PRODUCTION OF RADIOISOTOPES

BY 1.5M CYCLOTRON AND THEIR UTILIZATION

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ABSTRACT

Radioisotopes characterized by nuclear property and uses can be produced on the accelerator, especially those playing an important role in scientific researches and biomedical uses. The status of Radioisotopes produced by 1.5m cyclotron and their applications in our institute are summarized in this paper. The details of preparation and the results of use for radioactive sources, radiochemicals, radiopharmaceuticals of ^{57}Co, ^{109}Cd, ^{68}Ge- ^{68}Ga, and ^{167}Tm are given respectively.

INTRODUCTION

Cyclotron-produced neutron-deficient radioisotopes are playing an increasingly important role in radioisotope applications. They are produced via charged particle reactions and decay by emitting positron or -ray following electron capture. Because the resultant nuclide is frequently different from the target one, the product of carrier-free and high specific activity can be obtained with several methods of the radiochemical separation, ion-exchange and solvent-extraction chiefly. Cyclotron isotopes, as tracers, radioactive sources, labelled compounds and radiopharmaceuticals have extensively been applied to the researches on biomedicine, chemistry, physics, industry and agriculture. The building of small cyclotron for medical use and the preparation of short-lived radiopharmaceuticals are potential and brand -new development in the field of nuclear medicine recent decade.

More than ten radioisotopes, including ^{7}Be, ^{22}Na, ^{54}Mn, ^{55}Fe, ^{56}Co, ^{57}Co, ^{68}Ge, ^{85}Sr, ^{109}Cd, ^{167}Tm, and ^{207}Bi etc. were investigated and produced by 11 MeV p, 23

Table 1. Radioisotopes produced by 1.5m cyclotron at Lanzhou

Radio -nuclide	$T_{1/2}$	Decay	Gamma keV	production reaction	projectile energy,MeV	major uses
^{7}Be	53.3d	EC(100)	478(10)	$^{6}Li(d,n)^{7}Be$	22	radiotracer
^{22}Na	2.6d	β^+(90.5)	1274(99)	$^{24}Mg(d,\alpha)^{22}Na$	22	positron source soil tracing
^{54}Mn	312.5d	EC(~100)	834(100)	$^{56}Fe(d,\alpha)^{54}Mn$	14	γ-ray source
^{55}Fe	2.7a	EC(100)	5.9x	$^{55}Mn(d,2n)^{55}Fe$	15	x-fluorescent analysis
^{56}Co	78.5d	EC(77.5) β^+(23.9)	846(100)	$^{56}Fe(d,2n)^{56}Co$	22	radiotracer
^{57}Co	270d	EC(100)	122(85.2)	$^{56}Fe(d,n)^{57}Co$	7.5	Mössbauer source nuclear medicine
^{68}Ge	287d	EC(~100)	no	$^{66}Zn(\alpha,2n)^{68}Ge$	35	^{68}Ge-^{68}Ga generator
^{85}Sr	65.2d	EC(100)	514(100)	$^{85}Rb(d,2n)^{85}Sr$	22	scanning for bone
^{109}Cd	453d	EC(100)	88(4)	$^{109}Ag(d,2n)^{109}Cd$	12.8	x-fluorescent source
^{167}Tm	9.25d	EC(100)	208(41)	$^{165}Ho(\alpha,2n)^{167}Tm$	40	scanning for bone and tumour
^{207}Bi	30a	EC(~100)	567(98)	$Pb(d,xn)^{207}Bi$	22	source of internal electron conversion

MeV d, 48MeV α and 19.2 MeV HD^+ beams from our 1.5m cyclotron at Lanzhou (see table 1). Radioactive sources with specific property, such as mössbauer source, x-fluorescent source, γ-ray reference source, and radionuclide generator, radiopharmaceuticals were prepared using their isotope products and they were provided for user who had urgent need for them. Since 1.5m cyclotron can be used to accelerate charged particles to higher energy and greater beams can be acquired in internal target position, production of longer-lived isotopes are desirable and can bring the cyclotron into full play.

Production and application of four radioisotopes of great importance are described as follows.

