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Separation of yttrium-90 from strontium-90 via colloid formation

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Abstract No-carrier-added ^{90}Y was separated from ^{90}Sr via colloid formation of ^{90}Y in basic media. The mixture was passed through glass wool or membrane filter. The filtrate contained ^{90}Sr, while ^{90}Y was retained on glass wool/membrane filter. Yttrium-90 was extracted with 0.1 M HCl. Contamination of ^{90}Sr was <0.0001%. More than 98% labeling yield of ^{90}Y-EDTMP was confirmed by paper chromatography.

Keywords Strontium-90 · Yttrium-90 · Radiochemical separation · Colloid · Membrane filtration

Introduction

Radionuclide therapy using radiopharmaceuticals has been in existence for nearly 70 years and offers benefits to cancer patients, in particular, patients suffering from thyroid disorder. Radioisotopes of current interest for these applications include ^{90}Y ($T_{1/2}$ = 64 h) ^{131}I ($T_{1/2}$ = 8 days), ^{153}Sm ($T_{1/2}$ = 46.5 h), ^{166}Ho ($T_{1/2}$ = 26.8 h), ^{177}Lu ($T_{1/2}$ = 6.71 days), ^{186}Re ($T_{1/2}$ = 90.6 h), and ^{188}Re ($T_{1/2}$ = 16.7 h). Radioisotopes having short physical half-lives ranging from a few hours to a few days are quite useful for radionuclide therapy, and radionuclide generators represent an efficient means for making short lived therapeutic radionuclides more widely available throughout the developed and developing countries. A major advantage of generator produced radionuclides is that they have very high specific activity and can be used for the preparation of radiopharmaceuticals that target low density sites.

Yttrium-90 ($E_{\beta max}$ = 2.28 MeV) is a therapeutic radioisotope of enormous interest, and several established radiopharmaceuticals with this isotope are currently in use [1–4]. Yttrium-90 is a pure β^- particle emitter that can be prepared by the irradiation of ^{89}Y in a nuclear reactor or by the decay of ^{90}Sr ($T_{1/2}$ = 28.8 years) [5]. Strontium-90 is a major fission product and owing to the long physical half-life, a single batch can be used indefinitely. However, because of the long half-life, the technology required for fabrication of ^{90}Sr/^{90}Y generators is considerably different from that used for other generators such as the ^{68}Ge/^{68}Ga, ^{99}Mo/^{99m}Tc and ^{188}W/^{188}Re generator systems. The ^{90}Sr cannot be left in the column matrix for longer time, because of denaturation resulting from energy deposition of the high energy β^- particles from decay of parent and daughter radionuclides, which often results in ^{90}Sr breakthrough in the eluate. Yttrium-90 used for therapy should be of very high radionuclidic purity (>99.998%), as the contaminant ^{90}Sr is a bone seeker with a maximum permissible body burden (MPBB) of only 74 kBq (2 μCi). Currently, ^{90}Y is separated by using a combination of several separation techniques such as precipitation, solvent extraction and ion exchange chromatography, or by using ion selective resins [6–10].

In this paper we present the separation of ^{90}Y from ^{90}Sr via colloid formation of ^{90}Y and filtration by membrane filter and glass wool. Quantitative elution of ^{90}Y is achieved by 0.1 M HCl.

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Experimental

Materials and methods

All the chemicals used in the experiments were of analytical reagent grade and were purchased from E. Merck (Germany). Yttrium oxide powder and Strontium carbonate was product of Johnson and Mathey. Commercially available EDTMP was obtained from Dojin Laboratories (Kumamoto, Japan). Whatman 3 MM chromatography paper was used for ascending paper chromatography studies. Membrane filters were obtained from Millipore USA. Strontium-90 was purchased from Amersham UK.

Production of, strontium-85 and yttrium-90

Known Quantities of yttrium oxide/strontium carbonate targets were sealed in quartz ampoules and cold welded into aluminum cans. The irradiations were carried out inside the core of the 10 MW swimming pool type Pakistan Research reactor-I (PARR-I) for up to 120 h at a neutron flux of $\sim 1.5\times10^{14}$ cm^{-2} s^{-1}. The irradiated material was dissolved in concentrated hydrochloric acid, evaporated and taken in distilled water. These radionuclides were used for yield determinations.

Activity measurement

Yttrium-90 samples were measured in an ionization chamber (Capintec CRC 15R, USA) when used at the mega Becquerel (MBq) level and with a beta counter, when used at lower levels. The ^{90}Sr was also measured by beta counter. The ^{85}Sr ($T_{1/2} = 65.2$ days and γ peak 514 keV 99.3%) was measured by gamma spectrometry on an HpGe solid detector. The HpGe spectrometric system was calibrated using standard calibration radioactive sealed sources.

Filtration of ^{90}Y colloid by glass wool

Approximately 10 mCi of the radioactive solution was taken in 1 M HCl. The pH of solution was adjusted to 12 with concentrated NaOH and filtered slowly through a small glass wool column (1 cm $\varphi \times 4$ cm) The glass wool then washed with 0.1 N NaOH (15 mL). 0.1 M HCl was then slowly passed through glass wool column. The resulting filtrate was shown to contain only ^{90}Y as evidenced by a half-life measurement (Fig. 1).

