by aluminium shows the presence of a very short range component issuing from the platinum surface. This component makes a noticeable contribution to the count-rate up to an absorber thickness of 80 mg Al/cm^2. It is observed with approximately the same relative intensity if the needle is surrounded by platinum, but it is absent if the needle is surrounded by aluminium. It is reasonable to assume that this radiation is produced by the photoelectric effect in the platinum.

Conversion electrons due to Compton absorption must also be present, but these would not be recognized as a difference in absorption of radiation outside a platinum and outside an aluminium surface, the Compton mass attenuation coefficient being even a little higher in aluminium than in platinum. Compton electrons will certainly contribute to the count-rates measured above the gamma contribution through absorbers between 80 and 250 $mg/Al/cm^2$. However, this part of the absorption curve is very difficult to interpret. As the thickness of the aluminium absorber foil is raised the efficiency of the counter for gamma-rays is also increased. This in part compensates for the reduction of the count-rate from the softer radiation emitted by the needle. Evidently, if one would take a platinum needle surrounded by a sufficiently thick aluminium cylinder and if the aluminium absorber foils would then be fitted snugly around this cylinder, one would observe only a reduction of the count-rate due to gamma-absorption in the various layers of aluminium. We have actually observed a strong dependence of the shape of the absorption curve measured with aluminium covered needles on the geometry.

Thus we may conclude that there is a contribution from a low penetration component to the absorbed dose in the first one or two millimeters of tissue around a radium needle, but that this component cannot be noticeably reduced by increasing the thickness of the platinum wall.

In as far as this soft component consists of Compton electrons it only serves to establish the normal radiation equilibrium between photons and Compton electrons as it normally exists in tissue. (A slight difference will remain due to the transition from a high Z to low Z material). The photo-electrons, on the other hand, provide an extra contribution to the radiation field, which will penetrate for several decimeters the air around an uncovered needle. In therapy this short range radiation will hardly be noticed because of the $1/r$-dependence of the dose-rate. Under certain other circumstances, however, one might possibly wish to provide a shielding against this part of the radiation emitted by radium needles. This can easily be done by using 1 mm thickness of plastic or some similar light material.

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New Methods for Introducing 75Se into Radiopharmaceuticals

Introduction

To SYNTHESIZE a gamma-ray emitting radiopharmaceutical it is often necessary to introduce a radionuclide of an element not present in the original pharmaceutical. This process is sometimes referred to as foreign labeling.[1] The most common foreign label used in radiopharmaceuticals has been radioiodine because of the many, well-established, iodination methods currently available. Although selenium-75 has desirable physical characteristics for *in vivo* radiopharmaceutical imaging and can be a bioisosteric replacement for sulfur in many products, selenium labeled radiopharmaceuticals are not extensively available due to a lack of a simple method for introducing the label into the pharmaceutical.

A further consideration in the synthesis of labeled pharmaceuticals is the practice of introducing the label into the product at the latest possible synthetic step to prevent undue product handling thus decreasing personnel exposure and minimizing product decay. Iodinated radiopharmaceuticals, synthesized by isotope exchange, illustrate the principle of last step labeling. Until now, labeled selenium has not been available in a form suitable for last step labeling.

Selenium-75 has several advantages in radiopharmaceutical design over iodine-131: (a) The beta-particle absorbed dose is about 7% of that of iodine-131; (b) Between 100 and 400 keV there are 1.74 gamma rays per disintegration as compared to 0·91 for iodine-131; (c) The combined contribution of (a) and (b) means that smaller administered doses of 75Se rather than I^{131} radiopharmaceuticals would be needed; (d) The longer physical half-life of 75Se

means a longer shelf life for the radiopharmaceutical and thus reduced production costs.

We report a simple method for introducing ^{75}Se into an organic molecule during the later steps of chemical synthesis to produce a high specific activity ^{75}Se-radiopharmaceutical. This method is suitable for the synthesis of organic molecules that have the capability of forming a C–Se bond, e.g. selenourea and benzylselenol. The method relies on using the separate useful intermediate labeling reagents, NaH^{75}Se and Na$_2^{75}$Se$_2$, that are stable and can be used as stock solutions for labeling of a variety of radiopharmaceuticals.