I. Cobalt-57[1,2]

Radioisotope ^{57}Co ($T_{1/2}$=270d, EC 100%, γ122keV,85%) is most important one in cyclotron-produced isotopes. It was made by use of nuclear reaction $^{56}Fe(d,n)\ ^{57}Co$ on natural iron target. By controlling the energy of incident particle≤7.5MeV, radionuclidic purity of ^{57}Co product was about 98% while simultaneous radioimpurities ^{58}Co and ^{60}Co were below 0.01%, 2% respectively. The radiochemical separations involving Fe, Co, Mn, Cu were achieved by extraction of Fe from target materials with TBP or isopropylether and further anion-exchange process of the microamount element in HCl system(see Fig. 1). Radioisotope ^{54}Mn, produced by $^{56}Fe(d,\alpha)\ ^{54}Mn$ reaction, as by-product was recovered in the process. The contents of stable chemical impurities Fe, Co, Cu, were tens micrograms in the ^{57}Co product from an irradiated target respectively. The overamount of ferromagnetic impurities in the product has serious effects on the quality of Mössbauer source but there is no any effect on other applications.

Radioisotope ^{57}Co has extensive uses and in our laboratory it has been applied to preparation of radioactive sources and researches on nuclear medicine. (see table 2).

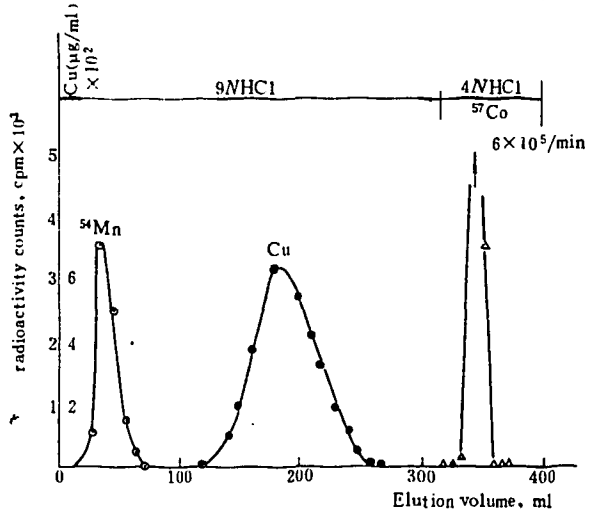

Fig. 1. Elution curve of ^{54}Mn-Cu-^{57}Co
Anion-exchange resin, type 717, 100-120 mesh
Size of column: φ12×300,mm
Flow rate: 0.5-1ml/min

Table 2. Uses of ^{57}Co products

Preparation	Performance	Application
^{57}Co-Mössbauer source	activity: 5-10 mCi line width: 0.104-0.114 mm/s drop: 9% Recoilless fraction: 0.6	analyzing chemical structure of iron and iron-containing material
^{57}Co-fluorescent source	activity: 10 mCi dimension:φ10×5,mm radioactivity area: 6mm	for analysis of uranium and thorium
large area source	activity: 0.5 mCi radioactivity area: φ320mm unconsistency: 10%	medical use
Reference source of energy series	activity: 0.1 mCi	calibering NaI(Tl) and Ge(Li)-spectrometer
^{57}Co-Bleomycin	Bleomycin solution, droping and stiring with ^{57}Co adjust pH to 6-7 Radiochemical purity: 99.5%	for diagnosing cancer

II. Cadmium-109[3,4]

Radioisotope ^{109}Cd of 453 days decays via EC to ^{109m}Ag and emits 22keV KX-ray and 88keV γ-ray of ^{109m}Ag, later productivity is about 4% of that of former. It is suitable for x-fluorescent analysis of molybdenum mineral etc. and worksite evaluating of petroleum exploiting when it equipped with radioactive densimeter. Carrier-free ^{109}Cd was obtained via ^{109}Ag (p,2n) ^{109}Cd reaction on the cyclotron and by completed anion-exchange technique in HBr system (see Fig. 2). The difference between the distribution coefficients of the complex anions of Cd and Ag on the column in 6.8N HBr system is so large that Cd complex anions are absorbed on it firmly while Ag complex anions are passed through rapidly. On the bass of this principle both Cd and Ag can reach a good quantitative separation. The recovery of ^{109}Cd radioactivity came to 99% by this process and no radioimpurities existed in γ-spectrum of ^{109}Cd product. We have prepared x-fluorescent sources using these products and provided for some universities and oil fields. The size of the source was φ10×5mm, the diameter of radioactivity area: 6mm, the thickness of Al window: 80μm, intensity: 1 - 3mCi.

