Nanozeolite bioconjugates labeled with 223Ra for targeted alpha therapy

Abstract:
Introduction: Alpha particle emitting isotopes are of considerable interest for radionuclide therapy because of their high cytotoxicity and short path length. Among the many α emitters, 223Ra exhibits very attractive nuclear properties for application in radionuclide therapy. The decay of this radioisotope and its daughters is accompanied by the emission of four α-particles, releasing 27.9 MeV of cumulative energy. Unfortunately the lack of an appropriate bifunctional ligand for radium has so far been a main obstacle for the application of 223Ra in receptor targeted therapy. In our studies we investigated the use of nanozeolite–Substance P bioconjugates as vehicles for 223Ra radionuclides for targeted α therapy. Methods: The sodium form of an A-type of nanozeolite (NaA) was synthesized using the template method. Next, the nanozeolite particles were conjugated to the Substance P (5–11) peptide fragment, which targets NK-1 receptors on glioma cells. The obtained bioconjugate was characterized by transmission emission spectroscopy, thermogravimetric analysis and dynamic light scattering analysis. The NaA-silane-PEG-SP(5-11) bioconjugates were labeled with 223Ra by exchange of the Na+ cation and the stability, receptor affinity and cytotoxicity of the obtained radiobioconjugates were tested. Results: The 223Ra-labeled nanozeolite bioconjugate almost quantitatively retains 223Ra in vitro after 6 days, while the retention of decay products varies from 90 to 95%. The synthesized 223RaA-silane-PEG-SP(5-11) showed high receptor affinity toward NK-1 receptor expressing glioma cells and exhibited a high cytotoxic effect in vitro. Conclusions: Substance P functionalized nanozeolite-A represents a viable solution for the use of the 223Ra in vivo generator as a therapeutic construct for targeting glioma cells.

Authors:
PIOTROWSKA A
MECYNSKA-WIELGOSZ Sylwia
MAJKOWSKA PILIP Agnieszka
KOZMINSKI P
WOJCIUK Grzegorz
CEDROWSKA Edyta
BRUCHERTSEIFER Frank
MORGENSTERN Alfred
KRUSZEWSKI M.
BILEWICZ Aleksander

Publication Year:
2017