Method

Selenium-75, was obtained from New England Nuclear (575 Albany St., Boston, Mass.) as a metal having a specific activity of 120·5 mCi/mg.
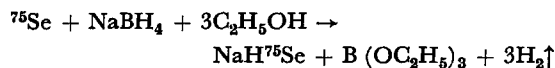
Preparation of NaH^{75}Se

To the vial containing 2·17 mg of ^{75}Se metal was added 50 μmoles of NaBH$_4$ in 0.2 ml of absolute ethanol. The reaction vial was purged with nitrogen and the effluent gas vented into a 5% lead-acetate solution to trap any potentially volatile hydrogen selenide (none was evolved). The reaction was allowed to proceed for 15 min until no further hydrogen was evolved. This solution can be used immediately or stored at room temperature with exclusion of O$_2$ under N$_2$. Aliquots of the solution can be removed and used as needed. The labeled product can be diluted with an alcoholic solution of NaHSe to lower the specific activity.

Preparation of Na$_2^{75}$Se$_2$

The diselenide is easily formed from the above NaH^{75}Se by adding an equimolar quantity of selenium metal to the ethanolic solution of NaH^{75}Se under nitrogen. The solution turns to a brownish red color, indicating the formation of Na$_2^{75}$Se$_2$. The reaction is complete within 15 min after complete dissolution of the selenium. This solution can be stored and used as above.

Results

The reaction involved in the production of NaH^{75}Se is:

$$^{75}\text{Se} + \text{NaBH}_4 + 3\text{C}_2\text{H}_5\text{OH} \rightarrow$$
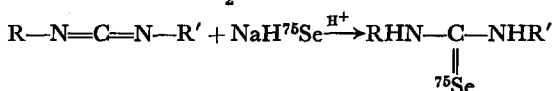$$\text{NaH}^{75}\text{Se} + \text{B}(\text{OC}_2\text{H}_5)_3 + 3\text{H}_2\uparrow$$

Since the triethyl borate byproduct of the reaction does not interfere with various displacement reactions, the highly nucleophilic hydroselenide anion solution can be used directly to displace aliphatic halides or *p*-toluene sulfonate ions to give selenols, monoselenides or diselenides. Typical displacements were accomplished in preparing benzylselenol–^{75}Se

and dibenzyl–diselenide–^{75}Se in quantitative yields on a 10 μmole scale by adding equimolar amounts of benzyl chloride to either NaH^{75}Se or Na$_2^{75}$Se$_2$.

The dibenzyldiselenide–^{75}Se can be reduced *in situ* using NaBH$_4$ to yield benzylselenol–^{75}Se which can be used to produce stable, soluble benzyl–alkyl-monoselenides. The protecting benzyl group may be easily cleaved by reduction with sodium in liquid ammonia[4] to yield selenols. The selenol may be converted to an alkyl selenide using an alkyl halide, or oxidized to the diselenide, or acylated in the presence of a base with an acyl chloride or acid anhydride to give a selenol ester.

Another useful ^{75}Se- containing intermediate is selenourea which can be prepared from NaH^{75}Se and cyanamide.[3] Symmetrical or asymmetrical disubstituted selenoureas can be prepared from carbodiimides and H$_2^{75}$Se in an acid media:

$$\text{R—N}{=}\text{C}{=}\text{N—R}' + \text{NaH}^{75}\text{Se} \xrightarrow{\text{H}^+} \text{RHN—C—NHR}'$$
$$\underset{^{75}\text{Se}}{\overset{\|}{}}$$

While benzylselenol and dibenzyldiselenide–^{75}Se are generally used in alkaline media, the neutral selenourea–^{75}Se is readily alkylated to give isoselenuronium salts in organic solvents which are readily hydrolyzed in base to selenols. Additional alkylation or acylation reactions on the selenol can be performed *in situ* (cf. ref. in 3).

