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# Abstract

At the Institute of Nuclear Physics a 150 cm cyclotron has been operating since 1965. In 1972 the cyclotron was converted to variable energy isochronous mode of operation<sup>1</sup>. Some time later a system of beam transport to external targets with formation of special transport modes<sup>2</sup> was modernized. All this in combination with high efficiency of cyclotron operation(up to 5200 hours of beam time a year) increased considerably the possibility to perform both fundamental and ap-plied scientific work. Especially valueable there appeared possibility to accelerate protons in a wide energy range from 6 to 30 MeV and realize correspondingly the nuclear reactions up to (A, 3n). Among different applied tasks performed at the cyclotron the special programme of cyclotron produc-tion of short-lived medical radioisotopes iodine-123, thallium-201, cadmium-109 in the first place and some others to satisfy clinic needs of Alma-Ata and its region has special importance. In accordance with this programme the preparation to produce iodine-123 is being held and regular production of "Thallium chloride, thallium-201" pharmaceptical is started.

#### Introduction

Thallium-201 based radiopharmacepticals are widely used in medical practice. Number of publications devoted to the conditions and possibility of use of this isotope, improvement of its production methods, analytical and radiometric control and so on is increasing. Great interest to this isotope is connected with the fact that it has found application for early diagnostics of heart diseases.

Thallium-201 radionuclide is produced in isotopes of hydrargyrum, plumbum, thallium and bismuth during irradiation with accelerated charged particles. To separate thallium-201 from target material different methods are used: ion charge chromatography, coprecipitation, extraction and other

methods<sup>3-9</sup>. Main requirments for thallium-201 production are maximum possible yield of necessary nuclide and minimum quantity of produced radionuclide contaminations.

## Experimental procedure and results

At the Institute of Nuclear Physics of the Kazakhstan Academy of Sciences technology of thallium-201 radionuclide production and production of "Thallium chloride, thallium-201" radiopharmaceptical on its basis are developed. The results obtained in report<sup>10</sup> were the basis of the development. Metallic thallium enriched by thalium-203 up to 97% was irradiated at the 150 cm isochronous cyclotron of the INP in Alma-Ata by protons with maximum (30.5±0.5) MeV energy. The target was duraluminium platcholder containing (5000 ± 30) um thick thallium disc 18 mm in diameter. From the side of incident proton beam the disc was covered by 140 mm thick copper foil that provided safety to thallium disc from the direct effect of proton beam and proton energy discarding down

to 28.5 MeV<sup>11</sup>. From the back side of the disc there was a copper foil which was water-cooled during irradiation. Remotely controlled irradiation device (Fig.1) allowed to perform target adjustment, subsequent target irradiation and its automatical discarding without disturbing vacuum in a beam line.



Fig. 1. Schematic drawing of the irradiation device (not to scale).

- 1 beam line
- 2 target

3 - target throwing pipe

- 4 target throwing barrel
- 5 drive screw

In the process of chemical treatment the radioactivity of nuclides of plumbum-200, 201 202<sup>M</sup>, 203 and thallium-200, 201, 202 produced in the irradiated target was measured by means of spectrometer on the basis of programmed multychannel analyser and germanium detector of 67 cm<sup>3</sup> working volume and 1.6 keV energy resolution at 1.33 MeV level. The developed programme allowed to perform erpress-analysis of radioactivity in all stages of reprocessing of the irradiated target. Separation of thallium-201 radionuclide

Separation of thallium-201 radionative out of the irradiated target was done in two stages. In the first stage the fraction of plumbums 200-203 was separated from target matrix by means of correcipitation with deposit of strontium sulfate. In the second stage after exposure of the solution with plumbum fraction during 30-32 hours the stored thallium-201 was extracted by mixture of butyl acetate with potassium bromate. After washing of the organic phase by chlorhydric acid thallium-201 was reextracted by sulphurous acid solution. Water phase was evaporated and the residue was dissolved in physiological solution<sup>10</sup>.

Overall activity of plumbum-201 in the irradiated target was 1.5-2.5 Curies after the irradiation was stopped. In gamma-spectra of plumbum fraction there were not found any radionuclides except of the principal ones (plumbum 200-203).

Exposure period of plumbum fraction to store thallium-201 was 24-32 hours for different targets. The yield of thallium-201 was in the range of 93-97% after the settling of plumbum fraction. Mean chemical yield of thallium-201 was 87-92%.

Volume concentration of ready pharmaceptical was in the range of 2-5 mC1/ml.

Determination of radiochemical purity of the pharmaceptical was performed by means of extraction method using butyl acetate. Inactive contaminations of thallium, strontium, copper and other elements were defined by means of plasma emission spectrum analyser. For more exact determination of concentrations of microcontaminations there were performed studies of dependence of sodium chloride concentration in the pharmaceptical from 0.1 to 0.9 mg/ml for 20 elements.

Content of inactive contaminations in the product did not exceed 0.5 mg/ml for thallium, 0.1 mg/ml for strontium, 0.25 mg/ml for ferrum and 0.1 mg/ml for copper. Overall concentration of all other contaminations is 1% for thallium-200, 0.05% for thallium-202 and 0.01% for plumbum-201, 203 (Fig.2). Qualitative purification of the pharma-

Qualitative purification of the pharmaceptical from inactive chemical and radionuclide contaminations allowed to make it more pure than in paper After thermal sterilization "Thallium chloride, thallium-201" pharmaceptical was used in clinics of Alma-Ata for myocardial studies.

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### References

- 1. A.A.Arzumanov, L.M.Nemenov. Nucl. Instr. and Meth., 106, N 2, (1973), 201.
- A.A.Arzumanov, V.N.Batischev, V.D.Berger et al. Proc. Tenth Int. Conf. Cycl. and their Appl. East Lansing, Michigan, USA, Edited by F.Marfi, (1984), 479.
- 3. E.Lebowits, M.Greene, R.Fairchid et al. Nucl. Med. 16, (1975), 151.
- S.M.Quaim, R.Weinrich and H.Ollig, Int. J. Appl. Radiat. Isot. 30, (1979), 85.
- V.G.Sodd, K.L.Schols and J.W.Blue.
  J. Radioanal. Chem. 68, (1982), 68.
- G.P.Kayfuss, T.E.Boothe, J.A.Campbell et al. J. Radioanal. Chem. 68, (1982), 289.
- M.Bonardi, Radiochem. Radioanal. Lett. 42, (1980), 35.
- 8. I.A.Watson, N.Ramamoorty, Radiochem. Radioanal. Lett. 39, (1979), 309.
- L.W.Makagonova, B.Z.Ioffe, Yu.G.Sevastyanov, Radiokhimiya, 22, (1984), 585.
- A.B.Malinin, M.D.Kozlova, A.S.Sevastyanova, Int. J. Appl. Radiat. Isot. 35, (1984), 685.
- N.I. Venikov, N.M. Volkova, M.D.Kozlova et al. Atommaya energiya, 60, (1986), 119.



Fig. 2. Ge(Li) gamma spectrum of "Thallium chloride, thallium-201" for production datum.