The ^{234m}Pa Generator

Aspects of Milking the "^{234}Th Cow"

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Principle of Nuclide Generators

Nuclear medical diagnosis (in vivo as well as in vitro) has gained much in importance over the last years. Only nuclides emitting a γ-component are applied in investigations in vivo because this radiation can be easily detected at the surface of the patient's body using a γ-scanner. In order to keep the radiation dose of the patient as low as possible, nuclides with a short biological and physical half-life are used (*1–4*).

The application of isotope generators is becoming more common in medicine as they provide ready availability of such radiodiagnostics. A long-lived parent nuclide is immobilized on an inert carrier (ion exchange resin, aluminum oxide) and its daughter is "milked" from it with isotonic common salt solution (Fig. 1) when needed.

Some suitable generator systems are compiled in the table. At the beginning of this century, Crookes (*5*) discovered that the radioactivity of uranium salt seemed to "vanish" after performing a certain precipitation procedure. As is known today (*6*), he removed the highly active granddaughter protactinium, the hard β-radiation of which was the only one that could be detected by his method (radioautography).

The uranium, however, *regained* activity after some time, while the separated material continued to decay. Crookes' discovery was the first observation of a parent/daughter system. Rutherford's mathematical formulation of this phenomenon (*7, 8*) was so successful, that he bore it on his coat

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Generator Systems Used in Nuclear Medicine

Mother Nuclide	$T_{1/2}$	Daughter Nuclide	$T_{1/2}$	Radiation of the Daughter Nuclide (Energy in MeV)	
$^{68}_{32}$Ge	280 d	$^{68}_{31}$Ga	68 min	β^+ 1.88;	γ 1.10
$^{87}_{39}$Y	80 h	$^{87m}_{38}$Sr	2.8 h		γ 0.388
$^{90}_{38}$Sr	27.7 y	$^{90}_{39}$Y	2.6 d	β^- 2.27	
$^{99}_{42}$Mo	67 h	$^{99m}_{43}$Tc	6 h	β^- 0.29;	γ 0.140
$^{113}_{50}$Sn	118 d	$^{113m}_{49}$In	1.7 h		γ 0.393
$^{115}_{48}$Cd	2.3 d	$^{115m}_{49}$In	4.5 h		γ 0.335
$^{132}_{52}$Te	3.2 d	$^{132}_{53}$I	2.3 h	β^- 0.7–2.12;	γ 0.58–2.20

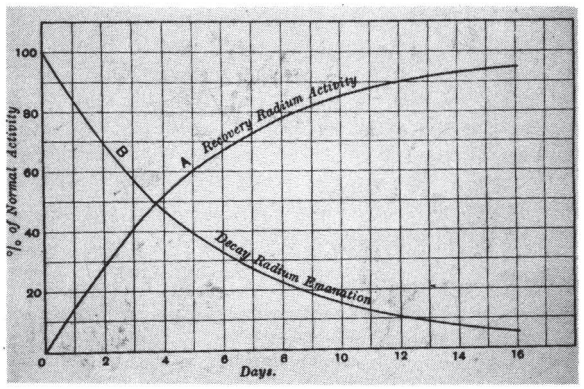

Figure 2. Decay and regeneration of a daughter after mother/daughter separation.

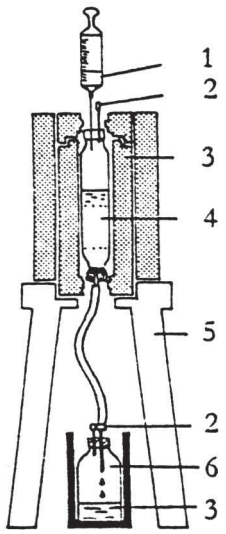

Figure 1. Schematic view of a generator system: 1, solvent for elution; 2, air cannula; 3, lead screening device; 4, generator; 5, stand; 6, vessel for eluted radioactive daughter substance.

Figure 3. Rutherford's coat of arms.