Sodium hydrogen selenide, disodium diselenide, dibenzyldiselenide, and selenourea can be used as labeling reagents to produce many high specific activity radiopharmaceuticals. These intermediates have enabled us to synthesize high specific activity 6-benzylseleno-19-norcholesterol specific for the adrenal cortex and alkylselenoanilide analogs o dopamine specific for the adrenal medulla.

Summary

Potential radiopharmaceuticals that have the capability of forming a C–Se bond can be easily labeled with NaH^{75}Se, Na$_2^{75}$Se$_2$ and dibenzyl-diselenide–^{75}Se. The synthesis of these useful intermediates from metallic radioactive selenium is described.

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The CdTe Sub-Miniature Semi-Conductor Detector: A Versatile Instrument for Detection of Gamma Radiation

Introduction

SEMI-CONDUCTOR detectors offer many advantages for clinical and experimental uses, chiefly because of their small size and excellent energy resolution. The energy resolution of a solid state detector is about twenty times higher than that of a conventional NaI(Tl) scintillation detector. In addition, the elimination of scattered radiation contributes to the improvement of image quality. The semi-conductors are considerably more efficient than miniature Geiger probes and their bias voltage is lower than that required by any other probe.

At present, solid state detectors are being used in the imaging techniques; however, thus far, attempts to make a high resolution semi-conductor gamma camera met with considerable difficulties. The choice application of miniature semi-conductors is the measurement of radiation in the immediate proximity of an anatomic structure, such as detection of eye tumors, measurement of cerebral blood flow, etc. Their special resolution is a function of the diameter of the probe and may be as small as 1 mm.

Solid state detectors became popular in the field of fluorescence X-ray assay. There are instruments on the market, allowing the thyroid scanning without any previous administration of radioactive iodine to the patient. The technique of fluorescence X-ray determination offers promises for the detection of trace elements in tissues and humors, as an alternate procedure to activation analysis.

The most commonly used probes are of Lithium–Germanium type, of relatively large size and cooled with liquid nitrogen. The miniature probes are considerably smaller, of the order of 1–2 mm dia. In this case, spacial resolution prevails over energy resolution. A recent application of a sub-miniature Si(Li) detector was used for the quantitative scanning of tissue slices, a procedure comparable to that used in radioautography.[1,2]

The development of Cadmium–Telluride probes, with a relatively good energy resolution at room temperature, rendered possible the performance of many radioactivity assays *in vitro* as well as *in vivo*.

CdTe has a relatively high atomic number (Cd = 48, Te = 52); consequently, its photoelectric efficiency, roughly proportional to Z^4–Z^5, is about hundredfold higher than that of silicon ($Z = 14$). Also, its low noise level (about 17 keV at room temperature) constitutes a desirable feature for the construction of medical probes.

This paper reports the use of the CdTe subminiature probe in experimental animals as well as in models simulating tissue slices containing one or two γ-emitting radionuclides. Also, some attempts to collimate the probe are being presented, some of them with the result of enhancing the actual count rate, by stimulating the X-ray fluorescence in a lead collimator.

Material and Methods

The present applications were carried out with a newly developed subminiature probe of Cadmium Telluride*. The semi-insulating CdTe crystal, of dia. 2·0 mm and a thickness of 1 mm, was housed in a cylindric steel can 15 mm long, of dia. 3·5 mm and a thickness of 0·13 mm. A bias voltage of 200 V was required for an efficient charge collection. The pulse shaping time constants for best energy resolution were:

$$\tau_{\text{integral}} = \tau_{\text{differ}} = 0\cdot8 \ \mu\text{sec}.$$

A multichannel analyzer with adjustable upper and lower discrimination levels was connected to the amplifier. Two adequate windows were selected and the accepted pulses were fed into separate scalers, especially in the experiments measuring two different radionuclides for the same sample.

(1) *Dual isotope scanning in a model*

The dual radioisotope mini-scanning procedure was carried out on a model containing point sources of ^{75}Se and ^{125}I of different strengths. Five holes of dia. 1 mm were drilled into a lucite plate, in a configuration as shown in Fig. 1a. The radionuclidic solutions were deposited and evaporated dropwise in

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* Kindly provided by SIMTEC, Montreal, Canada.