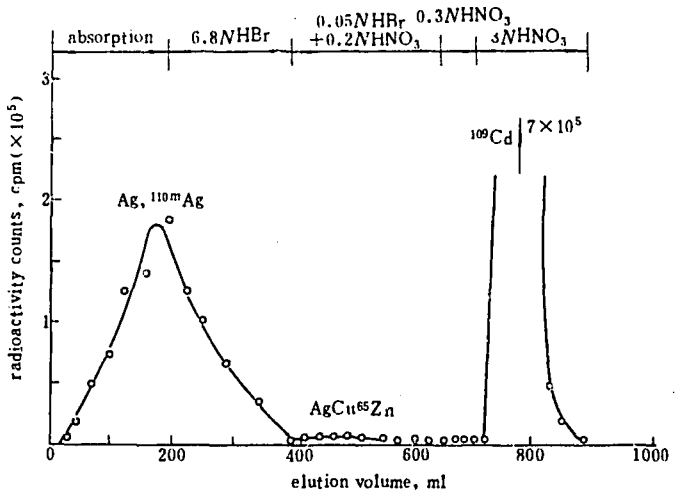

Fig. 2. Separation of ^{109}Cd from 3g irradiated Ag target
Anion-exchange resin, type 717, 100-200 mesh.
Size of column: φ10×400mm
Flow rate: 1-3ml/min

III. ^{68}Ge- ^{68}Ga generator[5-7]

^{68}Ge- ^{68}Ga radionuclide generator consists of parent ^{68}Ge ($T_{1/2}$=287d,EC 100%) and daughter ^{68}Ga ($T_{1/2}$=68.3min,90.5%,γ1, 077MeV,3%) and is growing in importance because of the applicability of ^{68}Ga as a lable for radiopharmaceuticals to be used in conjuctions with positron emission tomography. The combinations of half life provide a generator with a potential shelf life of about 2 years, which permits ^{68}Ga elutions every 3 - 5 hours. The generator is also used as a source of pure positrons in positron annihilation spectroscopy.

The production of parent ^{68}Ge was realized by α bombardment of Zn targets of high purity via $^{66}Zn(\alpha,2n)\ ^{68}Ge$ reaction on our cyclotron. The radiochemical separation of ^{68}Ge was brought to success using extraction process with CCl_4 in HCl system after the solution of irradiated Zn target and radiochemical recovery of ^{68}Ge was about 90% (see Fig. 3). The generator was prepared by ^{68}Ge adsorption on Al_2O_3 column when the product solution of lower acidity passed through it at a slower rate and percentage of the adsorption was above 90%. Fig. 4 shows the diagram of device of the generator.

