^{95}Zr AND ^{124}Sb IN ^{99}Mo-^{99m}Tc GENERATORS

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Radionuclide impurities in ^{99}Mo-^{99m}Tc generators have been recognized. In 1964 Smith (*1*) reported the presence of ^{99}Mo, ^{103}Ru, and ^{131}I in the eluant of generators using fission-produced ^{99}Mo. Smith observed that most of these radionuclidic impurities could be removed by washing the column. In 1969 Crosby (*2*) found ^{186}Re in several samples of "instant" ^{99m}Tc-sodium pertechnetate. Rhenium-186 levels were found to be equivalent to 0.1% of the injected dose to the patient (*2*). All radiopharmaceutical suppliers recommend that the eluate be assayed for ^{99}Mo content. No product should be used if the ^{99}Mo content is greater than 1 μCi/mCi^{99m}Tc, and no patient may be given any more than 5 μCi ^{99m}Mo/ administered dose.

While ^{99m}Mo can be produced as a fission product, the majority of generators apparently use ^{99}Mo produced by an n,γ irradiation reaction. A ^{99}Mo supplier records low levels of ^{92m}Nb, ^{187}W, ^{95}Nb, ^{86}Rb, ^{124}Sb, ^{65}Zn, ^{134}Cs, and ^{60}Co activity (*3*). Concentration of these radionuclidic impurities is less than 0.1% of the ^{99}Mo at the time of production.

In the course of a routine quality-control program, eluates of the generator purchased for hospital service were examined when insignificant amounts of ^{99m}Tc activity remained. It was expected that this study could show the degree of ^{99}Mo breakthrough and possibly could show identifiable quantities of other radionuclides. We found significant and unexpectedly high activity in the range of 0.250, 0.600, and 0.765 MeV in this generator. As a result of these findings, the survey was extended to include 20 generators from Supplier I (our supplier), eight generators from Supplier II, one generator from Supplier III, and two generators from Supplier IV.

The source of activity was identified in the following manner:

By pulse-height analysis. Using a Nuclear-Chicago RIDL Model 24, 400-channel analyzer connected to a 2 × 2-in. NaI(Tl) crystal (calibrated with 0.662-MeV peak of ^{137}Cs standard) the eluates were compared. Ranges of 0–1 MeV and 0–2 MeV were examined. Counting time, typically, was 20 min. All spectra of samples from Supplier I contained the peaks at approximately 0.250, 0.600, and 0.760 MeV. The other suppliers' samples did not display these peaks (Fig. 1). By splitting the screen and superimposing two spectra, two samples could be compared. Spectra peaks were normalized. Minor peaks could be seen at 0.300, 1.14, and 1.34 MeV in random samples from all suppliers.

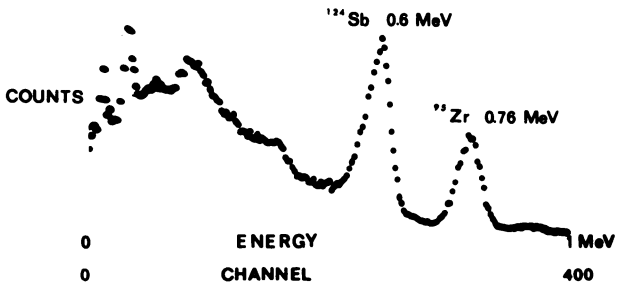

FIG. 1. Spectrum of activity seen in eluates from generators of Supplier I 3 days after elution showing contaminants.

By half-life. Half-life determinations were made in a 1½ × 3-in. NaI(Tl) well crystal. The half-lives of the activity appear to be between 60 and 70 days. Two samples containing impurities, which were eluted 3 months apart, were counted to 1,000 counts at the 0.600-MeV peak. The two curves again could be superimposed.

By relationship to aluminum breakthrough. Aluminum determinations were performed on several

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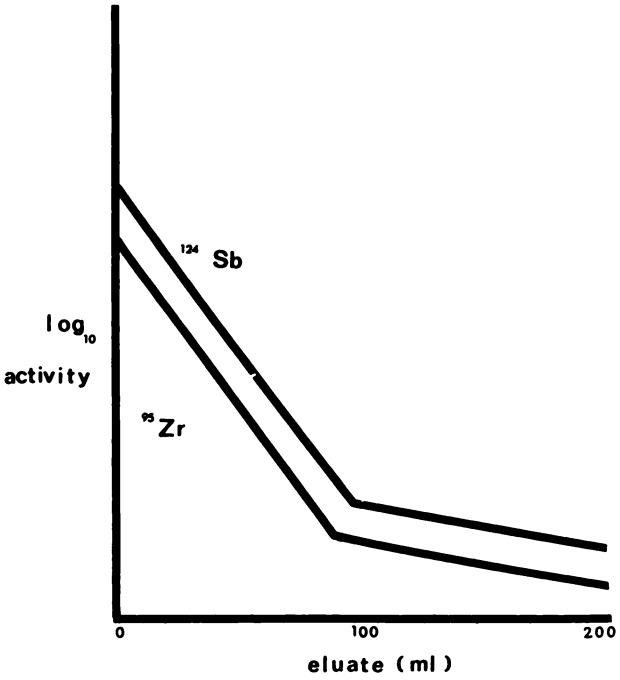

FIG. 2. Zirconium-95 and ^{124}Sb levels after repeated elutions of generator.

