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ASSESSMENT OF RADIOACTIVE AND CHEMICAL IMPURITIES IN PERTECHNETATE PRODUCED BY PHOTONUCLEAR TECHNOLOGY

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The results of the release of ^{99}Mo of molybdenum foil irradiated at LAE with E = 22 MeV and I = 700 μA are presented. The technology of electrolytic deposition ^{99m}Tc with its subsequent conversion into a radiopharmaceutical – pertechnetate – is considered. The content of chemical and radionuclide impurities in pertechnetate was monitored, as well as testing of the radiopharmaceutical with various carriers for the diagnosis of animal organs.

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INTRODUCTION

The beginning of the 21st century demonstrated high-quality developments in the production and clinical use of various radiopharmaceuticals (RPs). Unfortunately, medical isotopes are not produced in Ukraine but are bought abroad at high prices. In recent years, these have been mainly Poland and Uzbekistan. To date, more than a hundred radiopharmaceuticals have already been developed in the world, but only some isotopes are used in the clinic. This is due to many reasons: the development of the most economical technologies for obtaining a radioisotope, with its transfer into an appropriate biocompatible chemical form, with an assessment of the quality of radiopharmaceuticals, etc.

A limited number of isotopes are used in pure ionic form. Such isotopes include ^{123}I, ^{201}Tl, ^{82}Rb, ^{128}Cs. As an analysis of the state and main directions of development of nuclear medicine in the world shows, the most effective and promising in the field of clinical diagnostics and therapy are radiopharmaceuticals based on ^{99m}Tc, short-lived isotopes ^{123}I, ^{201}Tl, ^{67}Ga, ^{111}In, as well as ultrashort positron-emitting isotopes ^{11}C, ^{13}N, ^{15}O, ^{18}F.

In any case, the world's pharmacopeia dictates monitoring of the analytical parameters of the resulting isotope: radiochemical and radionuclide purity, hydrogen index, pyrogenicity, etc. The content of various impurities in the isotope makes it practically impossible for use in practical medicine. Removing impurities is usually a complex, expensive procedure and there is a risk of introducing new undesirable elements. In addition, the presence of chemical impurities can affect the diagnostic quality of radiopharmaceuticals. There are still no highly sensitive instrumental methods for analyzing impurity composition that can identify these impurities at a certain detection limit.

Radionuclide purity is the ratio of the main radionuclide activity to the drug's total activity, expressed as a percentage. The absence of any impurities in the form of elements other than those determines chemical purity.

Technetium-99m (^{99m}Tc) is one of the highest-priority medical isotopes worldwide for diagnostics and therapy. Approximately 85% of nuclear medicine uses this isotope. ^{99m}Tc is produced by the radioactive decay of ^{99}Mo, which is produced from a radioactive uranium target from which ^{99}Mo is extracted, followed by purification for use in a ^{99}Mo/^{99m}Tc generator. A similar technology is used in Belgium (IRE), Canada (AECL/Nordion), the Netherlands (Covidien), and South Africa (NTR). Demographic and medical trends suggest that the global need for the use of ^{99m}Tc will increase by an additional 8…10% in the future for diagnostic procedures using new markers [1].

The US National Academy of Science believes that the production of the medical isotope ^{99}Tc from highly enriched uranium is technologically and economically feasible. However, other alternatives and additional technologies for the production of ^{99}Mo/^{99m}Tc generators are also being considered. Some of the proposed technologies have not yet been commercially proven, and some are in the early stages of development. In any case, Canada, Europe, and the USA are trying to develop technologies for producing ^{99m}Tc without using highly enriched uranium to produce ^{99}Mo/^{99m}Tc. These are approaches that include the production of generators with high specific activity (fission product): neutron activation, photofission, transmutation, etc. However, when developing these technologies, such issues as disposal of radioactive waste, target material, radiochemistry, post-isotope separation, commercialization, etc. are necessarily considered [2].

The purpose of this work is to develop photonuclear technology for the production of the most common isotope in medical practice – ^{99m}Tc and ^{99m}Mo/^{99m}Tc – generator, with subsequent assessment of the quality of radiopharmaceutical.

1. MATERIALS AND RESEARCH METHODS

The molybdenum foil was used. It was irradiated at LUE with an energy of 22 MeV and a current of 700 μA [3].

