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Method for Determining the Radiochemical Purity of Radiopharmaceuticals Based on Iodine-125, Iodine-131 and Samarium-153-oxabifor

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ABSTRACT

Radionuclides ^{125}I, ^{131}I and ^{153}Sm are used to obtain labeled radiopharmaceuticals used in medicine for diagnostics, treatment, and anesthesia in various diseases.

Radionuclide ^{125}I was obtained by irradiation with neutrons of the enriched isotope ^{124}Xe in a nuclear reactor. ^{131}I was isolated from irradiated samples of TeO_2 enriched in ^{130}Te, and radionuclide ^{153}Sm was obtained by irradiation of samples $^{152}Sm_2O_3$ in a nuclear reactor.

The radiochemical purity of sodium iodide preparations labeled with ^{125}I or ^{131}I radionuclides was determined by the electrophoretic method, and the samarium-153-oxabifor preparation was determined by ascending paper chromatography. To determine the distribution of the activity of ^{125}I, ^{131}I, and ^{153}Sm-oxabiphor by electrophoregrams and chromatograms, a γ-radiometric device Ludlum-2200 was used, which makes it possible to determine the radiochemical purity at the level of 99.9%.

Key words: Electrophoresis, paper chromatography, radiopharmaceuticals, radionuclides ^{125}I, ^{131}I and ^{153}Sm, radiochemical purity,

1. INTRODUCTION

Currently, radioactive isotope-labeled drugs are widely used in nuclear medicine for the diagnosis and therapy of oncological diseases. These radionuclides include iodine-125 and iodine-131, which are used to prepare a number of radiopharmaceuticals used in nuclear medicine [1]. In particular, the iodine-125 radionuclide is widely used for the manufacture of microsources for the therapeutic treatment of prostate cancer in brachytherapy [2]. One of the main methods of treating thyrotoxicosis is radionuclide therapy with iodine-131, which is based on the peculiarity of the thyroid gland to accumulate a significant part of iodine entering the body [3].

In most cases, cancers such as breast cancer, prostate cancer (PC), lung cancer, and colon cancer lead to bone metastases. As a rule, bone metastasis is multiple in nature, which makes it impossible to perform surgery or external radiation therapy [4]. Various methods are used to suppress pain in prostate cancer patients with bone metastases: external beam radiation therapy, administration of bisphosphonates, hormone therapy, chemotherapy, symptomatic treatment (pain relievers, etc.), radionuclide therapy [5]. The radionuclide therapeutic method is based on the ability of some β-emitting drugs, for example, samarium-153-oxabifor, to accumulate in bone metastases or in foci of the border zones between the tumor and bone and to suppress pain [6].

This article presents preliminary experimental results on the determination of the radiochemical purity of sodium iodide preparations with iodine-125 or iodine-131 radionuclide without carrier and samarium-153-oxabifor by electrophoresis and paper chromatography (PC).

2. MATERIALS AND METODS

Determination of the radiochemical purity of sodium iodide with iodine-125 or iodine-131 radionuclide, without carrier

The radiochemical purity of sodium iodide labeled with iodine-125 or iodine-131 radionuclide was determined by electrophoresis (BPE TU5-375-4231-77). A mixture of sodium bicarbonate, potassium iodide, and iodic acid potassium was used as a carrier, and a phosphate buffer solution containing $0.025M K_2HPO_4$ and $0.0042M NaH_2PO_4$ with pH 7.0 ± 0.2 was used as an electrolyte. To determine the distribution of various chemical forms of iodine-125 or iodine-131 radionuclides by electrophoretogram, a γ-radiometric device Ludlum-2200 was used, which makes it possible to determine the radiochemical purity at the level of 99.9%.