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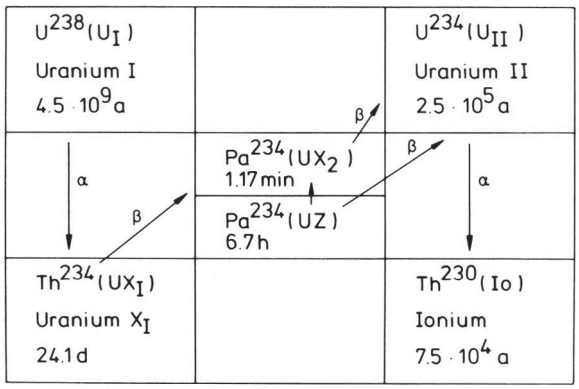

Figure 4. First members of the $4n + 2$ decay series.

of arms when he became Lord Nelson (Figs. 2 and 3). This coat of arms, composed of rather peculiar details (e.g., the kiwi on top alluding to Rutherford's New Zealand home), demonstrates his sense of humor and imagination. The shield is divided by two intersecting curved lines. A nuclear chemist will notice that this is a stylized version of the shape of the activity curves of mother and daughter products. Radiochemistry on a coat of arms is a novelty in heraldry, indeed.

The Radiochemical System U-238, Th-234, Pa-234

When looking for an easy-to-handle system that satisfies the condition for secular equilibrium, one finds that the first members of the $(4n + 2)$ series are both easily obtainable and unproblematic as far as security regulations are concerned (Fig. 4). In the following experiments the nuclides in question are separated by a classical method as well as by means of an ion exchanger. As can be derived from the half-lives, Th-234 ($T_{1/2}$ = 24.1 d) as mother and Pa-234m ($T_{1/2}$ = 70 s) as daughter form a convenient nuclear generator. Because of the very low activities involved, there is no radiation hazard. One must, however, bear in mind that uranium and its decay products have to be treated as toxic chemicals. All operations should be carrried out in a tray covered with tissue to avoid contamination. The uranyl nitrate used in the experiments should not have been purified for at least 6 mo, so as to contain a sufficient amount of decay products.

Experiment 1: Separation by Co-precipitation

About 1 g of commercial uranyl nitrate is dissolved in 5–10 ml H_2O, and 3–4 drops of a 3% solution of $FeCl_3$ are added. The activity of the solution is measured in a liquid counting vessel. One adds a solution of ammonium carbonate (0.25 *M*) drop by drop to the stirred solution until the precipitate formed has nearly dissolved again. The solution is then filtered (keep the filtrate), the precipitate dissolved in as much HCl (2 *M*) as the original volume, and its activity is measured in a liquid counter. The filtrate is counted as well. A plot of the obtained activities versus time will result in growth and decay curves similar to those in Rutherford's coat of arms. The precipitation with iron(III) chloride and ammonium carbonate is the above-mentioned procedure, with which Crookes (*5*) believed to have "deprived" uranium of its activity.

Experiment 2: Solvent Extraction and Identification of Th-234

(Note: Solvent extraction plays a vital role in nuclear fuel processing, e.g., the PUREX process).

Uranyl nitrate hexahydrate is soluble in ether because the compound loses some of its crystal water to form species of the formal type $UO_2(NO_3)_2 \times (6 - x)H_2O \; x Et_2O$ in the organic solvent. Th-234 can be enriched in the aqueous phase, the volume of which should be kept very low as the uranyl ion itself has a high affinity to water. The Th-234 can be characterized by determining its half-life.

Procedure: About 3g of uranyl nitrate hexahydrate are shaken in a separating funnel with about 50 ml of ether dried over $CaCl_2$ until a yellow solution is obtained (do not forget to deaerate the funnel). The counting rate at the bottom of the funnel and a few centimeters higher is measured from the outside by means of a Geiger counter. The results obtained differ only slightly, due to the geometry of the funnel. Now one drop of water is added, and the mixture is shaken again. After allowing it to settle the counting rates are determined again at the same places as before. As long as no considerable difference from the previous results is detected, more water is added drop by drop. Usually a *drastic* effect will be observed after adding about 3 drops of water: nearly all the activity is found in the barely visible aqueous phase, which contains practically all Th-234 plus a small amount of U-238. The Th-234 is well suited to demonstrate the study of physiological processes in plants using radioautography. Good results have been obtained with *Impatiens sultani* (Busy Lizzie). The aqueous phase from the separating funnel is carefully evaporated to dryness using an IR lamp. The residue is covered with a thin plastic foil (Mylar) and fixed at a distance of about 1 cm from a Geiger counter. The most efficient way to determine the half-life of Th-234 (which is about 1 mo) is to feed the output of the Geiger counter to a ratemeter, which in turn is connected to a chopper bar recorder. Using a time switch this equipment is turned on for 30 min every day.