2. RESULTS AND DISCUSSION

The use of electronic accelerators in the production of the ^{99}Mo isotope will radically solve the problems of radioactive waste disposal and significantly expand the diagnostic capabilities of radionuclide laboratories using the ^{99m}Tc eluate (elution - extraction of a substance by washing it out with an appropriate solvent - eluant). This approach can be implemented by creating and using high-power electron accelerators with a current of up to 1 mA and an energy of up to 25 MeV.

Studies on the yield of radioactive isotopes from a target of molybdenum foil were carried out using W and Ta converters of various thicknesses at a beam energy of 22 MeV.

The distance of the molybdenum foil target (weighing 160 mg) from the tantalum converter was 5 mm. The experimental design and the ^{99}Mo yield depending on the thickness of the converter are shown in Figs. 1, 2. Activity was recorded by a Ge-detector with an energy resolution of 2.8 keV along the 1332 keV ^{60}Co line. A smooth dependence of the ^{99}Mo yield on the converter thickness is visible, with a maximum value of 2 mm.

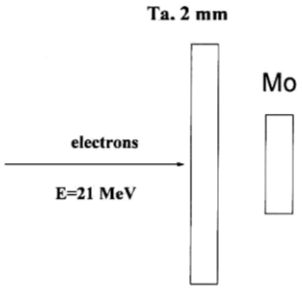

Fig. 1. Experimental scheme

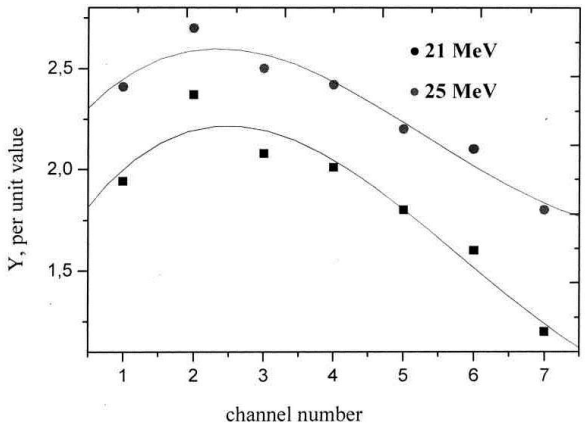

Fig. 2. Mo-99 yield depending on converter thickness

In a day, at the LAE with these parameters, it is possible to produce from 1 to 4 Ki of the parent isotope ^{99}Mo, using nuclear reactions: ^{100}Mo(γ,n)^{99}Mo ($T_{1/2}$ = 66.02 h), ^{98}Mo(n,γ)^{99}Mo ($T_{1/2}$ = 66.02 h).

The isotope ^{99}Mo is a beta- and gamma-emitter with a half-life of 66.02 h. The isotope ^{99}Mo is used to produce ^{99m}Tc. The isomeric state of ^{99m}Tc decays with a half-life of 6.066 h and a probability of 89.6% and with gamma line emission of 140.5 keV and 022% – 142.6 keV.

A technology has been developed for the electrolytic deposition of ^{99m}Tc onto a pyrographite substrate with subsequent transfer of ^{99m}Tc into a solution of technetium acid. The electrolysis method is a chemical reaction that occurs under the influence of an electric current on electrodes placed in a solution. Reduction occurs at the cathode, and oxidation of the ions that make up the electrolyte occurs at the anode. Using the electrolysis method, oxidation and reduction reactions occur with high yield and selectivity, which are difficult to achieve in conventional chemical processes.

In our proposed scheme, ^{99}Mo is produced from molybdenum foil at an electron accelerator. This sample is dissolved in a NaOH solution, followed by electrolytic deposition of ^{99m}Tc onto a pyrographite electrode relative to an analytical pure graphite electrode. The spent solution can be irradiated at an electron accelerator once more, and produce ^{99m}Tc within 10–15 days. This scheme has several significant advantages: 1 – the absence of radioactive waste that must be immobilized; 2 – the availability of ^{99m}Tc eluate expands the possibilities of carrying out diagnostic procedures in radionuclide laboratories.

The electrochemical separation of technetium from alkaline solutions (2N NaOH) occurs at a cathode potential of 1.1 V. The method is based on the selective electrolytic reduction of Tc(7) to TcO_2 and the deposition of the latter on the electrode. The optimal deposition mode of ^{99m}Tc was achieved at a current of 150 mA/cm^2 and intense stirring on a magnetic stirrer heated to 60 °C. After 60 min of electrolysis, the efficiency of ^{99m}Tc deposition on the pyrolytic carbon cathode is reduced by passivation (creation of a thin film ~ micrometer of released oxides and adsorption of surfactants on the electrode surface). After polishing the cathode, which was operated for 1 h, its ability to deposit TcO_2 is restored.

