Preparation and Surface Modification of Europium Doping Hydroxyapatite Luminescent Nanoparticles for Cell Labeling

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ARS 2016

08

The sensitivity of the detection techniques used in biological analysis primarily depends on the fluorescence labelling agent. A new generation of fluorophores such as Europium doped hydroxyapatite nanoparticle (Eu-HAPnps) has the ability to emit near infrared radiations which are of low absorptivity by tissue chromophores and especially suitable for biological system imaging.

Eu-HAP luminescent nanoparticles were prepared by co-precipitation method with the aim of seeking a compromise proposal for achieving high luminescence and nano-scale particles. Hence, the effect of reaction temperature and Eu^{3+} doping content on luminescence property as well as phase composition, crystal size and crystallinity of Eu-HAPnps were investigated. The 2% Eu doping content and reaction temperature of 121^0C were preferred for preparing Eu-HAPnps with strong luminescence.

We synthesised two sets of well stable Eu-HAPnps in the presence of different concentration of a low molecular weight capping agent, Polyacrylic acid (PAA) and different concentration of sodium heparin to investigate the best stabiliser and its productive concentration. Results of this characterization study showed that 0.3 PAA was an effective stabiliser concentration.

Furthermore, we also investigated on the modifications made by pluronic F 127 and targeting conjugation of folic acid on Eu-HAPnps. Thereafter, a tumour specific targeting ligand, folic acid is conjugated onto PF127-PAA-Eu-HAPnps to produce a multifunctional hydroxyapatite nanoparticle. According to characterization observations of synthesised nanoparticles, PF127 and its derivatives were grafted onto PAA-Eu-HAPnps by the chemical conjugation to yield more stable and smaller HAP clusters which could be stored in lyophilized form and rapidly re-suspended in double distilled water. Moreover, the surface coating polymer on PAA-Eu-HAPnps was also the determining factor for the efficiency of cellular uptake. FA-PF127-PAA-Eu-HAP having the FA moiety showed a better cellular internalisation in the folic receptor overexpressing cells. The biocompatibility of Eu-HAPnps was studied by hemolysis test and cytotoxicity experiment. Results showed that Eu-HAPnps has no hemolysis and cytotoxicity to L02 human normal liver cells. Therefore, the targeting experiment in vitro demonstrates that folic acid targeting Eu-HAPnps shows much higher cell uptake than non-folic acid conjugated Eu-HAPnps.

Keywords: hydroxyapatite, europium, nanoparticles, luminescent