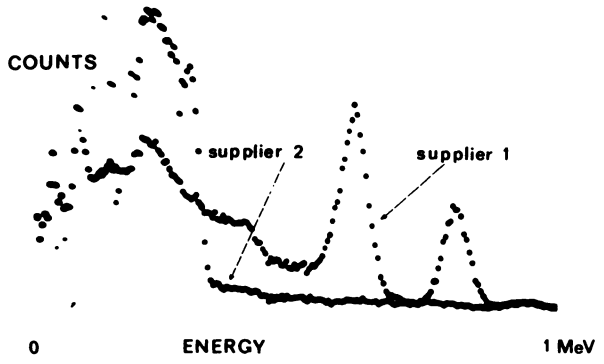

FIG. 3. Comparison of spectral characteristics of eluants from generators of Suppliers I and II.

eluates using the colorometric analysis of Neisler Laboratories (*4*). The breakthrough from eluates in generators of Supplier I ranged from 3.1 to 19.0 μg/ml of aluminum. Twenty-three eluates were studied. The activity in the eluates at the peaks did not bear any relationship to the amounts of aluminum in the sample. An eluate of a generator from Supplier II, which contained no impurities, had an aluminum breakthrough of 21.0 μg/ml.

By activities related to generator washing. A fresh, 200-μCi generator from Supplier I was eluted with eight, 25-ml aliquots of 0.9% sodium chloride. Each aliquot was assayed for ^{95}Zr and ^{124}Sb by pulse-height analysis. The levels of both radionuclides dropped with each elution. There was a progressive decrease in activity through each washing. The decrease was exponential through the first four washings, giving a steep slope on semilog paper. The remaining four washings contained little activity, and there was little variation between the eluates (Fig. 2).

By body retention. Body retention of the radionuclides was studied using the whole-body counter. At this time, the maximum administered activity appears to be between 0.1 and 5 μCi.

Peaks with energy of 0.250, 0.600, and 0.765 MeV and a half-life of 60–70 days must be considered due to radiocontaminant. Initial analysis suggested that the impurity might be ^{95m}Tc. Its half-life of 61 days and energies of 0.204, 0.584, and 0.780 MeV would support this hypothesis. However, after consultation with suppliers, it was felt that the ^{99}Mo used in at least three suppliers' generators is produced at the same location. One of these three was Supplier I. It would be difficult to explain the presence of ^{95m}Tc radiochemically. The spectra could also be produced by the decay of two nuclides of the same or similar half-lives. The peaks could be those of ^{95}Zr and ^{124}Sb.

Zirconium-95 has a half-life of 65 days and ^{124}Sb has a half-life of 61 days. The energies of zirconium are 0.724 MeV and 0.756 MeV. The energy of antimony is 0.600 MeV. The peak in the 250-MeV range could relate to ^{95}Nb (0.235 MeV), the daughter radionuclide of ^{95}Zr.

If ^{95}Zr and ^{124}Sb were bound to the aluminum oxide column, the levels of each in the eluants should be proportional to the aluminum breakthrough in the eluates. This should also hold true when a single generator is washed. No relationship between the aluminum breakthrough and the ^{95}Zr and ^{124}Sb could be seen in either case. The exponential nature of the levels of contaminant after successive elutions suggests that the ^{95}Zr and ^{124}Sb are loosely held in the column and merely removed with the eluate. One hundred milliliters of eluant lowers the contaminant to background levels (Fig. 2). The comparison between the two suppliers' eluates can be seen in Fig. 3. No contaminant appears in the eluate of Supplier II. Both suppliers' samples were counted under identical conditions.

DISCUSSION

It is reasonable to assume that the various manufecturers prepare their columns in different manners. Presumably Supplier I has not washed the columns or chemically separated the impurities as completely as the other three suppliers.

Although ^{95}Zr and ^{124}Sb may be demonstrated in

patients after administration of 10 mCi ^{99m}Tc-sodium pertechnetate used for brain scanning, it is too early to assess the significance of these contaminants. Before this can be determined, accurate measurement of the organ distribution and effective half-life of each radionuclide must be known along with the amount of each in the body.

Figure 3 shows that the two peaks may easily mask the ^{99}Mo 0.740-MeV peak, making its assay (using the method suggested by Supplier I) difficult to interpret. The potassium ethyl xanthate colorimetric assay avoids the ambiguity found with pulse-height determination. This fact becomes important in quality control.

The individual radiopharmacy is responsible for the quality of the radiopharmaceutical used. The results of this study suggest an extension of the customary parameters of quality control to include analysis of trace-metal levels. It would be reasonable to expect that the user should have data on these trace contaminants, either through his own work or through information provided by the supplier. If the user accepts the supplier's data, he should demand that the trace-contaminant level be stated clearly.

CONCLUSIONS

Zirconium-95 and ^{124}Sb have been reported in the eluates of a supplier's ^{99}Mo-^{99m}Tc generator. These contaminants do not appear in three other suppliers' generators included in this study. The contaminants may be washed off this column with about 100 ml of eluant. The biological significance of these contaminants is unknown.

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