Ac-225 ISOTOPES OBTAINING BY THE METOD OF SUPERCRITICAL FLUID EXTRACTION WITH CARBON DIOXIDE

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Actinium-225 is one of the most promising radionuclides for α-therapy of oncological diseases. In this work, the main world technologies for obtaining the isotope ^{225}Ac are analyzed, and a new approach to its production based on supercritical fluid extraction with carbon dioxide (SFE-CO_2) is proposed and theoretically substantiated. Based on the results of the conducted research in the field of extraction of heavy metal isotopes by the SFE-CO_2 method, it is assumed that this method is capable of providing high selectivity of ^{225}Ac, a reduction in the amount of liquid radioactive waste and automation of the technological cycle. The model proposed for the extraction of ^{225}Ac complexes is presented, the process parameters are discussed and the flowsheet is proposed.

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1. INTRODUCTION

1.1. CURRENT DEMAND OF ACTINIUM-225 FOR MEDICINE

The production of medical isotopes is essential for the development of modern accelerator technology and medicine. Currently, the actinium-225 medical isotope is widely used to develop advanced treatments for the patients who use targeted α-therapy, where ^{225}Ac can be attached to a molecule, that selectively targets it to the cancer cell, potentially treating diseases such as neuroendocrine cancer, melanoma, and lymphoma [1–3]. Drugs labeled with ^{225}Ac, once developed and approved, can kill cancer cells with minimal damage to nearby healthy cells [4].

The intensive development of targeted radionuclide therapy creates a need to increase the global production of ^{225}Ac, but existing methods for its production have significant limitations associated with a shortage of raw materials, low selectivity, high cost, or adverse environmental impact [5–7].

^{225}Ac is considered a key radionuclide for targeted α-therapy because it has: an appropriate half-life (9.9 days); the energy of α- lobes (5.8…8.6 MeV) sufficient to destroy tumor cells; and a family of daughter α- emitters that enhance the therapeutic effect.

By 2024 - 2025, global demand for ^{225}Ac is estimated to exceed global production capacity several times over. Accelerator - based technologies, such as linear accelerators, cyclotrons, and fission neutron sources, can meet the medical demand for these isotopes without the use of enriched uranium. Accelerator-based technology, which does not use enriched uranium, provides advantages in terms of radiation safety [8].

Modern production of medical isotopes, including ^{225}Ac, is focused on using natural decay methods without isotopic impurities. This allows for increased efficiency and automation of the process, as well as a stable supply of the radioisotope to the market. Currently, the majority of available ^{225}Ac is produced from ^{229}Th after the decay of ^{233}U, with a total yield of ^{225}Ac of only approximately 63 GBq per year. This method remains a focus of current scientific research, as it is unknown whether production by this method will be able to meet future global medical demand. In particular, by irradiating ^{226}Ra, it was possible to provide between 55.3 and 129.1 GBq of ^{225}Ac in a single cycle with use of an experimental fast reactor [9]. This value corresponds to approximately 86…200% of the current annual global supply, demonstrating the significant potential of the reactor method to exceed existing generator production capabilities.

2. COMPARISON OF THE MAIN TECHNOLOGIES FOR ^{225}Ac PRODUCING

Currently, three traditional methods are used: decomposition of the ^{229}Th isotope [10]; spallation of the ^{232}Th isotope by high-energy protons [10]; irradiation of the ^{226}Ra isotope [10] with protons in a cyclotron, reactor and accelerator, and it is proposed an innovative method based on supercritical CO_2, presented in this work.

Below there is a comparative analysis of existing methods for producing ^{225}Ac.

2.1. THORIUM/ACTINIUM GENERATOR [11]

Source: ^{229}Th – decay product of ^{233}U (^{233}U (α) ^{229}Th (α)^{225}Ra (β^-) ^{225}Ac). The world reserve of ^{229}Th is estimated at tens of grams [12].

Problems: ^{229}Th deficiency; the need for high-precision radiochemistry; low industrial scalability.

2.2. THE SPALLATION OF ^{232}Th [13]

Reactions (p,x) with energies of 0.6…2 GeV (^{232}Th(p,x)^{225}Ac).

Advantages: high potential yield; availability of thorium.

Disadvantages: formation of ^{226}Ac and ^{227}Ac impurities; need for complex separation of products; energy consumption of the accelerator.

2.3. PHOTONUCLEAR PRODUCTION [14]

Reactions on radium isotopes (**^{226}Ra (p,2n) ^{225}Ac, ^{226}Ra (γ,2n) ^{225}Ra, ^{226}Ra (3n,2β) ^{229}Th, ^{226}Ra (n,2n) ^{225}Ac**).**

The advantage of this method is its relatively simple technology. Disadvantages include low yields, difficulties in handling radium raw materials, and the need for remote radiation processing.

