Photoporphyrin IX- superparamagnetic iron oxide nanoparticle (SPION) nanoclusters for MR imaging and photodynamic therapy

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Introduction: Photodynamic therapy (PDT) has recently attracted widespread attention as a non-invasive and highly selective approach for cancer treatment. Many nanoparticle-based photosensitizers (i.e. nanophotosensitizers) have been developed due to the nanoparticle unique properties. However, one of the major challenges for most nanophotosensitizers is the low capability for their clinical translation since they cannot be produced in large-scale. In this work, we used a facile approach for the preparation photoporphyrin IX (PpIX) SPION nanoclusters. It was found this simple method could produce nanophotosensitizers with a high PpIX loading efficiency, a high loading capacity, stable behavior, high potency, and mass producibility. Moreover, PpIX- SPION nanoclusters were shown to cause a significant reduction in 4T1 tumor growth rate compared with both free PpIX and PpIX-loaded PEG-PCL micelles. Considering the simple synthesis, the nanoclusters presented in this work will be a promising agent for fast clinical translation.

Results:

Photoporphyrin IX (PpIX)- superparamagnetic iron oxide nanoparticle (SPION) nanoclusters were prepared. The diameter of SPION utilized here was at 7 nm and demonstrated paramagnetic properties. The as-prepared PpIX SPIO-NPs are highly water soluble. The average diameter of generated nanoclusters was 34.8 nm with a polydispersity index (PDI) of 0.23. TEM was used to determine the morphology of the nanoclusters. As seen in TEM, a narrow distribution of fine spherical structures with tightly packed SPION was observed. Moreover, these clusters maintain a stable size over days based on DLS measurements. *In vitro* release study demonstrated that 25% of adsorbed PpIX was released from nanoclusters in fetal bovine serum (FBS, 37 °C) at 24 hours, while paramagnetism was still maintained based on relaxometry measurements, which agreed with DLS measurements. Relaxometry measurements showed an R2 value of 220.57. MR imaging of nanoclusters showed high T2 signal at the developed concentration on phantom imaging relative to controls. Finally, PDT treatment was carried out using the 4T1 tumor model on Balb/c mice. As expected, outstanding *in vivo* tumor therapeutic efficacy with dramatically delayed tumor growth was achieved using the PpIX SPION nanoclusters as the photodynamic agent following a single dose administration, compared to both free PpIX and PpIX-loaded PEG-PCL micelles.

Conclusion:

In summary, a PpIX SPION nanocluster platform was developed for MRI imaging and photodynamic therapy. Our results suggest that the nanoclusters might represent a promising contrast and photodynamic agent for clinical translation.