Filtration of ^{90}Y colloid by membrane filter

Approximately 10 mCi of the radioactive solution was taken in 1 M HCl. The pH of solution was adjusted to 12 with concentrated NaOH and filtered slowly through a membrane filter (0.22 μm). The membrane filter then washed with 0.1 N NaOH (15 mL). 0.1 M HCl was then slowly passed through membrane filter. The resulting filtrate was shown to contain only ^{90}Y as evidenced by a half-life measurement. Similarly the chloride solution of ^{90}Sr in equilibrium with ^{90}Y was neutralized with NH_4OH and passed through Millipore membrane filter. Washing was performed by 1 M NH_4OH. Removal of ^{90}Y was achieved by 0.1 M HCl.

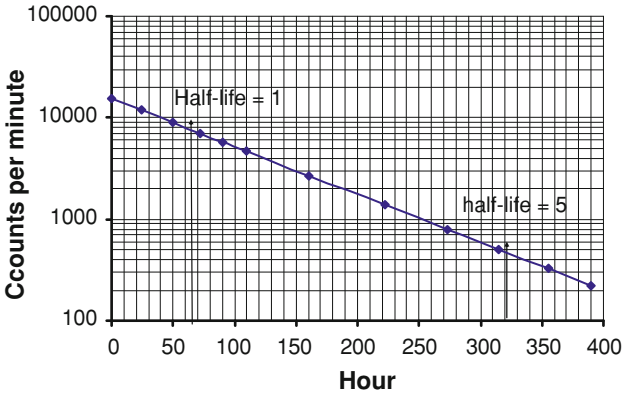

Fig. 1 Decay of Yttrium-90 (half-life = 64 h)

Preparation of ^{90}Y-EDTMP

EDTMP was dissolved in distilled water or dilute NaOH. ^{90}Y chloride solution was added to the EDTMP solution. The pH was adjusted to 8.

Paper chromatography

Five microlitre (μL) of the test solution was spotted at 2 cm from one end (bottom end) of Whatman 3 MM chromatography paper strips (14 × 2 cm). The strips were developed in pyridine/ethanol/water (1:2:4), dried, cut into 1 cm segments and the activity was measured. Some times strips were scanned by 2π Scanner (Berthold, Germany).

Results and discussion

The present investigation was planned to study the retention of carrier free ^{90}Y colloid in filtration process with glass wool column and membrane filters. The Millipore bacteria filter is effectively impermeable to particles of colloid size, and by the constant area and uniform pore size of the filters, it would be expected to obtain more quantitative results.

Various experiments were carried out for the separation of ^{90}Y from ^{90}Sr using colloid formation behavior of ^{90}Y in

basic pH range. When the acidic solution of $^{90}Sr/^{90}Y$ was treated with NaOH and passed through a small glass wool column, more than 95% ^{90}Y was retained on glass wool, which was further washed with 0.1 M NaOH. The ^{90}Y was extracted in 0.1 M HCl. Radionuclidic purity was determined by half life measurement (Fig. 1), which confirms the half life of 64 h of extracted isotope. The contamination of parent was less than 0.0001%. Table 1 shows the recovery of ^{90}Y from $^{90}Sr/^{90}Y$ mixture using a small glass wool column. The glass wool column was reused after washing with 30 mL of deionized water. Similarly when the colloid was passed through membrane filter more than 99% ^{90}Y was retained which was also recovered by 0.1 M HCl. The contamination of ^{90}Sr was less than 0.0001%. New membrane filter was used for each experiment. Similar experiments were carried out using reactor produced ^{90}Y and ^{85}Sr to determine the purity and yield of separation. Table 2 shows the recovery of ^{90}Y from $^{90}Sr/^{90}Y$ mixture using membrane filters.

Similar results were also obtained when first experiment was performed by neutralization of stock solution of $^{90}Sr/^{90}Y$ in HCl by NH_4OH. However when the stock solution of $^{90}Sr/^{90}Y$ in NH_4OH was again passed through Millipore filter paper or glass wool after 1 week equilibrium time, the retention of ^{90}Y was insignificant. The equilibrium mixture of $^{90}Sr/^{90}Y$ was acidified with HCl and again precipitated with addition of NH_4OH. The basic solution was passed through the Millipore filter or glass wool. More than 90% activity of ^{90}Y was retained, which was finally extracted in 0.1 M HCl. It was concluded that for recovery of ^{90}Y from ^{90}Sr by colloid formation, the acidic solution of $^{90}Sr/^{90}Y$ shall be freshly precipitated by NH_4OH. Presence of NH_4Cl has significant effect on the retention of ^{90}Y on membrane filter. After third neutralization cycle the retention of ^{90}Y colloid was very low, since NH_4Cl dissolves the $Y(OH)_3$.