3. PHYSICOCHEMICAL TECHNOLOGIES FOR OBTAINING USEFUL ELEMENTS FROM MONAZITE MINERAL CONCENTRATE

One of the main directions of obtaining ^{225}Ac is the technological processing of mineral monazite using physicochemical methods. Monazite is a phosphate of rare earth elements with the general formula (Ce, La, Nd, Th)PO_4. It contains significant concentrations of cerium, lanthanum, neodymium and impurities of thorium and uranium, which leads to its natural radioactivity. The typical chemical composition of monazite consists of cerium (Ce) – 40…50%; lanthanum (La) – 15…25%; neodymium (Nd) – 10…20%; thorium (ThO_2) – 3…12%; uranium (UO_2) 0.1…0.4% [15].

Rare earth elements and thorium play a key role in the development of modern nuclear energy and medical technologies. To obtain rare earth elements as daughter products from monazite sand, chemical processing is used, which typically begins with treatment of the raw material with sulfuric acid followed by aqueous extraction [16]. Extraction is a method of separating substances into their component parts using a solvent in which they dissolve differently. This process involves multiple neutralization and filtration steps, resulting in thorium phosphate concentrate, rare earth metal hydroxides, and uranium concentrate. At first, the ore is treated with sulfuric acid to decompose the mineral. After acid treatment, aqueous extraction is performed to further separate the components. These steps are repeated multiple times to isolate different fractions. The result is several concentrates, such as thorium phosphate concentrate, rare earth metal hydroxides, and uranium concentrate. Thus, monazite sand is an invaluable source of useful elements that can be used in various fields of scientific research, technology and medicine.

The chemical method for producing ^{225}Ac involves keeping the ^{229}Th radionuclide and its decay daughter compounds in a nitric acid solution with a concentration of 10.0 to 11.0 mol/l [17]. This nitric acid solution becomes enriched with impurities of the ^{229}Th and ^{228}Th radionuclides during a chemical reaction. The solution is then passed through a column with a cation exchanger (a compound that ensures the exchange of positive ions in the solution), and then the solution is passed through a column with an anion exchanger (a compound that ensures the exchange of negative ions in the solution). The sequence of such operations leads to the release of the radionuclide ^{225}Ac in the solution. It is sufficient to carry out four distillations, successively changing the concentration of nitric acid to 3.0 mol/l, and ^{225}Ac remains in the column with the cation exchanger, and the radionuclides ^{225}Ra and ^{224}Ra remain at the outlet. The remaining daughter decay products freely pass through the column [18].

To obtain thorium from the mineral monazite using the oxygen method under industrial production conditions, the monazite concentrate is treated with hot concentrated sulfuric acid (temperature 200 ºC), sometimes with the addition of hydrofluoric acid [19]. This results in a concentrated phosphate-free solution. The sulfation products are dissolved in water. This solution also contains dissolved sulfates of thorium, uranium, and other rare earth elements. This is followed by neutralization and treatment with hydrochloric acid. Separation of associated elements is based on the difference in solubility of the resulting chlorides. Extraction with tributyl phosphate (TBP) is sometimes used, allowing the removal of impurities. When treating monazite with sulfuric acid, the excess is retained for a lighter solution of thorium sulfate in a mixture of sulfuric and phosphoric acids.

When obtaining thorium from the mineral monazite using the alkaline method, monazite is fused with caustic soda (400 ºC), sodium carbonate (800 ºC) or lime at high temperature [20].

The technology for producing ^{225}Ac by physicochemical methods involves irradiating accelerators with a target and shell made of metallic thorium with a flow of charged particles [21]. The next step is the selective dissolution of the target and shell with hydrofluoric and nitric acid in order to obtain ^{225}Ac, where the final stage is the isolation of ^{225}Ac by passing the extraction solution through a chromatographic column.

Research centers such as Oak Ridge National Laboratory (ORNL), Canada's National Particle Accelerator Centre (TRIUMF), and Los Alamos National Laboratory (LANL) employ acid-complex methods. However, extraction and ion-exchange methods for ^{225}Ac extraction have the following limitations: the use of concentrated acids; multiple extraction/sorption stages; significant volumes of liquid waste. Since existing methods for producing ^{225}Ac have a number of technological, radiation, and logistical limitations, it is advisable to further explore alternative approaches.