Decay of Pa-234

In the previous experiments we did not stress the fact that the β-radiation of Th-234 has low energy (0.19 MeV) and is absorbed even by thin layers of glass. In contrast, the counting efficiency for the more penetrating radiation of its daughter Pa-234m (2.28 MeV) is high. Thus when determining the half-life of Th-234 (as in the previous section), one really measures the radiation of Pa-234m in equilibrium with its mother.

In 1921 Otto Hahn showed by means of chemical methods that the Pa in the $4n + 2$ decay series occurs in two isomeric forms—Pa-234 (UX_2) and Pa-234 (UZ) (*9*). This was the first known case of nuclear isomerism. As we know now, nearly 100% of the Pa-234m (which is in a metastable excited state) decays directly to U-234 (U_{II}) with a half-life of 1.17 min. However, a small percentage of Th-234 (UX_I) decays to the ground state of Pa-234 (UZ), which in turn forms U-234 (U_{II}) with a half-life of 6.7 h.

Model Generator

We shall describe the setup and the way of working of an easy-to-build Pa generator that can be run with 1–3 g of uranyl salt.

Setup of the Generator

A solution of uranyl nitrate is poured on a cation exchanger previously loaded with Na^+, so that the uranium and its daughter products (Th-234, Pa-234m, Pa-234, U-234) are fixed on the column. (In radioactive equilibrium with 1 g U-238 there are $1.42 \cdot 10^{-11}$ g Th-234 and $3.96 \cdot 10^{-16}$ g (0.4 fg) Pa-234m.) Since uranium forms a soluble stable chloro complex ($UO_2Cl_4^{2-}$), it can be removed selectively, whereas its daughters remain fixed on the column. Pa-234m (together with Pa-234 which is not relevant for the experiment) can be eluted with citrate solution. At least 10 min should elapse before the next elution takes place, so that a sufficient amount of protoactinium can form again. The decay time of the mother nuclide (Th-234) being 24.1 d, a generator can be used up to 3 mo.

Procedure:

A: Dowex 50 W-X8 ion exchanger (commercial grade) is soaked overnight in 1 *M* NaOH and introduced into the ion exchange column which, at its lower end above the stopcock, contains a glass wool wad or a sintered glass frit.

B: The column is washed with distilled water until a pH of 7 is reached.

C: 3 g of uranyl nitrate, dissolved in 10 ml of H_2O, is poured onto the column. The stopcock is turned so that the liquid is allowed to pass very slowly through the column.

D: After some 25 min the uranium is eluted with about 200 ml of 2 *M* HCl. At the end of this procedure the pH of the last 2–3 ml of the eluate is increased with sodium acetate, then 1 ml of 5% potassium hexacyanoferrate(II) is added. The solution should not turn brown (which would indicate the formation of $K_2UO_2[Fe(CN)_6]$, because of uranium tailing).

E: After this test for uranium is negative, the hydrochloric acid is eluted by washing the column with about 50 ml of distilled H_2O (control with pH paper). The column is now ready for use.

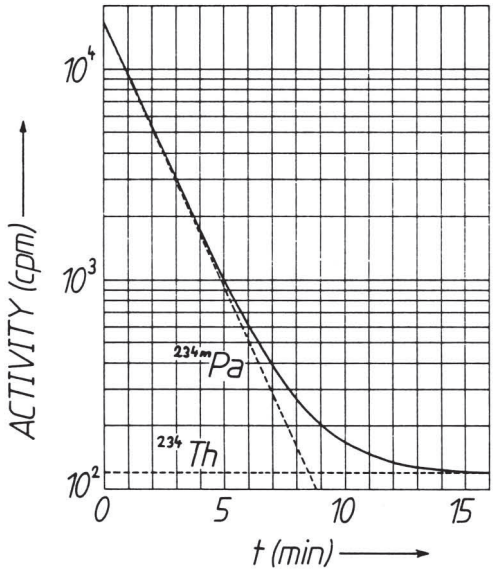

Figure 5. Half-life of Pa-234.

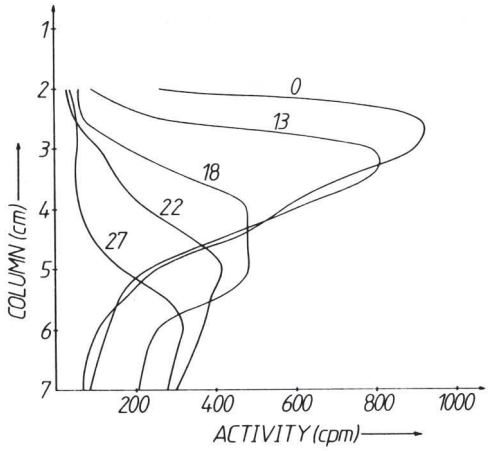

Figure 6. Distribution of activity on the ion-exchange column as a function of the number of elutions.

