{131}I^-$: 0.8 - 0.85.

Biological controls

Test sterility, pyrogens and toxicity according to general methods.

Biological affinity

The percentage of activity in lungs must be not less than 80% and activity in liver not more than 5%, 30 minutes after administration, in rats.

Physical controls

Determination of particle size and number is done by optical microscopy with a micro metric ocular and a cell counter chamber. Particles should not exceed 100 µ.

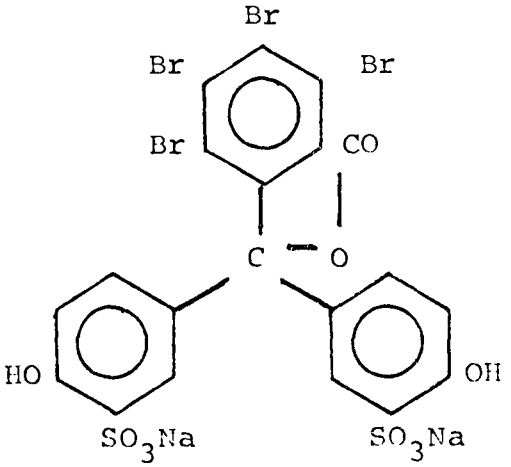
Activity

Count in an ionization chamber.

Use and dose

Use for lung scanning. Inject intravenously 150 - 300 µCi.

^{131} I Bromosulfophthalein



Aqueous solution, isotonic, sterile, pyrogen-free. Keep in darkness at 4°C.

pH : 6.0 - 8.0.

Radiochemical purity

Backing: S.G.

Solvent: ClH IN.

Time: 15 minutes.

Rf.: ^{131} IBSP : 0.0.

Rf.: ^{131} I^- : 0.9 - 1.0.

Biological controls

Test isotonicity, pyrogens, sterility and toxicity according to general methods.

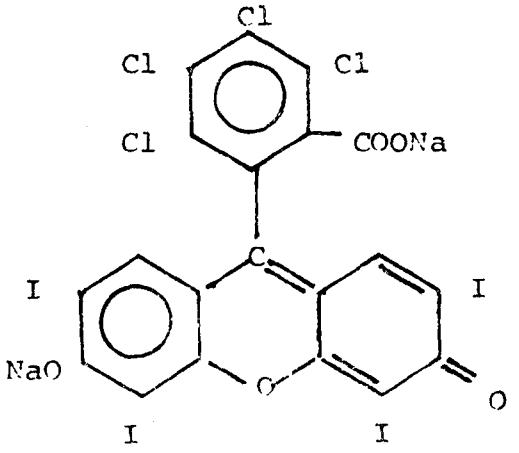
Activity

Count in an ionization chamber.

Use and dose

Use for liver scanning. Inject intravenously 100 - 300 µCi.

^{131}I - Bengal Rose



Aqueous solution, dark red, isotonic, sterile, pyrogen-free. Keep in darkness at 4°C.

pH : 6.0 - 8.5.

Biological purity

Backing: ITLC S.G.	Whatman N°1.
Solvent: Cl_3CH: Acetic acid (9:1).	Acetic acid 1 N.
Time: 5 minutes.	2 hours.
Rf.: ^{131} IR.B. : 0.8.	Rf.: I R.B. : 0.0
Rf.: less iodinat.fluoresc $<$ 0.2.	Rf.: $^{131}I^-$: 1.0.

Biological controls

Test isotonicity, pyrogens, sterility and toxicity according to general methods.

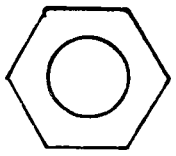
Activity

Count in an ionization chamber.

Use and dose

Use for liver scanning. Inject intravenously 100 - 250 µCi.

^{131} I Sodium O.Iodohipurate



CO.NH.CH_2-COONa

I

Aqueous solution, injectable, isotonic, sterile, pyrogen-free.
pH : 7.0 - 8.5.

