IAEA-CN-310/324

Direct Radiolabeling of PVP-Nanogel from 99mtco4- Reaction

Tatiana Santana Balogh, Fabio NAVARRO MARQUES, Sławomir Kadłubowski, Ademar Benevolo Lugao

Instituto de Pesquisas Energéticas e Nucleares IPEN-CNEN, São Paulo, Brazil

Nanogels are considered promising drug delivery systems for different pathologies, mainly associated with neurological disease, by intranasal administration since drug transport occurs via the olfactory nerve, causing rapid delivery to the brain. The present work aimed to evaluate a protocol for 99mTc labeling of poly(N-vinylpyrrolidone) (PVP) nanogel synthesized by an electron beam for future in vivo biodistribution assays. 10 mM PVP K-90 solution saturated with N2O was irradiated by e-beam using a dose of 7 kGy and a dose rate of 5.35 kGy/s. Nanoparticles characteristic was evaluated by DLS technique to determine the Rh and SLS to determine the Mw and Rg. Rg/Rh and ρcoil were calculated. The sample was morphologically characterized using AFM. The same analyzes were performed with a non-irradiated PVP solution. Radiolabeling was performed by mixing 0.55 mg of SnCl2.2H2O in 50 µL of HCl 0.1 M with (A) 450 µL 0.2 M NaOAc buffer, pH 4.1; (B) 200 µL 0.2 M NaOAc buffer, pH 4.1 and 0.5 M NaHCO3 buffer, pH 7.26; (C) filtered solution B in a 0.22 µm syringe filter. To the solutions (A), (B), and (C) were added 200 µL of nanogel (8.9 mg of PVP K-90), 100 µL of 99mTcO4- (860-980 µCi), and the samples were stirred at 500 rpm for 90 minutes at room temperature. The reaction was assessed by W3MM paper/acetone chromatography at the end of the process. All solutions were filtered through a 0.22 µm filter to remove 99mTcO2, as a previously validated process, and the radioactivity in the filter and the solution was measured. Finally, the solutions were concentred in the Amicon® (10 kD), and the radioactivity of the filtered and retained solution were measured too. The solution remaining on the filter was diluted with 300 µl of purified water and the concentration process was repeated twice. Filter content and the sum of filtered solutions 1 and 2 had the radioactivity measured to check labeling efficiency. Nanogel was obtained with an average for Rh of 12.49 nm, Rg of 6.8 nm, Mw of 1.32 x 106 g/mol, ρcoil of 786.98, and Rg/Rh of 0.620. High relief spherical structures were observed in the AFM images instead of the low roughness film observed in the non-irradiated PVP solution. Chromatographic analysis of the sample prepared only with NaOAc buffer (final pH 3.8) and of the sample with the mixture of buffers without previous filtration (final pH 6.8) indicated, respectively, 99.89 and 99.68% associated with the formation of 99mTc-PVP nanogel or 9mTc-colloid. In contrast, the sample prepared with the mixture of buffers and previously filtered (final pH 6.8) showed 80.10% of nonreduced 99mTcO4. Filtration results at 0.22 µm showed that the 9mTc-colloid remains 100% retained in the filter, while free 99mTcO4 and 99mTc-PVP nanogel are filtered. Amicon® filtration confirmed 95.75% and 92% of 99mTc-PVP nanogel formation in the samples with NaOAc buffer and a mixture of buffers without previous filtration, respectively. It was possible to synthesize nanogel by electron beam, obtaining an average Rh of 12.49 nm. The labeling process with 99mTcO4- showed a high radiochemical yield in samples prepared with NaOAc buffer and a mixture of buffers without previous filtration.