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NEUTRONDEFICIENT NUCLIDES FOR POSITRON EMISSION TOMOGRAPHY. VII. SEPARATION OF ^{55}Co AND ^{64}Cu FROM NI TARGET

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NEUTRONDEFICIENT NUCLIDES FOR POSITRON EMISSION TOMOGRAPHY.

VII. SEPARATION OF ^{55}Co AND ^{64}Cu FROM NI TARGET: Preprint ITEP 19-94/

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The method for simultaneous production of copper-64 and cobalt-55 is described. An improved procedure for radio chemical separation of radionuclides is suggested. The procedure provides high radionuclidic purity of products.

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INTRODUCTION

This work is a part of a larger scheme with the aim of finding ways to produce radionuclides for positron emission tomography (PET) and with the following criterias:

- Half-lives of several hours in order to allow for kinetic studies of fairly slow physiological processes (like the uptake and distribution of antibodies).

-Stable labelling procedures of organic molecules should be possible (e.g. covalent or cehelating techniques).

-Production should be possible at low energy accelerators commonly used in context with PET (below 20 MeV protons, preferably at 12-16 MeV)

Within the framework of this program production methods of ^{45}Ti ($T_{1/2}$= 3,09 hours), ^{61}Cu ($T_{1/2}$ =3,4 hours), ^{76}Br ($T_{1/2}$=16 hours), ^{110}In ($T_{1/2}$=69 min) has been studied.

Cobalt and copper isotopes are known to be good chelators

and can easily be used to label large bio-molecules. Co has been used for the labelling of e.g. bleomicin, cyanocobolamine and antibodies for diagnostic purpose [1, 2,3]. A specific interest for ^{64}Cu-labelled antibodies is also for in vivo dosimetry in context with radioimmunotheraphy with ^{67}Cu [4]. The physical characteristicsfor ^{55}Co and ^{64}Cu is given below

Table 1. Physical properties of ^{55}Co and ^{64}Cu

Nuclide	^{64}Cu	^{55}Co
Half-life	12,7 hours	17,53 hours
Mode of decay	β^- 39%/0.578 MeV β^+19%/1.67 MeV EC 42%	β^+ 77%, 1,5 MeV EC 41%
Gamma energies (MeV)	1,346 (0.48%)	0,477 (20.2%) 0,931 (75%) 1,408 (16,9%)

A chemical separation method described in the litterature [5] for ^{55}Co was used and modified in order to simplify and to avoid manual work with strongly radioactive targets. For the separation of ^{64}Cu we applied an extraction technique with dithizone, earlier applied in the separation of copper from zink [6], and with good results.

MATERIAL AND METHODS

Targets of natural nickel with a chemical purity of 99.95% was used. Two foils (0.25 mm thick and with a diameter of 8 mm) were irradiated at a small cyclotron (MC17, Scanditronix AB, Uppsala) at the Uppsala PET-Centre. Proton energy on target was 16.2 MeV.

For the analysis of the radioactivity of different radionuclides in the target as well as in different fractions during the separation procedure an ultra pure germanium detector, conected to a PC-based multi-channel analyzer, was used.

Analysis of labelled proteins was carried out using HPLC (Column-GF-250, eluent -0,1 M phosphate buffer (pH 7,0)).

SEPARATION TECHNIQUES AND RESULTS

Dissolving of Ni target.

Irradiated Ni- targets were dissolved in minimal amount of boiled aqua regia. To remove any traces of nitric acid, the solution was evaporated to dryness. The remnant was taken up in 2 ml of concentrated hydrochloric acid and evaporated to dryness again. The last procedure was repeated two times.

Dissolving of the target and removing of nitric acid takes about 40-60 minutes.

Separation of ^{64}Cu.

Since ^{64}Cu is practically a pure positron emitter and has no specific gamma linem, it is rather difficult to estimate its amount in a crude solution, containing several positron emitting nuclides. Due to this reason ^{61}Cu was chosen for the assessment of copper recovery. Thus, the experimental work was carried out 8

hours after irradiation, before the decay of this isotope. For the estimation of purification from nickel, the isotope ^{57}Ni was chosen.