The maximum release productivity ^{99m}Tc at a current of 150 mA/cm^2 and an electrolyte temperature of 60 °C was ~ 2 MBq/(h·cm^2) in a 2N NaOH solution. An increase in the productivity of ^{99m}Tc separation at the carbon cathode is achieved by using a rotating electrode. As is known, the process of electrochemical release of ^{99m}Tc is limited by diffusion processes. In a fluid at rest, the current density i_d is:

$$i_d = n F D_{ox}(C_{ox}/\delta),$$

where n is the number of electrons corresponding to the discharge of one particle, F is the Faraday number ($0.964 \cdot 10^5$ Coul·mol^{-1}), D_{ox} is the diffusion coefficient of the substance x, C_{ox} is the volume concentration of the desired component the thickness of the diffusion layer. Therefore, it is possible to influence the limiting current density only by changing D_{ox}, which is practically impossible, as well as by temperature, the thickness of the boundary layer, and changing its kinematic viscosity.

Limit diffusion current id for a rotating electrode:υ

$$i_d = 0.62 F D^{2/3} \omega^{1/2} \upsilon^{-1/6} C,$$

where ω is the angular velocity of rotation of the electrode, υ is the kinematic viscosity; C is the

concentration of the desired component in the volume and D is the diffusion coefficient.

Therefore, by changing the speed of rotation of the electrode, the limiting diffusion current density. Extraction of ^{99m}Tc deposited on the cathode surface is carried out with a 10% solution of hydrogen peroxide after washing it in distilled water, followed by the conversion of ^{99m}Tc into technetium acid (H_2TcO_4), and this is a radiopharmaceutical. This is a technological cycle for processing irradiated material, which includes the preparation of the radiopharmaceutical itself. The concentration of ^{99m}Tc in NaOH solution is usually $10^{-15}…10^{-13}$ atom/cm^2.

Control of the decomposition of the hydrogen peroxide residue in a solution of technetium acid is carried out using the titration method. This method is based on measuring the amount of reagent required to react with certain components in a solution. The permanganatometry method with 0.1 N $KMnO_4$ was used. If a pink color appears when 0.1 ml of permanganate is added during the titration of technetium acid, in that case, this means that not all of the peroxide has decomposed and must be decomposed again.

More precise control of the hydrogen peroxide content in a solution of technetium acid was carried out using sodium hypochlorite (ClO^-) on a quantum metric installation with PhEM-140 (photoelectric multiplier) with an interference filter in the 630 nm according to the reaction [4]: $H_2O_2 + OCl^- \rightarrow Cl^- + O°_2 + H_2O$ by detecting light quanta with a wavelength of 632 nm, due to the generation of singlet oxygen ($O°_2$). The detection limit of hydrogen peroxide by this method is 0.0005%.

The content of radioactive impurities in technetium acid was controlled by measuring emission spectra with a Ge-detector. The only impurity in technetium acid was ^{99}Mo (Fig. 3). Its activity during a single electrolytic deposition of TcO_2 did not exceed ~ 1.5%. Considering the quantum yield of ^{99}Mo radiation with an energy of 739 keV (12.8%), the intensity of the impurity radiation was ~ 0.19%.

As a rule, during the electrolysis process, intensive contamination of the electrolyte occurs with glass dissolution products. For example, when using a Pyrex electrolysis cell, 84 mg of glass is lost when boiled for three hours with a solution of 2N NaOH per 100 cm^2 of surface. In our case, quartz cell were preferable, in which such losses are significantly lower, except Si losses. Electrolyte impurities passivate the electrode surface with released oxides; therefore, restoration of the electrode surface is required, for example, by rotating the electrode in a special device by bringing it into contact with abrasive materials. A monolayer of substance on the surface contains ~ 10^{15} mol./cm^2. A new layer of substance can form if the concentration of the impurity in the solution is ~10^{-7} mol./cm^{-2}. Reducing the electrolyte temperature and increasing the limiting current will be significant for optimizing the electrolytic release of ^{99m}Tc.

Biological testing of radionuclide ^{99m}Tc. The radiopharmaceutical pertechnetate was tested in animal experiments at the Kharkiv Institute of Medical Radiology to discover possibilities for radionuclide diagnostics.