Radiochemical purity

Backing: ITLC S.G.
Solvent: Cl_3CH: Acetic acid (9:1).
Time: 5 - 6 minutes.
Rf.: ^{131} I Hip. : 1.0.
Rf.: ^{131} I^- : 0.1.

Whatman N°1 (descendent).
Benzene: Acetic acid-H_2O (2:2:1) (organic layer).
3 hours.
Rf.: ^{131} I Hip.: 0.5.
Rf.: ^{131} I Iodo Benz.: 0.9.
Rf.: ^{131} I^- : 0.0.

Biological controls

Test pyrogens, sterility and toxicity according to general methods.

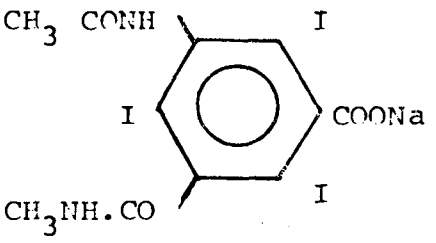
Activity

Count in an ionization chamber.

Use and dose

Use for determination of kidney function. Inject intravenously 250 - 300 µCi.

^{131}I Sodium iodotalamate



Aqueous solution, colourless or slightly yellow, isotonic, sterile, pyrogen-free.
Keep in darkness at 4°C.
pH : 7.0 - 8.0.

Radiochemical purity

Backing: S.G.	ITLC S.G.
Solvent: ClH 1 N.	Benzene: Acetic acid-water(2:2:1).
Time: 15 minutes.	5 minutes.
Rf.: ^{131}I tal. : 0.0 - 0.4.	Rf.: ^{131}I tal. : 0.2.
Rf.: $^{131}I^-$: 0.9 - 1.0.	Rf.: $^{131}I^-$: 1.0.

Biological controls

Test pyrogens, sterility, isotonicity and toxicity according to general methods.

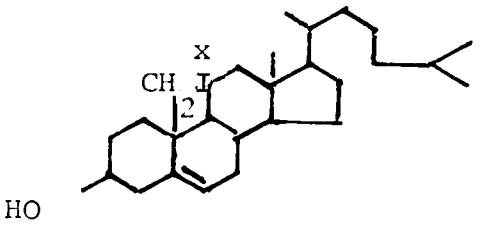
Activity

Count in an ionization chamber.

Use and dose

Inject intravenously 250 - 300 µCi.

^{131} I. 19 Iodocholesterol



Clear and colourless or slightly yellow solution, pyrogen-free, sterile.

pH : 3.0 - 5.0.

Radiochemical purity

Backing: ITLC S.G.
Solvent: Cl_3CH.
Time: 5 minutes.
Rf.: ^{131} I 19 Chol. : 0.6.
Rf.Imp. : 1.0.
Rf.: $^{131}I^-$: 0.1.

Radiochemical controls

Test sterility, pyrogens and toxicity according to general methods.

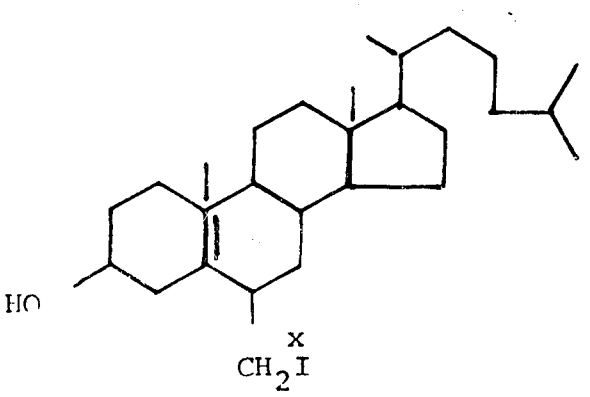
Activity

Count in an ionization chamber.

Use and dose

Use for adrenaline gland scanning. Inject intravenously 1 - 2 mCi.

