SYNTHESIS AND PURIFICATION OF 15-(PARA-[^{123}I] IODOPHENIL)-PENTADECANOIC ACID (*IPPDA)

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Lately radiopharmaceuticals, based on fatty acids and labelled by the shortlived isotope iodine-123 (13.3 h) in ω-position, are used abroad for diagnosis of heart diseases [1, 2]. Of these radiofarmaceuticals *IPPDA attracts much attention, because radioactive iodine-123 is firmly bound with phenil ring of a molecule of the acid and is not deiodinated during processes of metabolism [3].

The aims of this investigation were preparation of *IPPDA and its purification without using preparative high pure liquid chromatography.

*IPPDA was produced by a method of halogen isotopic exchange in presence of $CuCl$ [4, 5] and purified by simple column chromatography.

The scheme of synthesis of nonactive IPPDA was following:

$$PhBr \xrightarrow{Li} PhLi \xrightarrow{CuBr} PhCuLi \longrightarrow Br(CH_2)_4COEt \longrightarrow$$

$$\longrightarrow Ph(CH_2)_{14}COEt \xrightarrow{a)KOH,b)H^+} Ph(CH_2)_{14}COOH \xrightarrow{KI,KNO_2,CF_3COOH} IPPDA$$

The process was organized in St-Petersburg's Pharmaceutical institute. This method of synthesis gives a mixture of two isomers 15-(para-iodophenil)- and 15-(ortho-iodophenil) of pentadecanoic acids. The needed para-isomer was separated by repeated crystallization of raw product from hexane (6–7 times). IPPDA is a white-yellow powder (melt.temp.93–95°). Admixture of iodide-ions was also removed from the product by crystallization from a mixture ethylalchocol-water (7 : 1). The analysis showed absence of this admixture (sensitivity of the instrument for iodide-ion 0.01%). The final characterization of the product was performed by ^1H method of NMR.

Isotope iodine-123 for labelling of IPPDA was produced at LNPI synchrocyclotrone of 1 GeV protons. The method is based on irradiation of Cs-target, extraction on line Xe-isotopes from the target by a He-stream, preliminary purification and absorption in original special trap at -196°C for $6h + 12h$ of decay.

The trap is made of glass and filled with SiO_2 (Silochrom-S-80 or SCH-1); at the end of trap a small quantity of Al_2O_3 is added for absorbing tellurium isotopes, which appear during decay of radioactive xenone isotopes in the trap (Fig.1).

The main advantages of such a trap are 100% efficiency for sorbing Xe-isotopes from He-stream and also quantitative retention on oxide of aluminium Te-isotopes during elution of ^{123}I from the trap.

For elution of iodine-123 from the trap we used a solution of 1% NH_4OH. The process of ^{123}I elution is presented in Fig.2. It is important, that ^{123}I is removed from the trap with radiochemical yield 94–95% and ~90% of it is collected in a volume 1 ml. Fig.2 also shows, that radiochemical purity of ^{123}I is high enough (~90% in a form of iodid-ions). All these factors make the synthesis of *IPPDA easier and faster.

The obtained solution with ^{123}I is dried in a vial using a rotational evaporator at 100°C in vacuo. Then 1 ml of ethylalhochol is added to the dried precipitate and 1.5–2 μg $CuSO_4$ in H_2O solution (1–2 drops), 3 μg $SnSO_4$ and finally 1–2 mg of IPPDA. The vial is germetized

with a rubber cork and *Ar*-stream is passed through the reacting mixture for removing oxygen.

Time of the mixture heating (100°C) is one hour.

Labelled products of the reaction are presented in Fig.3. (TLC-method [6]). It is shown, that besides *IPPDA there are many other radioactive products.

$^{123}I^-$ and $^{123}IO_3^-$ removing from the reaction mixture was achieved by passing through a column, filled with anionite ARA-8P.

Purification of nonionic compounds ($^{123}I_x$ etc. was performed by passing solution without $^{123}I^-$ and $^{123}IO_3^-$ through a column (20 cm long and 8 mm wide) filled with Sylipore (0.125–0.165 mm). Series of operations was as follows:

1) washing the column by petroleum ether (35–60°) (PE);
2) introducing *IPPDA in 1 ml of hexane;
3) washing with 5 ml PE;
4) washing with 8 ml mixture PE and ether (E) (19.8:0.2);
5) washing with 6 ml mixture PE-E (19.5:0.5);
6) finally *IPPDA is eluted with mixture of PE-E (15:5).

The purified *IPPDA is depicted in Fig.4. The radiochemical purity of *IPPDA ≥98%.

The synthesized product was analyzed by TLC-method as well as by neutron activation. There were no *Cu* and *Sn*, which were used when preparing *IPPDA.

In general, it is clear, that *IPPDA may be used for experimental investigation of heart in a form for injection.