4. OBTAINING ^{225}Ac by SFE-CO_2 METHOD

One of the new environmentally hazardous radiochemical methods is the extraction of uranium from man-made deposits using supercritical fluid extraction [22]. This method was developed at the Kharkiv Institute of Physics and Technology of the National Academy of Sciences of Ukraine. To implement this method, a pilot plant for supercritical fluid extraction of uranium complexes in a carbon dioxide medium was constructed (Fig. 1).

Fig. 1. General view of SFE -U installation

The SFE-U facility is designed to develop a technology for producing radionuclides using supercritical fluid extraction in carbon dioxide medium (CO_2). This method utilizes supercritical temperature and pressure to extract useful materials from mineral raw materials. The process is carried out in a CO_2 medium in a closed volume, without emissions into the atmosphere. This allows for research to be conducted in a non-toxic environment at temperatures above 37 ºC and pressures above 7.3 MPa. Studying supercritical extraction processes for target isotopes for various purposes, including medicine, as well as rare earth metals and actinides, can be of great practical importance, since the substance extracted under such conditions has a small amount of excess impurities compared to liquid extraction. It has been proven that supercritical CO_2 has a low viscosity (like a gas); high solubility properties (like a liquid); controlled parameters (pressure and temperature); chemical inertness; environmentally friendly if used in a closed cycle.

At KIPT, by use of the SFE-CO_2 method such substances were successfully extracted: uranium complexes (UO_2^{2+}–TBP); oxide forms of Mo and MoO_3; thorium complexes; actinides of III–IV groups [23–27]. As a result of the conducted studies, the formation of stable adducts of metals with tributyl phosphate was proven; their high solubility in supercritical CO_2; and the possibility of separation by temperature gradient.

4.1. PHYSICS AND CHEMISTRY OF THE PROCESS FOR OBTAINING ^{225}Ac UNDER SFE – CO_2 CONDITIONS (THEORY)

Hypothetically, $^{225}Ac^{3+}$ could form a complex of TBP that is soluble in supercritical CO_2, since the valence and chemical properties are identical to stable Ac^{3+}.

$$Ac^{3+} + 3\ TBP \rightarrow [Ac(TBP)_3]^{3+}. \quad (1)$$

Typically, such complexes exhibit: high stability; low susceptibility to hydrolysis; and solubility in supercritical CO_2. Extraction is expected to occur in three stages:

Formation of the complex:

$$Ac^{3+} + nL \rightleftharpoons AcL_n^{3+}. \quad (2)$$

Transition of the complex to the supercritical phase:

$$AcL_n\ (\text{liquid}) \rightarrow AcL_n\ (\text{supercritical } CO_2). \quad (3)$$

Temperature distribution:

$$\partial S / \partial T \neq 0 \quad (4)$$

ensures convection of the complex along the column of the reactor.

4.2. THE FLOWSHEET OF ^{225}Ac ISOLATION PROCESS

It is assumed that thorium can be obtained by processing monazite concentrate at Ukrainian enterprises for the extraction of thorium ores, obtaining thorium oxides and metallic thorium. Monazite ore contains a large amount of the isotope ^{232}Th. The isotope ^{229}Th, during the decay of which it is possible to obtain ^{225}Ac, is not a decay product of ^{232}Th. Th-229 is a daughter product after α-decay of U-233. In turn, Th-232 is converted into U-233 by neutron capture with subsequent β-decays.

$$Th-232 \xrightarrow{(n,\gamma)} Th-233 \xrightarrow{\beta^-} Pa-233 \xrightarrow{\beta^-} U-233\ (\text{in a reactor}). \quad (5)$$

In special nuclear reactors, U-233 is accumulated in the thorium cycle. The U-233 stockpile is the main source of thorium-229. This is a long-lived isotope [10] that can be used to produce medical ^{225}Ac.

$$U\text{-}233\ (\text{after a reactor}) \xrightarrow{\alpha} Th\text{-}229 \xrightarrow{\alpha} Ra\text{-}225 \xrightarrow{\beta^-} Ac\text{-}225. \quad (6)$$

In scientific research, in the presence of accelerators, the method of proton irradiation of Th-232 (^{232}Th(p,x)^{225}Ac) is also widely used to obtain ^{225}Ac. In particular, the use of an accelerator is also possible at the NSC KPTI. Further, the formation of complexes for the extraction of actinium by the FE-CO_2 method is assumed. The main stages of the process of isolating ^{225}Ac by the SFE-CO_2 method are shown in Fig. 2.