^{131} I - 6 β Iodomethyl-19-Norcholestirol (NP-59)



Colourless or slightly yellow solution sterile, pyrogen-free.

pH : 3.5 - 6.0.

Radiochemical purity

Backing: ITLC S.G.

Solvent: Cl_3Ch.

Rf.: ^{131} I 6 β 19n: 0.6.

Rf.: 19 I Chol. : 1.0.

Rf.: $^{131}I^-$: 0.1.

Biological controls

Test pyrogens, sterility, toxicity according to general methods.

Activity

Count in an ionization chamber.

Use and dose

Use for adrenaline gland scanning. Inject intravenously 1.5 - 2.0 mCi.

BIBLIOGRAPHY

1 - Farmacopea Nacional Argentina.
VI Edición 1978.

2 - The United States Pharmacopeia.
XX Edición 1980.

3 - ALVAREZ, J.C.; SALAS, G.N.B. de ; RABAN, P. y MITTA A.E.A.
J.Chrom. 45 , 328 (1969).

4 - CORREIA, R.J. y MITTA, A.E.A.
Radiochim. Acta 12 , 118 (1969).

5 - MITTA, A.E.A.; CAMIN, L.L. y TROPAREVSKY, M.L.P. de.
Radiochim. Acta 6 , 112 (1966).

6 - STRUFALDI, B.; EUGELSTEIN, E.; BARBERIO, J.C. y MITTA, A.E.A.
Publicazao N°120 IEA Sao Paolo (1963).

7 - ALVAREZ, J.; SALAS, G.N.B. de; MITTA, A.E.A.
Informe CNEA N°285 (1970).

8 - SALAS, G.N.B. de ; TROPAREVSKY, M.L.P. de y MITTA, A.E.A.
Radiochim. Acta 8 , 224 (1968).

9 - PLIEGO, O.H. y MITTA, A.E.A.
Informe CNEA N°459 (1980).

10 - SUÑER, A.A. y MITTA, A.E.A.
Informe CNEA N°458 (1980).

11 - RECCHI, N.
Manual de Controles Radiofarmaceúticos C.N.E.A. (1965).

12 - MASSAGLIA, A. y ROSA, U.
JChromatog. 14 , 516 (1964).

13 - LOGUSSO, N.A. y MITTA, A.E.A.
Informe CNEA N°294 (1973).

14 - SALAS, G.N.B. de; ALVAREZ, J. y MITTA, A.E.A.
Radiochim. Acta 17 , 58 (1972).

15 - CORREIA, R. y MITTA, A.E.A.
Informe CNEA N°373 (1973).

16 - SANCHEZ, M.V.; SALAS, G.N.B. de; y MITTA, A.E.A.
Informe CNEA N°342 (1972).

Carbon ^{14} - Mercure ^{197} - Chrome ^{51} etc.

1 - ^{14} C Glycine.

2 - ^{197} Hg Neohydrin.

3 - ^{51} Cr Sodium chromate.

4 - ^{75} Se Selenium methionine.

5 - ^{198} Au Colloidal gold.

6 - ^{196} Yb D.T.P.A.

7 - ^{32} P Sodium phosphate.

8 - ^{32} P Colloidal chromium phosphate "B" and "C".

9 - ^{57} Co Cyanocobalamin.

^{14}C Glycine

Aqueous solution, injectable, isotonic, sterile. Keep at 4°C.
pH : 7.

Radiochemical purity

Backing: Whatman N°1.
Solvent: Butanol: Acetic acid: H_2O (12:3:5).
Time: 16 hours.
Rf.: Simultaneously a standard glycim must be developed. Use as developer a solution of ninhydrine in acetone 0.2%. Prepare fixer dissolving 1 ml saturated cupric nitrate and two drops of NO_3H in 100 methanol.

Biological controls

Test sterility, pyrogens and toxicity according to general methods.

Activity

Count in an ionization chamber.