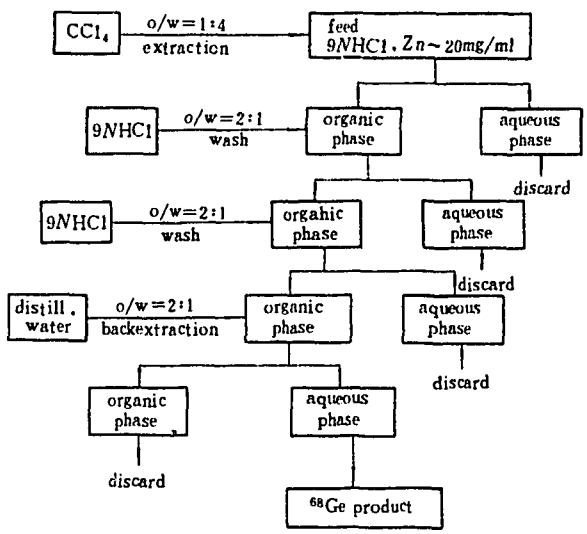

Fig. 3. The diagram of separation process of ^{68}Ge

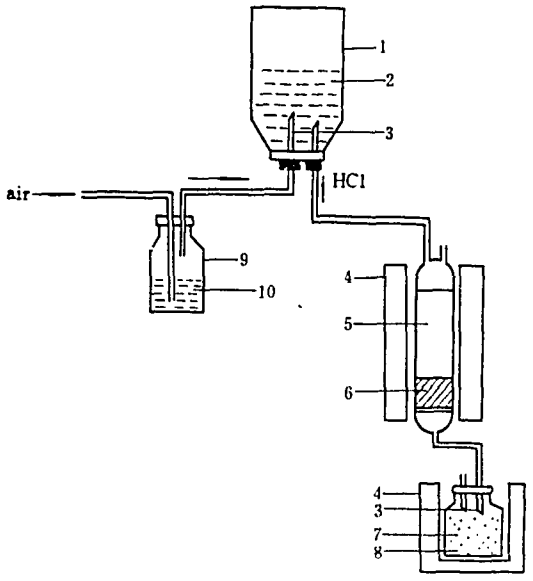

Fig. 4. The diagram of device of ^{68}Ge- ^{68}Ga generator
1. Eluant bottle 2. Eluant (HCl)
3. Injection pin 4. Lead protector
5. Glass column 6. Al_2O_3 bed
7. Penicillin bottle 8. ^{68}Ga eluate
9. Air sterilizer 10. $KMnO_4$ solution

The principle parameters of the generator investigated by us are as follows:

elution solution: 0.05-0.15HCl
elution volume: 5ml
elution rate: 1-6ml/min
elution yield of ^{68}Ga; 40-50%
chemical form of ^{68}Ga eluate: ionic
breakthrough of ^{68}Ge: 10^{-5}
Al content of ^{68}Ga eluent:
in range of 20-30μg/ml
Total intensity of ^{68}Ge radioactivity on column:
to the amount of millicuries.
sterile, pyrogen-free.

The generator was installed in a hospital at Shanghai and ^{68}Ga eluate was converted into ^{68}Ga-citrate and ^{68}Ga labelled colloid and in vivo-distribution of ^{68}Ga radioactivity in normal and tumour-bearing mice and viscera scanning in liver of rabbit and dog were investigated. The results showed higher concentration of ^{68}Ga radioactivity in tumour and bone of mice thirty minutes after injection and scanning of animal visceras had clear outline and even distributions of radioactivity.

IV. Thulium-167[8-10]

Radioisotope ^{167}Tm(T=9.25d,EC 100% γ208keV,41%) is a useful bone and tumour scanning agent in nuclear diagnosis medicine. ^{167}Tm of high radionuclidic purity was produced by 40 MeV α particle bombardment on metallic Ho target via ^{165}Ho (α,2n) ^{167}Tm reaction on the cyclotron. D_2EHPA extraction chromatography technique was used for separation of ^{167}Tm radioactivity from irradiated Ho target. Previously elution solution for Ho was selected as 2.5N HNO_3, the strip of Tm fraction was completed with 6N HNO_3, and tracer experiments were carried out by reactor-produced ^{170}Tm (see Fig. 5). The recovery of ^{167}Tm was above 90% and Ho content in Tm fraction was below 4μg/ml. Based on these results, the hot target processing was fulfilled and radionuclidic purity of ^{167}Tm product was above 99% and radioactive contamination of long-lived ^{168}Tm wasn't observed on γ-spectrum of the product during the measurements. The ^{167}Tm-citrate solution as final product was sterile, pyrogen-free, and suitable for medical use.