To establish the accumulation of pertechnetate in certain organs and systems of the animal body, standard sets of carrier reagents for radionuclide diagnostics were used. These are drugs such as “Technefit”, “Pentatekh”, “Citratekh”. Drugs were prepared according to standard procedures supplied with these kits. The volume and dose of the drug were calculated according to the weight of the animals (see Fig 3).

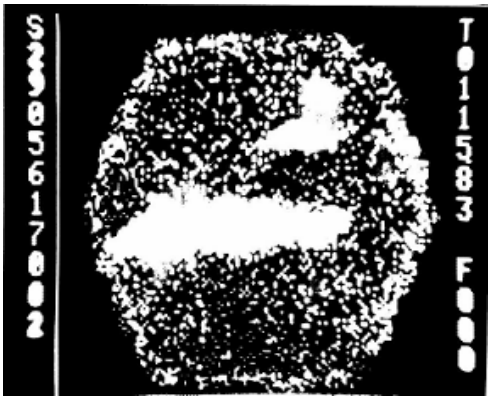

Fig. 3. ^{99m}Tc-pertechnetate distribution in the rat body

The drugs “Pentatekh” and “Citratekh” are intended mainly for diagnosing the function of the kidneys and urinary system. According to the attached instructions, pertechnetate in saline solution was added to the drug to an activity of 0.4 MBq in 1.5 ml. The prepared drug was administered to rats at 1.2 ml. As in the previous experiment, 20 min after drug administration, clear visualization of the kidneys and bladder was noted.

The health status of the animals was monitored for 7 days. There were no deaths or adverse consequences associated with the procedures performed.

CONCLUSIONS

1. Requirements for the selection of conditions for the production of ^{99m}Mo/^{99m}Tc generators are formulated.

2. The effect of irradiation conditions of targets made of molybdenum foil on the yield of ^{99}Mo when using bremsstrahlung from an electron accelerator was studied. The ^{99}Mo yield for molybdenum foil was 2 Ci per day at an electron energy of 22 MeV and a current of 700 μA.

3. The influence of the conditions of electrochemical separation of ^{99m}Tc from an alkaline solution of ^{99}Mo on the degree of extraction of ^{99m}Tc was studied. The productivity of ^{99m}Tc release on a carbon substrate at a current of 150 mA/cm^2 and an electrolyte temperature of 60 °C was 2 MBq/(h·cm^2). A model of an installation for the electrolytic separation of ^{99m}Tc (at 200 MBq/h) has been developed. The only impurity in technetium acid was ^{99}Mo.

4. Biological testing of the produced pertechnetate was carried out using special sets of reagent carriers for radionuclide diagnostics of individual animal organs at the Kharkiv Institute of Medical Radiology.

REFERENCES

1. R.G. Bennett, J.D. Christian, D.A. Petti, et al. A system of ^{99m}Tc production based on distributed electron accelerators and thermal separation // *Nuclear Technology*. 1999, v. 126, p. 102-121.
2. V. Husak, P. Kopecky. Quality assessment of radiopharmaceuticals // *J. Nucl. Med. Biol.* 1989, v. 1, p. 78-92.
3. N. Dikiy et al. Development of new electron irradiation based technology for technetium-99m production // *Proceeding of the Sixth European Particle Accelerator Conference*, Stockholm, 22-26 June 1998 / S. Myers, L. Liljeby, Ch. Petit-Jean-Genaz, J. Poole, K.-G. Rensfet (Eds). Institute of Physics Publishing, Bristol and Philadelphia, 1998, p. 2389-2391.
4. E. Lengfelder, E. Cadenes, H. Sies. Effect of DABCO (1,4-diazabicyclo (2,2,20-octane) on singlet oxygen monomol (1270 nm) and dimol (634 and 703 nm) emission // *FEBS Lett*. 1983, v. 164, p. 366-370.

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ОЦІНКА РАДІОАКТИВНИХ ТА ХІМІЧНИХ ДОМІШОК У ПЕРТЕХНЕТАТІ, ОДЕРЖАНОГО ЗА ФОТОЯДЕРНОЮ ТЕХНОЛОГІЄЮ

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Представлено результати виходу ^{99}Mo з мішені фольги молібдену, опроміненої на ЛПЕ з E = 22 МеВ та I = 700 мкА. Розглянуто технологію електролітичного осадження ^{99m}Tc з подальшим переведенням його у радіофармпрепарат – пертехнетат. Проведено контроль вмісту хімічних та радіонуклідних домішок у пертехнетаті, а також апробацію радіофармпрепарату з носіями при діагностиці органів тварин.