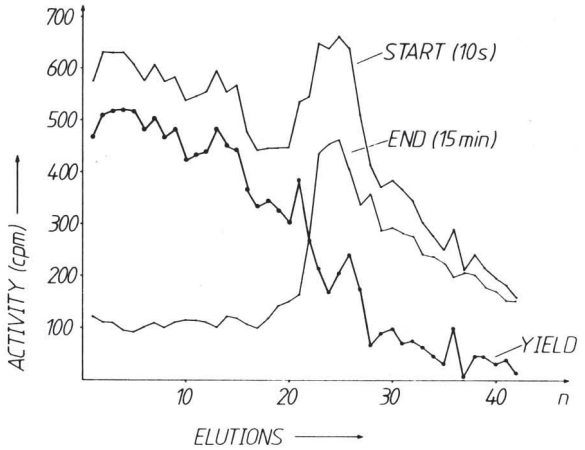

Figure 7. "Milking behavior" of the model generator (initial and residual activity and yield of Pa-234m).

Elution and Identification of Femtogram Amounts of Pa-234

A 5% solution of citric acid in water is prepared and a pinch of salicylic acid is added for conservation. The mixture is brought to pH 2.5 with ammonia. As the half-life of Pa-234 m is very short, the elution must take place as fast as possible. Therefore, a stopper pierced with a small glass tube is put on the upper end of the column. The glass tube is connected to either a pressurized air inlet or a rubber bulb. By applying suitable pressure the time needed for elution can be shortened to a few seconds. The volume of the eluate should be such as to fill the liquid counting vessel.

Measurement is started immediately after elution and the number of pulses counted is recorded every 15 s for 6 or 7 min. After 10 min the residual activity is determined. This activity is then subtracted and the resulting values are plotted versus time (Fig. 5). The half-life of Pa-234m can be determined graphically to be about 70 s.

Milking Behavior of the Generator

In order to examine the properties of the model generator over a longer period of time, a series of experiments was carried out in which the generator was milked until the parent substance was nearly completely eluted and, as a result, the yield of Pa-234m became very low. At the same time the downward movement of the Th-234 band in the column could be monitored using a Geiger counter. A typical example is described below.

Procedure: A Geiger counter is placed so that it directly touches the column (the glass of which should be as thin as possible). The distribution of activity is measured in steps of 1 cm alongside the contents of the column. Curve 0 of Figure 6 represents the activity distribution after loading the column with uranyl nitrate (see Setup of the Generator above); this profile is hardly altered when the uranium is washed out. After this up to 42 elutions of Pa-234m have been performed, with a minimum regeneration time of 15 min. The distribution of activity is measured several times between the elutions. The active zone can be seen to spread out and move downwards (see Figure 6). The yield of Pa-234m is also determined as a function of the number of elutions. It is (approximately) calculated as the difference between the initial and the residual activity (after 12 min, corresponding to 10 half-lives of Pa-234) of the eluate. As can be seen from Figure 6, the Th-234 is not completely immobilized on the column, but slowly moves downwards and is eventually washed out. At this state, the lifespan of the generator is over, since the yield approaches zero. The big increase of the initial and residual activity (but not the yield) after some 20 "milkings" (see Fig. 7) occurs when the Th-234 band has reached the bottom of the column and is partly eluted together with its daughter. Intense "milking" showed that Pa elution can be repeated for about two dozen times in a period of 2 or 3 d until the "cow" gets "exhausted." In the experiments stretched over longer periods of time the half-life of the parent nuclide becomes an additional limiting factor. Satisfying results can be obtained for up to one month with one elution per day.

The life-span of the generator is shortened if the ion exchange resin is moved (i.e., mixed) when working with the column. Using longer and thinner columns instead of short and thick ones (with the same volume) results in a longer life-span of the generator.

It should be added that the rapid regeneration of Pa-234m on the column after each elution cannot be measured quantitatively with our simple equipment.

We hope to have shown again (as in (*10*) and (*11*)) that some of the oldest concepts of radiochemistry have not lost their importance in regard to practical applications as well as to instructional demonstrations.

Acknowledgment

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