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Modified Inorganic Nanoparticles as a Vehicles for Alpha Emitters in Radionuclide therapy

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Alpha particle emitting isotopes are in considerable interest for radionuclide therapy because of their high cytotoxicity and short path length [1]. Unfortunately, all available emitters have serious disadvantages: ^{211}At forms weak bond with carbon atoms in the biomolecule and in the case of ^{212}Bi , ^{213}Bi and ^{226}Th short half-life often limits the application of these nuclides. However, the short half-life of ^{212}Bi and ^{213}Bi could be effectively lengthened by binding the parent radionuclide ^{212}Pb ($t_{1/2} = 10.6$ h) or ^{225}Ac ($t_{1/2} = 10$ d) to a biomolecule, thereby effectively extending the use of short half-life ^{212}Bi and ^{213}Bi . In addition, in vivo generator delivers much greater dose per unit of administered activity compared to ^{212}Bi and ^{213}Bi alone. Also three radium radionuclides ^{223}Ra , ^{224}Ra and ^{225}Ra exhibit very attractive nuclear properties for radiotherapy, but the lack of appropriate bifunctional ligand for radium was the reason why these radionuclides did not find application in receptor targeted therapy. In our studies we investigated the use of TiO_2 nanoparticles as potential carriers for $^{225}\text{Ac}/^{213}\text{Bi}$ in vivo generator and nanozeolite particles as vehicles for $^{223,225}\text{Ra}$ radionuclides.

The TiO_2 nanoparticles have unique properties like: high specific surface, high affinity for multivalent cations and simple way of synthesis, which are useful in the process of labelling. Commercially available (e.g. P-25 Degussa) and synthesised in our laboratory nanoparticles were used in experiments. The nanoparticles were characterized by TEM, SEM, DLS and NanoSight techniques.

In our experiments we tested two different methods of labeling. The first one was based on the possibility of formation strong bonds with certain cations on the surface of the nanoparticles. In the second one, TiO_2 nanoparticles were doped with ^{225}Ac during the process of synthesis. In both cases we obtained high yields of labelling (>99%).

Afterwards, the stability of labelled nanoparticles was examined in 0.9 % NaCl, 10-3 M EDTA, solutions of biologically active substances (cysteine, glutathione) and human serum. In case of TiO_2 nanoparticles labelled with Ac-225, which was built in the crystalline structure, the leakage of ^{225}Ac and its daughter radionuclides was not significant in any of solutions, even when the incubation time was extended to 10 days. In the case of nanoparticles with adsorbed ^{225}Ac on surface the leakage in serum was slightly higher, but still insignificant. Also the NaA nanozeolite as a carrier for radium radionuclides has been studied. ^{223}Ra , and ^{225}Ra , the α -particle emitting radionuclides, have been absorbed in the nanometer-sized NaA zeolite through simple ion-exchange. $^{223,225}\text{Ra}$ -nanozeolites have shown very good stability in solutions containing: physiological salt, EDTA, amino acid and human serum. To make NaA nanozeolite particles dispersed in water their surface has been modified with silane coupling agent containing poly(ethylene glycol) (PEG) molecules.

To obtain conjugates specific for receptors on glioma cancer cells short peptide substance P were covalently attached to the PEG- TiO_2 and PEG-nanozeolite surface. The obtained bioconjugate were labeled with ^{225}Ac and ^{223}Ra respectively. The serum stability of labelled bioconjugates was similar or little better than unmodified nanoparticles. The cell affinity, cytotoxicity and biodistribution studies of the obtained radiobioconjugate are in progress.

References

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