RADIOPHARMACEUTICALS ON THE BASE OF TECHNETIUM-99m IN THE NEXT DECADE

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One of the main positions, which determine the level of Nuclear Medicine state and development, is the possibility to choose and to get radiopharmaceuticals (RP) for concrete clinical situation.

In the closing half of the past century technetium-99m was the most used radionuclide in the world and each country. It is due to the excellent coincidence of nuclear-physical and chemical properties of the radionuclide. So it is clear that ^{99m}Tc-radiopharmaceuticals will be used more and more in all directions of nuclear medicine.

The great number of RP such as ^{99m}Tc-DTPA (diethylenetriaminpentaacetate), ^{99m}Tc-MDP (methylenediphosphonate), ^{99m}Tc-MAG_3 (mercaptoacetyltriglycine), ^{99m}Tc-MIBI (methoxyisobutylisonitryl) and many others became useful in daily routine clinical practice and it will be so in future. These RP and special methods of radionuclide diagnostics are of considerable current use also in paediatric practice. Last decade novel ^{99m}Tc-RP were developed. Most of them are labeling peptides, which bind up with specific cell membrane receptors and provide in vivo high level of specificity and sensitivity in obtained diagnostic information.

^{99m}Tc-labelled peptides were described to be useful in vitally important clinical trends:

Oncology - octreotide, deptreotide, vapreotide, bombesine analogues, MSH (melanotropin stimulation hormone) analogous, neurotensin, calcitonin, VIP (vasoactive intestinal peptide) and others;

Cardiology and angiology - annexin V, endothelin analogous, apticide, bitistatin and others.

One of the last modern and important trends - **RP for the imaging of the inflammation and infection:** interleukine-2,8, leucocyte-avid ^{99m}Tc-labelled peptide (P483H), containing heparin-binding platelet factor-4 fragments, antimicrobal peptides and others.

There are many examples in the literature. First clinical results with such RP are extremely encouraging.

Compared with larger molecules, like proteins and MoAbs, peptides are rapidly taken up and retained in target tissues, in accordance with usually rapid plasma clearance due to the

renal excretion. At the same time they are not usually immunogenic and have high receptor binding affinity.

There are some methods for peptide labeling with ^{99m}Tc:

- *Direct labeling (S-S bounds)*

The method includes both reduction of ^{99m}Tc and peptide S-S- moieties followed by binding of the reduced Tc with thiol, carboxyl or amino-groups of peptides. $SnCl_2$ in a tartrate/phthalate buffer or Sn-glucoheptonate or sodium ditionite are used for the ^{99m}Tc-reduction. The most interesting is the method of direct incorporation of $[^{99m}Tc(CO)_3(H_2O)_3]^+$ - cations into peptide molecules.

- *Via chelators (post-synthesis conjugation of metal chelator)*

Chelators included N_2S_2, N_3S or N_4-donor groups, which form five coordinated Tc-complexes, are used for such methods.

- *Incorporation of a metal chelator during the synthesis*

HYNIC (6-hydrozinenicotinamid) was appeared to be more useful for this purpose.

A particularly attractive approach is to use mixed-ligand systems (for example, with tricine, EDDA, phosphines and others), in which variations of the ligands can radically alter the biodistribution pattern.

Thus one can assume that the main directions in the development of the new radiopharmaceuticals in the next decade would be:

- an active search of the new synthesis and investigation of the physical-chemical properties of the mixed-ligand technetium complexes using different combination of biologically active ligands, chelators and co-ligands;
- study of the biodistribution of the synthesized complexes and their stability in vitro and in vivo.

The synthesis and investigation of the analogues compounds of rhenium is also the main exceptionally urgent direction both in the view of the establishment of the chemical analogy or its absence and in the view of the development of the new radiopharmaceuticals on the base of ^{186}Re and ^{188}Re for radionuclide therapy.