For the analysis, the analyzed preparation was diluted to a volumetric activity of 370 MBq / ml. Double distilled water was used as a diluent. Chromatographic paper, grade "C" was prepared as follows. The paper was cut into 15 x 250 mm strips. Departing from one of the edges by 50 mm (starting line), we applied (1% sodium bicarbonate solution, 0.1% potassium iodide,

and 0.2% potassium iodic acid) a carrier with a volume of 10-20 μL. After drying the spot in air, a sample of the preparation with a volume of 1-2 μL (activity 0.37-0.74 MBq) was applied to the same place. The strip was moistened with phosphate buffered saline at pH 7.0 ± 0.2.

The paper strips were placed in a horizontal electrophoresis chamber. The electrophoresis process was carried out at a voltage of 400 V for 50 min.

The resulting electrophoretogram was dried at room temperature, pasted over from both sides with a polyethylene film with a sticky layer. The developed electrophoretogram was used to determine the distribution of the activity of iodine-125 or iodine-131 along its length on a γ-radiometric device Ludlum-2200. The first 45 mm and the last 65 mm electropherograms were cut and discarded. The remaining part was marked into 10 mm long segments, numbered starting from the side of the starting line, and used to determine the radiochemical purity of the preparation. This results in 14 measurement segments.

Before measurements, the background of the γ-radiometric device Ludlum-2200 was determined. The background was measured 3 times for 10 seconds and the result was averaged.

Then, each successive segment of the electrophoretogram was cut off and placed for activity measurement in a Ludlum-2200 γ-radiometric device. Measurement time 10 sec.

The radiochemical purity was calculated from the ratio of the areas of the peaks corresponding to the main and impurity chemical forms of iodine.

Determination of the radiochemical purity of samarium-153-oxabifor

When using the drug "Samarium ^{153}Sm-oxabifor" in nuclear medicine, stringent requirements for radiochemical purity are imposed on it, since the main active ingredient is a complex of phosphorus-containing reagents of oxabiforic acid with samarium-153 radionuclide, which accumulates in bone cells, and impurity free ions $^{153}Sm^{3+}$ do not accumulate in bone cells and damage other organs.

The radiochemical purity of ^{153}Sm-oxabifor was determined by ascending paper chromatography. A phosphate buffer containing 0.0036 M K_2HPO_4 and 0.0076 M NaH_2PO_4, pH = 7.5 ± 0.2, was used as a mobile phase.

To determine the distribution of $^{153}Sm^{3+}$ ions and ^{153}Sm-oxabiphor of the complex on the chromatogram, a γ-radiometric device Ludlum-2200 was used, which makes it possible to determine the radiochemical purity at the level of 99.9%.

For the analysis, we used the analyzed preparation samarium-153-oxabifor with a volumetric activity of 1500 MBq / ml.

Whatmann ET-31 chromatographic paper (catalog no: 3031915) was prepared as follows: 3 strips of 15 × 200 mm were cut off, a sample of 0.5-1 μL of drug solution was applied to the start line (15 mm from the edge of the strip) (activity 0,75–1,5 MBq).

The separation of the main product from impurities was carried out in a chromatographic chamber for 35–40 min, until the front of the mobile phase reached a level of 120–140 mm from the starting line. At the end of the process, the strip was removed and dried in air and pasted over it on both sides with a polyethylene film with a sticky layer. For the developed chromatogram, the distribution of the activity of samarium-153 along its length was determined on a γ-radiometric device Ludlum-2200. The last 60 mm strips (from the finish side) were cut and discarded. The remaining part was marked into 10 mm segments, numbered starting from the side of the starting line, and used to determine the radiochemical purity of the preparation. It turns out 14 pieces of segments for measurements. Before measurements, the γ-background was determined using a Ludlum-2200 radiometric device. The background was measured 3 times. Then, each successive chromatogram segment was cut and placed for activity measurement in a Ludlum-2200 γ-radiometric device. The measurement time for each segment is 10 sec.

The radiochemical purity was calculated from the ratio of the areas of the peaks corresponding to the basic and impurity chemical forms of samarium.