On the other hand, in case of NaOH multiple separations of ^{90}Y from ^{90}Sr were performed successfully. The stock solution of ^{90}Sr kept in 0.1 NaOH can be used many times for the separation of colloidal ^{90}Y by filtering through glass wool or Millipore filter. Nearly 3 mL 0.1 M HCl was required for extraction of ^{90}Y from glass wool column or Millipore filter. Various separation techniques reported in the literature [6–10], use multiple steps to achieve high purity ^{90}Y needed for medical applications, while few are cumbersome and not suitable for remote handling. Ion exchange chromatography is frequently used ^{90}Y isolation technique, however due to radiation damage of resin, high level of ^{90}Sr breakthrough occurs. Inorganic adsorbent supported generator system gives low yields of ^{90}Y, while solvent extractions suffer contamination from organic components and incomplete separation from parent

Table 1 The recovery of ^{90}Y from $^{90}Sr/^{90}Y$ mixture using a small glass wool column

^{90}Sr (MBq/mCi)	^{90}Y growth period day	^{90}Y expected (MBq/mCi)	^{90}Y recovered (MBq/mCi)	^{90}Y recovered (%)
370.0/10.000	1	84.65/2.288	79.55/2.150	94
369.96/9.999	5	268.99/7.270	257.52/6.906	95
369.85/9.996	7	309.69/8.370	297.29/8.035	96
369.66/9.991	12	352.98/9.540	331.78/8.967	94
369.37/9.983	15	361.49/9.770	343.39/9.281	95
369.00/9.973	10	341.32/9.225	327.67/8.856	96
368.77/9.967	7	308.80/8.346	290.26/7.845	94
368.59/9.962	7	308.65/8.342	290.11/7.841	94
368.41/9.957	14	358.38/9.686	344.02/9.298	96
368.0/9.948	10	340.47/9.202	321.71/8.695	95

Table 2 The recovery of ^{90}Y from $^{90}Sr/^{90}Y$ mixture using membrane filters

^{90}Sr (MBq/mCi)	^{90}Y growth period day	^{90}Y expected (MBq/mCi)	^{90}Y recovered (MBq/mCi)	^{90}Y recovered (%)
370.0/10.00	5	268.99/7.270	260.92/7.052	97
369.85/9.996	7	309.72/8.371	303.51/8.203	98
369.70/9.992	10	341.95/9.242	335.11/9.057	98
369.44/9.985	15	361.56/9.772	347.10/9.381	96
369.07/9.975	5	268.32/7.252	260.29/7.035	97
368.96/9.972	10	341.28/9.224	331.04/8.947	97
368.70/9.965	7	308.69/8.343	302.51/8.176	98
368.48/9.959	7	308.54/8.339	299.28/8.088	97

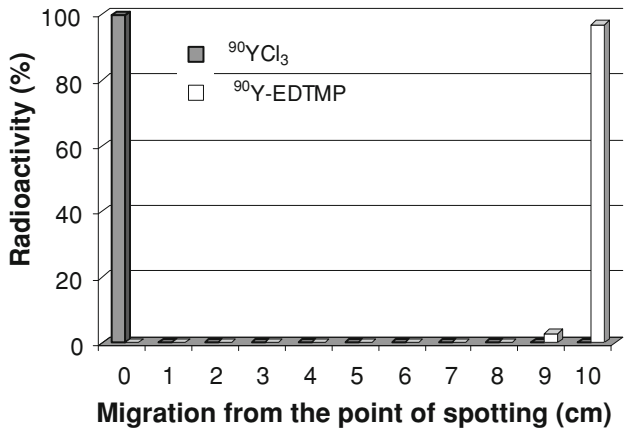

Fig. 2 Paper chromatography pattern of the ^{90}Y-EDTMP complex and $^{90}YCl_3$ in pyridine:ethanol:water (1:2:4)

radionuclide. ^{90}Sr/^{90}Y generators based on supported liquid membrane and electrochemical deposition require two stages to obtain highly pure ^{90}Y suitable for preparation of radiopharmaceuticals [6]. The method described in this paper gives high yields of ^{90}Y and it can easily be adopted by using spent Tc-99 m generator body for remote handling needed for safety of operator and environment [11].

It was also observed that the adsorption of ^{90}Y in basic solution was quite high when the ^{90}Sr solution was left in a glass vial for the growth of ^{90}Y. However it can be easily extracted after keeping it in boiling water bath for few minutes.

The separated ^{90}Y via colloid formation was used for the labeling of EDTMP. Labeling efficiency of ^{90}Y-EDTMP was more than 98%. Figure 2 show the chromatographic and behavior of ^{90}Y-EDTMP.

Conclusion

The separation of ^{90}Y from ^{90}Sr via colloid formation is simple, but not suitable for hospital radiopharmacy. Such procedure can be adopted in radiochemistry lab, where Curie level ^{90}Y may be separated and supplied to its users. Stock solution of ^{90}Sr can be kept in 0.1 M NaOH for growth of ^{90}Y colloid, which can be retained on glass wool or membrane filter and finally extracted by using 0.1 M HCl for labeling purposes.

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