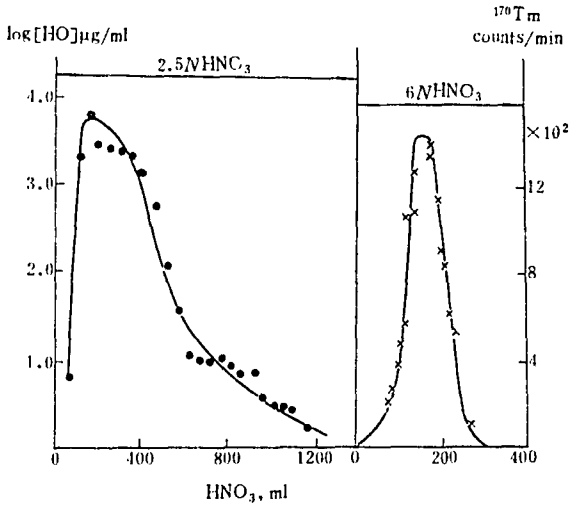

Fig. 5. Elution curve of Ho-^{170}Tm D_2EHPA-containing resin, type M, 100-120 mesh
Ho-loaded quantity: 1.1455g
Eluate: 2.5N HNO_3

Tm citric acid solution was sent to a hospital at Lanzhou for animal tests and clinical studies. The experiments on the in-vivo distribution and uptake of ^{167}Tm preparations in normal and tumour-bearing mice and scanning of whole body of rabbit were completed. (see tables 3 - 5). The results showed that ^{167}Tm radioactivity mainly accumulated in bone and tumour of the mice and radiodensities in liver and spleen were lower and the lowest in muscle. It was cleaned in the blood very rapidly and excreted out by the kidney. Radioactivity concentrations in the tissue of tumour S-180 and cancers of other visceras were higher than the circumambiencies, and this indicates that radioactive ^{167}Tm has affinity for some kinds of tumours of soft tissue. Based on animal experiments, the investigations of clinical diagnosis for the patients who suffered from malignant bone tumour and liver cancer etc. have been performed and these results were similar those of the mice.

Table 3. Distribution of ^{167}Tm Radioactivity in normal mice*

Time(h)	Mice	Blood	Kidney	Liver	Spleen	Muscle	Bone
2	3	5.7±0.640	18.3±3.555	6.5±1.130	3.7±1.860	1.0±0.043	28.3±8.141
3	3	2.9±0.363	19.8±7.066	6.3±1.032	2.4±1.382	1.2±0.265	28.1±7.220
6	4	1.2±0.110	16.5±5.594	6.3±0.219	1.8±0.620	0.4±0.129	41.9±11.282
24	3	0.3±0.250	14.5±6.896	4.7±0.727	2.1±0.704	0.5±0.140	61.2±10.593
48	3	0.3±0.297	17.0±4.808	4.0±0.727	3.2±0.822	0.3±0.130	37.6±4.521
72	3	0.5±0.331	10.9±0.278	3.7±1.050	1.9±0.352	0.8±0.089	33.4±4.558
96	4	0.2±0.197	4.3±0.612	2.2±0.317	1.0±0.456	0.2±0.037	26.9±9.116
120	3	0.2±0.041	2.2±0.041	2.1±0.627	1.4±0.367	0.2±0.069	25.3±3.156

* In tissue per gram or blood per millilitre

Table 4. Distribution rate of ^{167}Tm in tumour S-180 and each viscera in mice

time(h)	tumour/blood	tumour/kidney	tumour/liver	tumour/spleen	tumour/muscle	tumour/bone
3	3.6	0.50	1.6	3.5	10	0.31
6	4.4	0.47	1.9	5.6	9.3	0.27
24	11.8	0.30	1.8	2.96	10.37	0.20
48	18.0	0.18	1.35	2.10	18.0	0.13
72	31.5	0.68	2.7	4.2	21.0	0.21

Table 5. Distribution of ^{167}Tm radioactivity in tumour-bearing mice*

Time(h)	S-180	Liver Cancer	Lung Cancer	Brain Cancer
6	8.4±2.342	2.6±1.443	6.2±0.402	5.6±0.924
24	8.3±1.194	8.6±1.874	12.9±1.450	7.4±1.410
48	5.4±1.926	8.4±2.470	8.8±0.790	8.9±1.900
72	6.3±3.590	6.5±0.664	5.7±0.830	
		3.3±0.391		

* In tumour per gram

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