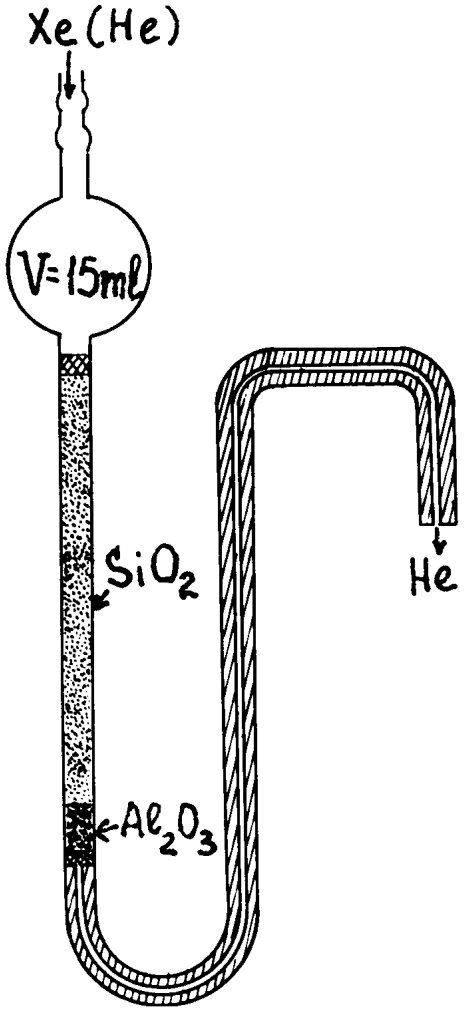

Fig.1. Trap for xenone radioisotopes

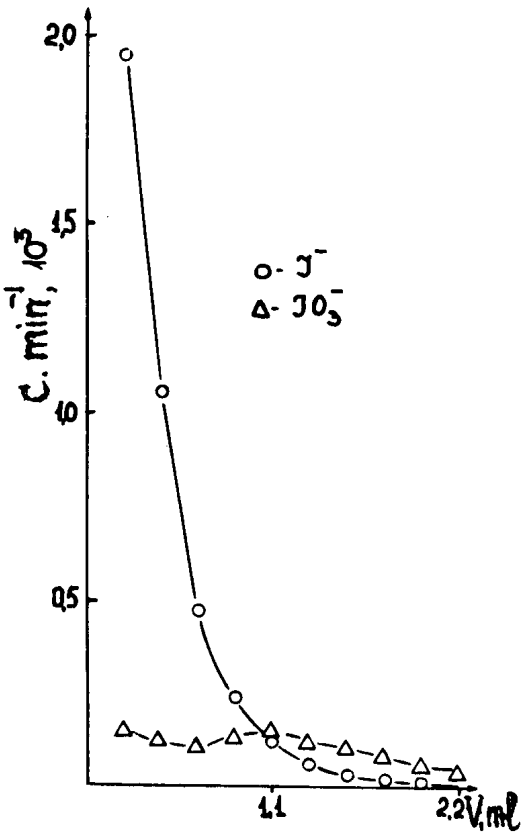

Fig.2. Curve for elution of iodine-123

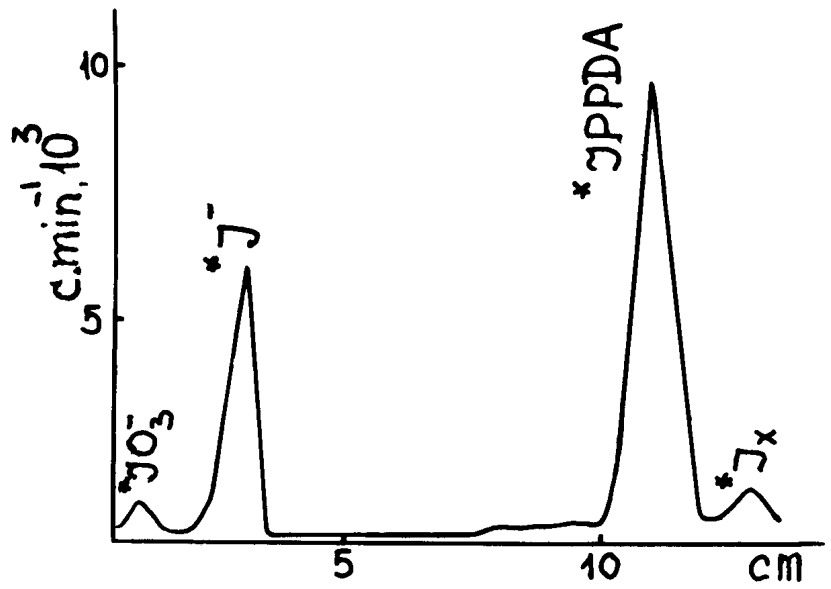

Fig.3. Labelled products of reaction (TLC)

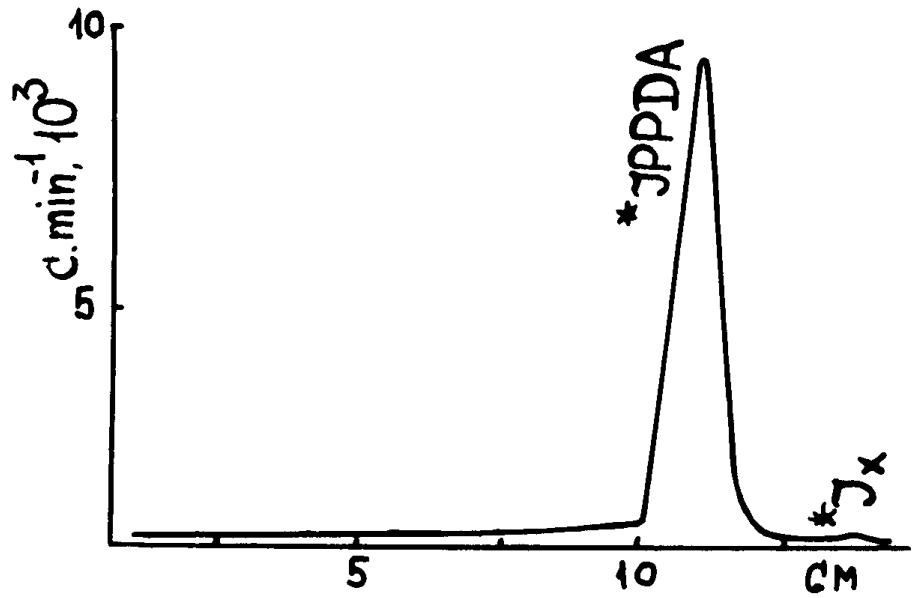

Fig.4. Purified *IPPDA (TLC)

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