SYNTHESIS OF RADIOACTIVE GOLD 198 NANOPARTICLE ENCAPSULATED BY ALBUMIN AS CANCER THERANOSTICS AGENT

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Resumo:
Albumin is a natural drug nanocarrier as it has equivalent diameter of about 5 nm and has natural affinity for hydrophobic and hydrophilic drugs. They can be bound in a reversible way and the delivery controlled by endogenous mechanism. Albumin can be crosslinked by radiation alternatively to conventional systems, in such way that dialdehydes or toxic chemicals are avoided. On the theranostic side, radioactive ions are commonly employed for diagnostic and therapeutic applications. As an example, radioactive gold nanoparticles are currently employed in radiotherapy whether to increase local dose deposition in tissue during radiotherapy or as a local emitter of gamma and beta rays. The radioactive properties of gold include: 198Au (?max=0.96 MeV; t1/2 = 2.7 days) and 199Au (?max =0.46 MeV; t1/2 = 3.14 days), making it a strong candidate for theranostics . Conjugation of such materials with sugars, peptides, antibodies, proteins among others is routinely used nowadays for targeting. While radioactive nanoparticles can offer a much higher dose payload than ions for therapy and diagnostic, in addition to the the huge surface to bind targeting species presented by the nanoparticles, functionalization with proteins may potentially increases the particle uptake by tumors or tissues. The main purpose of this work was the development of one pot in situ synthesis of radioactive gold 198 nanoparticle encapsulated by albumin for application in cancer Theranostics. While crosslinked albumin may provide a nontoxic coating on AuNPs with a controllable hydrodynamic diameter, conventional AuNP can be activated by nuclear reactor to produce 198AuNP. The gamma or beta radiation originated from the gold nanoparticle was used to crosslink the Albumin layer. The use of a radioactive particle able to emit radiation for crosslinking of the Albumin layer and simultaneous theranostic application was tried for the first time. The elegant procedure and ease of produc¬tion combined with the properties of 198Au and the safety of HSA-198AuNP make this new particle an exciting advancement in cancer therapy and diagnosis. For such purpose, radioactive tetrachloroauric acid H198AuCl4 was produced from gold foils of high purity by neutron irradiation in IPEN research nuclear reactor. 198AuNP/BSA were synthesized by stirring aqueous solutions of BSA and radioactive tetrachloroauric acid H198AuCl4. The reaction mixtures were stirred continuously at 25 °C. The color of the mixture become purple-red from pale yellow within 15 minutes indicating the formation of gold nanoparticles. The reaction mixture was stirred for an additional 20 minutes. The 198AuNP/BSA formed were characterized by UV-Vis spectrophotometry, DLS and TEM analysis. The spectra were recorded at first day of preparation and after 1 month. Radioactive gold nanoparticle encapsulated by crosslinked Albumin was prepared in reproducible way. The gold nanoparticle core size measured by TEM was about 20 nm and about 60 to 70 nm with the albumin layer as measured by DLS. Bityrosine formation was measured by fluorescence and it was an evidence of intramolecular and intermolecular crosslinking. In conclusion the technique was suitable for the in situ production of the crosslinked albumin functionalized radioactive gold nanoparticles. Acknowledgements The authors would like to thank Conselho Nacional de Desenvolvimento Cientifico e Tecnológico (CNPq) project number 402887/2013-1 and 401438/2014-7 and International Atomic Energy Agency (IAEA) (CRP code F22064) for financial support.