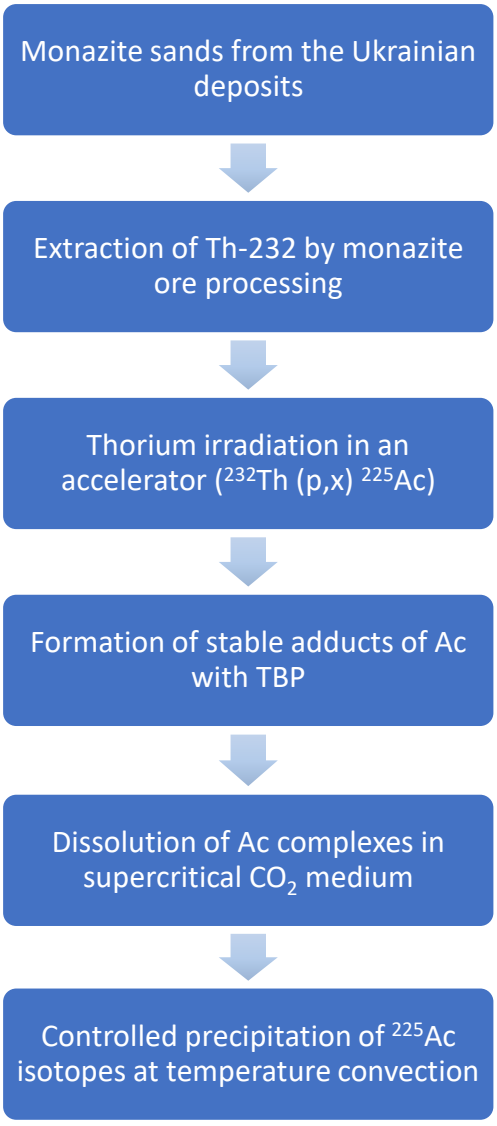

Fig. 2. The flowsheet of ^{225}Ac isolation (SFE-CO_2)

5. TECHNOLOGY EVALUATION. ADVANTAGES OF THE SFE-CO_2 METHOD

During the selectivity assessment, it was found that SFE-CO_2 exhibits: high selectivity with respect to Ra^{2+}; low extraction of thorium impurities; no matrix dissolution. Comparison of the ecological parameters of the SFE-CO_2 process with classic extraction is presented in Table.

Ecological extraction parameters

Parameter	Classic extraction	SFE-CO_2
Volume of liquid waste	1…3 l	<10 ml
Acid load	High	Zero
Impact on staff	Average (2–4 people)	Minimum (1–2 people)
Automation	Limited	Maximum

For radiochemistry, the following are important: the absence of liquid waste; minimal personnel contact with solutions; and the possibility of full automation. The SFE-CO_2 method combines the advantages of: solvent-free technology; selective complexation; fractionation capabilities; and comparatively low cost. It also eliminates the need for acid distillations; ensures process repeatability; reduces radiation exposure; and is scalable to industrial volumes.

CONCLUSIONS

1. The production of ^{225}Ac is a complex multi-step process combining hydrometallurgical, nuclear and radiochemical technologies. Monazite ore plays a key role as a source of thorium for this process.

2. An analysis of traditional methods of processing thorium isotopes to obtain ^{225}Ac was conducted and it was shown that each of them has limitations in terms of the main technological requirements: selectivity, environmental friendliness, scalability.

3. As an innovative approach for obtaining medical ^{225}Ac, the method of supercritical fluid extraction in carbon dioxide medium (SFE-CO_2) is proposed

4. The model for obtaining medical ^{225}Ac based on the SFE-CO_2 technology is presented, which ensures the minimization of liquid radioactive waste, that indicates ecological advantages of the proposed approach.

5. It is expected that the proposed method for obtaining ^{225}Ac is capable of environmentally safe scaling up the production of ^{225}Ac with the potential for industrial implementation.

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ОТРИМАННЯ ІЗОТОПУ Ac-225 МЕТОДОМ НАДКРИТИЧНОЇ ФЛЮЇДНОЇ ЕКСТРАКЦІЇ ДІОКСИДОМ ВУГЛЕЦЮ

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Актиній-225 є одним із найбільш перспективних радіонуклідів для α-терапії онкологічних захворювань. Проведено аналіз основних світових технологій отримання ізотопу ^{225}Ac, а також запропоновано та теоретично обґрунтовано новий підхід його отримання, заснований на надкритичній флюїдній екстракції діоксидом вуглецю (НФЕ-CO_2). На підставі результатів проведених досліджень у галузі екстракції методом НФЕ-CO_2 ізотопів важких металів передбачається, що даний метод здатний забезпечити: високу селективність ^{225}Ac, зниження кількості рідких радіоактивних відходів і автоматизацію технологічного циклу. Надано модель екстракції комплексів ^{225}Ac, обговорено параметри процесу та запропоновано технологічну схему.