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Pharmaceutical development of the theurapetic radiopharmaceutical based on β-emitting samarium-153 in heat-sensitive carrier for brachytherapy of tumors of various location

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The present development is aimed at creation of thermo-collapsing radiopharmaceuticals for brachytherapy based on thermo-sensitive copolymers with chelated beta-emitting radionuclide 153Sm. The preparation is a polymer solution and is made of two components, each loads individual function.
The task set in this development is solved with component-wise division of the radiopharmaceutical's key functions. Primarily, the first functional subsystem is prepared: this is a thermo-sensitive copolymer of n-isopropylacrylamide and allylamine which is exposed to etherification on aminogen groups by the chelating agent of diethylenetriaminepentaacetic acid dianhydride, and to the following labeling of 153Sm3+ due to formation of chelate complexes. Separation of the labeled copolymer component from low-molecular active and inactive compounds in the reaction mixture is performed by elution with acetate buffer on a chromatographic column filled with swollen sephadex. Column effluent containing active copolymer fractions actually is the first functional system which serves as a hybrid solvent to prepare a semidelute solution of the polymer –gelifier. Gelifier's role is to build a fluctuation quasi network which is formed by contacts of links from different chains.
Auxiliary materials such as copolymer-carrier and polymer-gelifier are responsible for formation of the required conditions in the preparation to hold the active substance tightly by creation a firm compact gel, while acetate buffer and salt component provide the required pH and isotonicity of the solution.
Action mechanism is the following –radiopharmaceutical solution after intratumoral injection at the injection site quickly achieves the body temperature and due to self-collapsing of the heat-sensitive polymer-gelifier turns into a firm polymeric clot. This phenomenon provides fast loss of translational mobility of immobilized radionuclides chelated with linear chains of the copolymer-carrier. As a result, there are formed sources of local therapeutic irradiation which affect cancer cells and destroy them almost without any impact of healthy tissues. When therapeutic action is completed the polymer coils are naturally removed from the body.
There were performed the pre-clinical trials of the radiopharmaceutical for brachytherapy of a number of prostate malignancies and other solid tumors. According to the pre-clinical trials results the preparation is recommended for clinical trials for local therapy (brachytherapy) of tumors of various location. First phase of clinical trials is reasonable to be performed with patients of the one clinical entity of the disease –prostate cancer.
The preparation injection should be performed intratumorally and to the several tumor points (at the rate of 1 injection / 1 cm3 of tumor tissue), 0.1 ml in volume. Recommended dosage of the injection for patients with average body weight (70 kg) is 1.6 GBq.

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