3. RESULTS AND DISCUSSION

According to the requirements for the drug, which are used in medical practice, radiochemical purity (the proportion of iodine in the main form - the form of iodide) must be at least 98%.

The results of measurements of sodium iodide preparations with iodine-125 and iodine-131, without a carrier are shown in Table 1.

Table 1: Results of electrophoretogram measurements.

segment №	Number of impulses in 10 sec	
	Iodine-125	Iodine-131
1	208	316
2	205	260
3	202	284
4	208	**430**
5	**220**	**1147**
6	209	**438**
7	226	352
8	232	304
9	208	316
10	**1016**	**3060**
11	**16578**	**19308**
12	**25786**	**850100**
13	**15785**	**180423**
14	208	261

The histograms of the distribution of the activity of iodine-125 and iodine-131, obtained according to the data in Table 1, are shown in Fig. 1 and Fig. 2.

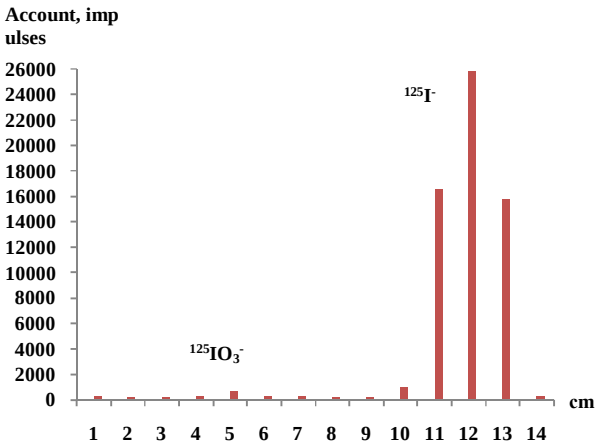

Figure 1: Histogram of the distribution of iodine-125 activity along the length of the electrophoretogram.

The histogram shows the zones of different chemical forms of iodine.

Table 2: Rf value for $^{125}I^-$, $^{125}IO^{3-}$ and $^{125}IO^{4-}$

Chemical form	*Rf*
Iodide $^{125}I^-$ (basic)	0,8 – 0,85
Iodate $^{125}IO^{3-}$ (impurity)	0,3 – 0,4
Periodat $^{125}IO^{4-}$ (impurity)	0,0

As can be seen from the histogram, the minimum distance between the $^{125}I^-$ (main) and $^{125}IO^{3-}$ (impurity) peaks is 4 cm, so their mutual influence is excluded. It is for this reason that the technique gives a reliable result.

Radiochemical purity is calculated by the formula:

$$RCP = \frac{\sum_p 58365}{\sum_t 58491} \times 100\% = 99{,}8\%$$

where:

Σ_p – the sum of pulses in the peak of iodide ions with background subtraction;

Σ_t– total amount of impulses with background subtraction;

RCP - radiochemical purity.

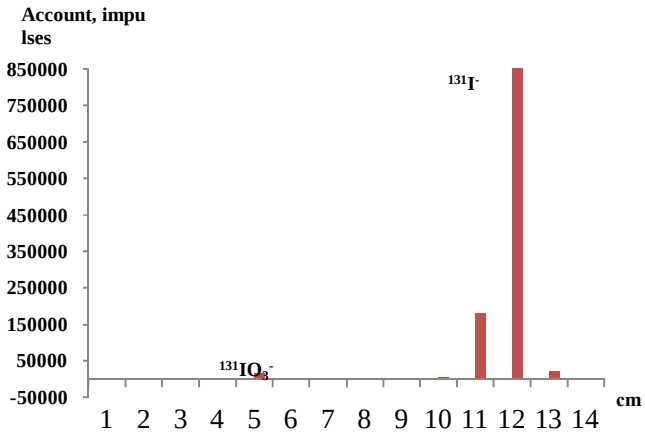

Figure 2: Histogram of the distribution of iodine-131 activity along the length of the electrophoretogram.