Use and dose

Research.

^{197} Hg Neohydrin

Aqueous solution, injectable, sterile, pyrogen-free.
pH : 7 - 8 .

Radiochemical purity

Backing: ITLC S.G.
Solvent : NaOH 1N.
Time: 5 minutes.
Rf.: ^{197} Hg Neoh. : 1.0.
Rf.: Hg^{++} : 0.0.

Whatman N°1.
Methanol: Buatnol: NH_3(0.15N): H_2O.
4 hours (7:5:3:1).
Rf.: ^{197} Hg Neoh. : 0.5.
Rf.: Hg^{++} : 0.0.

Biological controls

Test sterility, pyrogens and toxicity according to general methods.

Activity

Count in an ionization chamber.

Use and dose

Use for kidney and brain scanning. Inject intravenously 100 - 200 µCi.

^{51}Cr - Sodium chromate

Limpid, slightly yellow solution, sterile, pyrogen-free, isotonic. Keep in darkness at 4°C.
pH : 6.0 - 7.5.

Radiochemical purity

Backing: Whatman N°1.
Solvent Water: alcohol 95° NH_4OHconc. (5:2:1).
Time: 2 - 3 hours.
Rf.: $^{51}CrO_4Na_2$: 0.9.
Rf.: $^{51}Cr^{+++}$: 0.0.

Concentration

Determine concentration by spectrophotometry at 370 mμ. Previously adjust pH to 8 ± 0.5 with CO_3HNa (see The United States Pharmacopeia XX page 150).

Special tests

Determine the affinity of sodium chromate for red blood cells, incubating at 38°C with heparinized rabbit blood. Centrifugate and wash labelled blood cells. 90% of used dose should be in blood cells. No hemolisis should be observed.

Activity

Count in an ionization chamber.

Use and dose

Use determination of volemia and erythrocyte survival. Inject intravenously 15 - 200 μCi.

^{75} Se Soleniummethionine

$$CH_3-{}^{75}Se-CH_2-CH_2-CHNH_2-COOH$$

Aqueous solution, injectable, isotonic, sterile, pyrogen-free. Keep in darkness at 4°C.

pH : 5.0 - 8.0.

Radiochemical purity

Backing: ITLC S.G.

Solvent: Isopropanol: n butanol: H_2O (1:3:1).

Time: 15 minutes.

Rf.: ^{75} Se Met. : 1.0.

Rf.: ^{75} Se Selenoxymet: 0.4.

Biological controls

Test sterility, pyrogens and toxicity according to general methods.

Activity

Count in an ionization chamber.

Use and dose

Use for pancreas or parathyroid scanning. Inject intravenously 200 - 350 µCi.

^{198}Au Colloidal gold

Aqueous suspension, injectable, sterile, pyrogen-free. Colloidal gold protected with polyvinylpirrolidone or with getaline. Particle size 3 - 6 mμ por "colloidal germ" and 20 - 30 mμ en el "grown colloid".
pH : 5.0 - 7.0.

Radiochemical purity

Backing: Whatman N°1.	Whatman N°1.
Solvent: Acetone: H_2O: ClH conc. (7:2:1).	Acetone: H_2O (3:1).
Time: 1 hour.	1 hour.
Rf.: ^{198}Au colgel. : 0.0.	Rf.: ^{198}Au col.PVP: 0.0.
Rf.: $^{198}Au^{+++}$: 1.0.	Rf.: $^{198}Au^{+++}$: 1.0.

Biological controls

Test pyrogens, sterility and toxicity according to general methods.

Particle size

Determine by either spectrophotometry or electronic microscopy.

Activity

Count in an ionization chamber.

Chemical concentration

By spectrophotometry.

Use

Therapy.

^{169}Yb Ca D.T.P.A.

Aqueous solution, injectable, isotonic, sterile.
pH : 7.0 - 7.5.

