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Determining the retention of recoiling daughter nuclides of 225Ac in polymeric nano-carriers

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Alpha radionuclide therapy has a great potential in the fight against cancer as proven by a large number of pre-clinical and clinical studies. In vivo generators capable of delivering a highly efficient cascade of alpha particles are also steadily gaining importance. At the moment 225Ac is the most relevant radionuclide that can serve as an in vivo generator, providing four alpha particles with a total energy of 28 MeV. However, due to the recoil effects the daughter recoil atoms, most of which are alpha emitters as well, receive energies that are much higher (> 100 keV) than the energies of chemical bonds (typically around 2- 8 eV) resulting in decoupling of the radionuclide from common targeting agents such as antibodies. The escaped daughter atoms are free to spread in the body and can cause severe harm to healthy tissue, which is considered to be the major challenge in alpha radionuclide therapy. Here, we demonstrate that polymer vesicles (i.e. polymersomes) can retain recoiling daughter nuclei based on an experimental study examining the retention of 221Fr and 213Bi when encapsulating 225Ac. Furthermore, we examined the retention of 209Pb, the daughter nuclide of 213Po, when enclosing 213Bi in the vesicles.
Polymersomes composed of poly(butadiene-b-ethylene oxide) were successfully loaded with 225Ac and 213Bi reaching an efficiency of more than 60 % in both cases with negligible loss. The recoil retention of 221Fr and 213Bi were found to increase with the size of the polymersomes, reaching respectively 69 ± 1.5 % and 53 ± 4 for polymersomes having a diameter of 800 nm. The retention of 209Pb subsequent to a single recoil step (i.e. 213Po decaying to 209Pb) was found to be 59 % ± 17 in the case of polymersomes having the same diameter as reported above. Finally, the polymersomes were found to accumulate around the nucleus in tumor cells (HeLa cell line) which is expected to further reduce the harm caused by recoiling alpha emitters, provided that the nano-carriers have favorable pharmacokinetics.

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