The histogram shows the zones of different chemical forms of iodine.

As can be seen from the histogram, the minimum distance between the $^{131}I^-$ (main) and $^{131}IO^{3-}$ (impurity) peaks is 4 cm, therefore, mutual influence is excluded. It is for this reason that the technique gives a reliable result.

Radiochemical purity is calculated by the formula:

$$RCP = \frac{\sum_p 1052091}{\sum_t 1054199} \times 100\% = 99{,}8\%$$

where:

Σ_p – the sum of pulses in the peak of iodide ions with background subtraction;

Σ_t– total amount of impulses with background subtraction;

RCP - radiochemical purity.

The calculated values of radiochemical purity for both drugs were 99.8%.

The radiochemical purity (RCP) of the radiopharmaceutical drug "Samarium-153 oxabifor", according to the requirements of regulatory documents, must be at least 90%.

The results of measurements of the drug "Samarium-153 oxabifor" are shown in table 2.

Table 3: Results of chromatogram measurements.

segment№	Number of impulses in 10 sec
	153Sm-oxabifor
1	**7675**
2	**633**
3	**501**
4	286
5	246
6	209
7	233
8	223
9	224
10	240
11	**611**
12	**616296**
13	**310199**
14	312

Measurement conditions: The length of each segment of the electrophoretogram is 1 cm; Background - 200 pulses.

The histogram of the ^{153}Sm-oxabifor activity distribution obtained from the data in Table 2 is shown in Fig. 3.

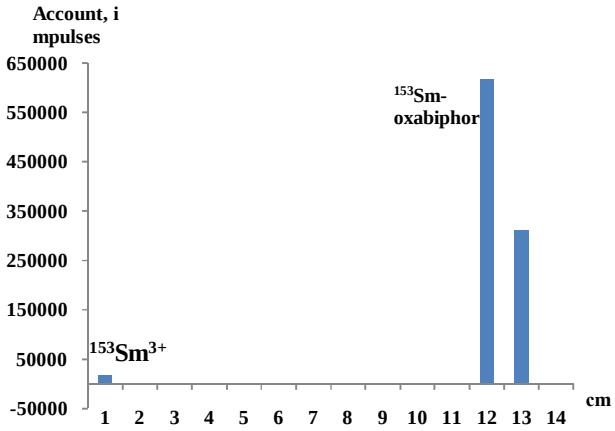

Figure 3: Histogram of the ^{153}Sm-oxabifor activity distribution over the chromatogram.

The histogram shows zones of different chemical forms: $^{153}Sm^{3+}$ ions and ^{153}Sm-oxabiphor complex.

Table 4: Rf value for ^{153}Sm-oxabifor and $^{153}Sm^{3+}$

Chemical form	*Rf*
^{153}Sm-oxabiphor (main form of the complex)	0,9-1,0
Samarium $^{153}Sm^{3+}$ (as impurity)	0,0-0,1

As can be seen from the histogram, the minimum distance between the ^{153}Sm-oxabiphor peak (the main form of the complex) and $^{153}Sm^{3+}$ (as an impurity) is 8-10 cm; therefore, the mutual influence of the peaks is excluded, which indicates the reliability of the results obtained.

The activity corresponding to the peak of the ^{153}Sm-oxabiphor complex referred to the total activity of the strip, taken as 100%, showed radiochemical purity, which should be at least 95% by the expiration date. The radiochemical purity was calculated from the results of three repeated tests based on the data on peak areas minus the background using the following formula:

$$RCP = \frac{\sum_p 926506}{\sum_t 935288} \times 100\% = 99{,}1\%$$

Where:
Σ_p – the sum of pulses at the peak of the ^{153}Sm-oxabifor complex;
Σ_t– total amount of impulses;

RCP - radiochemical purity.

The calculated value of the radiochemical purity of the preparation "Samarium-153 oxabifor" was 99.1%.

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