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Chlorin e6 loaded lactoferrin nanoparticles for enhanced photodynamic therapy

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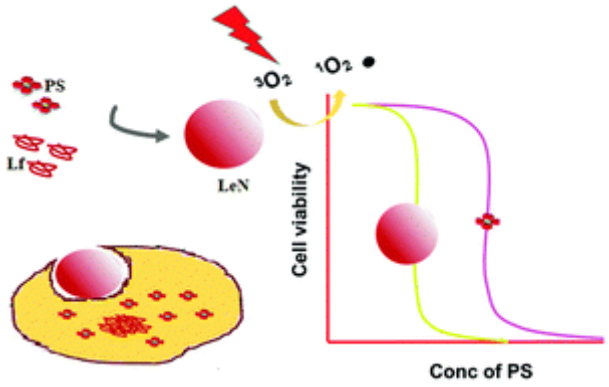
Abstract

Photosensitizer (PS) mediated Photodynamic Therapy (PDT) is a preferred treatment modality for certain cancers. Some of the factors limiting the expansion of PDT to other clinical conditions are the aggregation of hydrophobic PS in aqueous media and the inefficient biodistribution of photosensitizers. Formulations containing the PS have overcome some of the limitations by controlling aggregation-dependent quenching of PS and by improving the biodistribution of PS. We report a photosensitizer delivery system with protein nanoparticles that does not involve any chemical modifications. Using Lactoferrin, an iron-carrying milk protein, as sole matrix and Chlorine e6 (Ce6), an FDA-approved PS. The nanoparticles were prepared by the water-in-oil emulsion method. The spectral and physical properties of the particles were analyzed. Production of reactive oxygen was enhanced in the formulations (LeN) compared to free Ce6 as indicated by the water-soluble and -insoluble dyes. LeN show a specific Ce6 release at low pH, which is an advantage in the acidic environment of tumors and in endosomes. The uptake and intracellular concentrations of Ce6 by SK-OV-3, estimated by confocal microscopy, FACS and fluorescence spectroscopy, were significantly higher with LeN compared to free Ce6. Upon light exposure, LeN showed a substantial decrease (>4 times) in Ce6 requirement compared to free Ce6 in its ability to cause light-mediated cell death in the SK-OV-3 and MDA-MD 231 cells. LeN were shown to be non-toxic to the cells even at concentrations ten times that used in the PDT study. Safety, efficient loading and significant uptake by cells and more importantly a significant decrease in IC_{50} values demonstrate that LeN have potential in PDT.


PS
Lf
LeN
Cell viability
Conc of PS