Radiochemical purity

Backing: Whatman 3 MM.
Solvent: Ammonium sulfate (0.025 M): Acetone: NH_4OH 10% (110:50:0.1).
Time: 3 hours.
Rf.: ^{169}Yb DTPA: 0.8.
Rf.: $^{169}Yb^{+++}$: 0.0.

Biological controls

Test sterility, pyrogens and toxicity according to general methods. Determine for 3 mice percentage of remaining activity 48 hours after injection. Mean value should be 1.4%.

Activity

Count in an ionization chamber.

Use and dose

Use in cysternography. Inject by intrathecal or rachidic 1 mCi.

^{32}P Sodium phosphate

$^{32}PO_4HNa_2$

Limpid and colourless solution. Colourless or with slight of bacteriostatic agent used in the preparation. Sterile and isotonic.
pH : 5.0 - 6.0.

Radiochemical purity

Backing: Whatman N°1 (descendent).
Solvent: Isopropanol (75 ml): trichloroacetic acid (5g): NH_3 δ 20°C: 0.921 (0.3ml).
Time: 16 hours.
Rf. orthophosphates: 0.75.
Rf. pyrophosphates : 0.45.
Rf. polyphosphats : 0.35.

Biological controls

Test sterility, pyrogens and toxicity according to general methods.

Activity

Count in an ionization chamber.

Use and dose

Use in therapy. Inject intravenously or orally.

^{32}P Colloidal Chromium phosphate "B" and "C"

$^{32}PO_4Cr$

Aqueous suspension, injectable, isotonic, sterile, pyrogen-free. Particle size 300 - 700 Å for "B" and 100 - 300 Å for "C".
pH : 6.0 - 7.0.

Radiochemical purity

Backing: Whatman N°1.
Solevent: ClH 1 N.
Time: 1 hour.
Rf.: $^{32}PO_4Cr$: 0.0 - 0.1.
Rf.: $^{32}PO_4^{---}$: 0.8 - 0.9.

Biological controls

Test sterility, pyrogens and toxicity according to general methods.

Activity

Count in an ionization chamber.

Use and dose

Use in therapy.

^{57} Co Cyano cobalamin

Aqueous solution. Colourless or pink

pH : 4.0 - 5.5.

Radiochemical purity

Backing: ITLC S.G.

Solvent: NaCl 10%.

Time: 3 minutes.

Rf.: ^{57} Co cia. : 0.2 - 0.5.

Rf.: ^{57} Co^{+++} : 1.0.

Spot one drop of standard.

Biological controls

Test of toxicity according to general methods.

Activity

Count in an ionization chamber.

Use and dose

Use for schilling test. Administer orally 0.5 µCi.

BIBLIOGRAPHY

1 - ALVAREZ, J.; SALAS, G.N.B. de y MITTA, A.E.A.
Informe CNEA N°285 (1970).

2 - CARO, R. y INGRAND, R.
Revew d'Optique 6 , 281 (1965).

3 - CARO, R.; NICOLINI, J.O. y RADICELLA, R.
Int. J.Appl.Rad. and Isotopes 19 , 547 (1968).

4 - ANGHILERI, L.
Informe CNEA N°125 (1964).

5 - ANGHILERI, L. y MARQUES, R.O.
Informe CNEA N°154.

6 - Farmacopea Argentina.
VI Edición 1978.

7 - The United States Pharmacopeia Ed. XX 1980.

8 - BUHLER, M.F.; CASTRILLON, J.P.A.; MITTA, A.E.A. y DANKERT, M.A.
Informe CNEA N°42 (1960).

9 - Farmacopea Francesa (1965).

10 - COHEN, Y.; INGRAND, I. CEA (francia).
Informe N°1618 (1960).

11 - WAGNER, H.
Principles of Nuclear Medicine Ed. Sauders W.B. Company-Filadelfia (1968).

12 - Radiopharmaceuticals and Labelled Compounds STI/PUB/344.
IAEA (1973 - Pag. 145).