Nickel chloride, containing isotopes of cobalt and copper was taken up in 3 ml 0,1 M HCl and transferred into test tube. 3 ml of freshly prepared 0,001% dithizone solution in CCl_4 was added into the test tube. Content of test tube was stirred during 3 min. After the stirring and phase separation the organic phase (lower layer) was transferred into an other test tube. The extraction was carried out twice. The organic fractions were collected and washed twice with 3 ml of 0,1 M HCl to remove any traces of nickel and cobalt isotopes.

Copper isotopes were reextracted quantitatively via 3 minutes long stirring with 6 M HCl. To get rid of dithizone traces, the solution was washed with 3 ml of CCl_4.

Only peeks of ^{61}Cu and ^{64}Cu were seen in the gamma-spectrum of the final product.

The solution was evaporated to dryness and radiocopper was redissolved in hydrochloric acid with desirable molarity.

The described procedure took about 40 minutes (starting from dry nickel chloride). Average yield of ^{61}Cu was about 95% (decay corrected).

Separation of ^{55}Co.

In order to study the influence upon cobalt separation, this procedure was carried out without and with primary copper extraction. When no Cu-separation was carried out, dry nickel

chloride containing cobalt and copper isotopes was dissolved in 3 ml of 10 M HCl. In order to reduce copper to oxidation state (1), 2ml of 2% solution of $SnCl_2$ in 10 M hydrochloric acid were added. Then the solution was loaded on the top of the ion-exchange column (AG 1x8, 100-200 mesh, 2 ml). Nickel and copper passed the column without retention. The column was additionally washed with 5 ml 10 M HCl after which the gamma spectrum of the column was taken.

The spectrum showed no trace of gamma- lines of nickel and copper isotopes.

Cobalt was eluted from the column with 5 ml of 0,05 M HCl. Total yield of cobalt separation was in the level of 80%, but the eluate contained certain amounts of Sn. By adjusting of pH value for labeling, the tin was hydrolized and precipitated. About 50 % of cobalt activity coprecipitated with tin.

When a preliminary copper extraction was made the nickel chloride solution containing radiocobalt was additionally shaken three times with 0,001% solution of dithizone in carbon tetrachloride. Gamma-spectrum of acidic solution shows no peeks of copper isotopes. To get rid of dithizone traces, the solution was washed with 3 ml of CCl_4.

After the removing of copper the water phase was evaporated to dryness and the remnant was redissolved in 3 ml of 10 M HCl. This solution passed through the ion-exchange column (AG 1x8, 100-200 mesh, 2 ml), preconditioned with 10 M HCl. Column was additionally washed with 5 ml 10 M HCl. Cobalt isotopes were eluted from column with 5 ml of 0,05 M HCl. Eluate was evaporated to dryness. Co was redissolved in hydrochloric acid

with desirable molarity.

This procedure took 35-40 minutes. The yield of separation is 80%. No differences were observed in the ion-exchange behavior of cobalt in the two separation methods.

At the described irradiation conditions Co-55 contained 0.83% of Co-57.

Labeling of dextrane with ^{55}Co and ^{64}Cu.

Produced nuclides were used for the labelling of dextrane with attached thiosemicarbazide groups, which served as a model compound for labeling procedure.

Yield of labelling was independent on reaction time (in time span 20 - 120 minutes) but showed strong dependence on pH value of reaction mixture. Optimal conditions were as described below.

Into 20 microliters of solution, containing 2 mg/ml of dextrane with 5% of 4-methylthiosemicarbazide groups, 200 microliters of borate buffer (pH 9,0) and 25 MBq of Co-55 in 20 mkl of 0,01 M HCl was added. Final pH value of solution was 8,5. Analyses were carried out after 20 min- 2 hours long incubation at 25 C.

Into 20 microliters of solution containing 2 mg/ml of dextrane with 5% of 4-methylthiosemicarbazide groups, 200 microliters of acetate buffer (pH 5,6) and 25 MBq of Cu-64 in 20 mkl of 0,01 M HCl were added. Final pH value of solution was 5,3. Analyses were carried out after 20 min- 2 hours long incubation at 25 C.

Yield of labeling under these conditions amounts to 80% for ^{64}Cu and 92% for ^{55}Co.

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