Role of Mn2+ Doping in the Preparation of Core-Shell Structured Fe3O4@upconversion Nanoparticles and Their Applications in T1/T2-Weighted Magnetic Resonance Imaging, Upconversion Luminescent Imaging and Near-Infrared Activated Photodynamic Therapy

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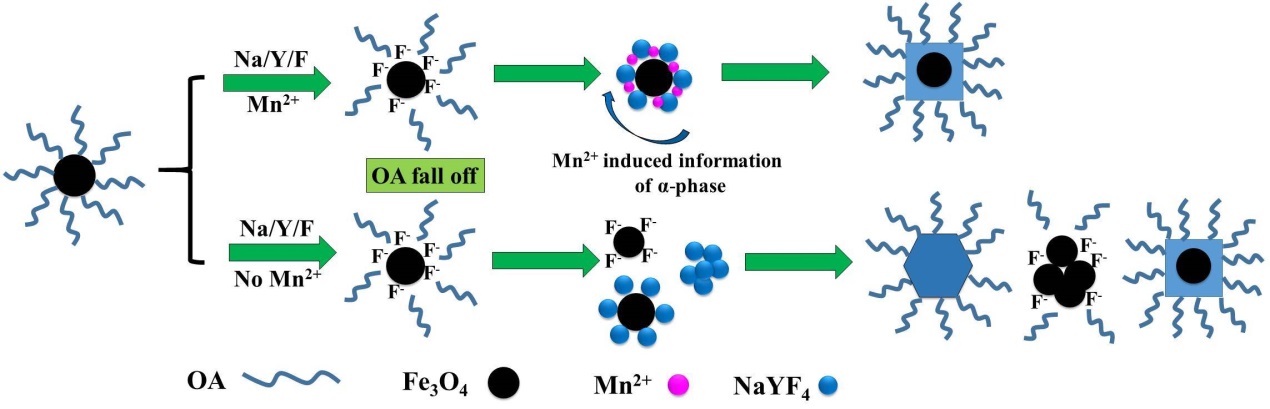
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**Abstract:** Core-shell (C/S) structured upconversion coated Fe3O4 nanoparticles (NPs) are of great interest due to their potential as magnetic resonance imaging (MRI) and upconversion luminescent (UCL) imaging agents, as well as near-infrared activated photodynamic therapy (PDT) platforms. When C/S structured Fe3O4@Mn2+-doped NaYF4:Yb/Er NPs were prepared previously, well-defined C/S-NPs could not be formed without the doping of Mn2+ during synthesis. Here, the role of Mn2+ doping on the synthesis of core-shell structured magnetic-upconversion nanoparticles (MUCNPs) is investigated in detail. Core-shell-shell nanoparticles (C/S/S-MUCNPs) with Fe3O4 as the core, an inert layer of Mn2+-doped NaYF4 and an outer shell consisting of Mn2+-doped NaYF4:Yb/Er were prepared. To further develop C/S/S-MUCNPs applications in the biological field, amphiphilic poly(maleic anhydride-alt-1-octadecene) (C18PMH) modified with amine functionalized methoxy poly(ethylene glycol) (C18PMH-mPEG) was used as a capping ligand to modify the surface of C/S/S-MUCNPs to improve biocompatibility. UCL imaging, T1-weighted MRI ascribed to the Mn2+ ions and T2-weighted MRI ascribed to the Fe3O4 core of C/S/S-MUCNPs were then evaluated. Finally, chlorine e6 (Ce6) was loaded on the C/S/S-MUCNPs and the PDT performance of these NPs was explored. Mn2+ doping is an effective method to control the formation of core-shell structured MUCNPs, which would be potential candidate as multifunctional nanoprobes for future T1/T2-weighted MR/UCL imaging and PDT platforms.

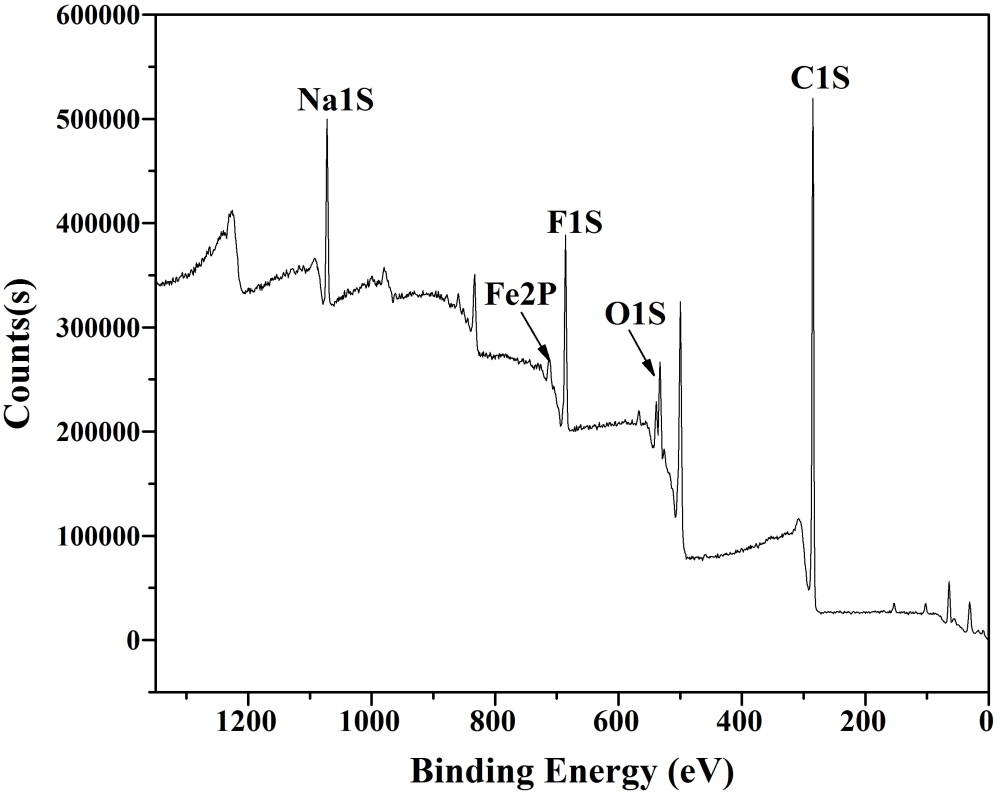
**Keywords:** Mn2+; Fe3O4; upconversion; core-shell-shell; MR/UCL imaging; PDT platforms

**Scheme S1**

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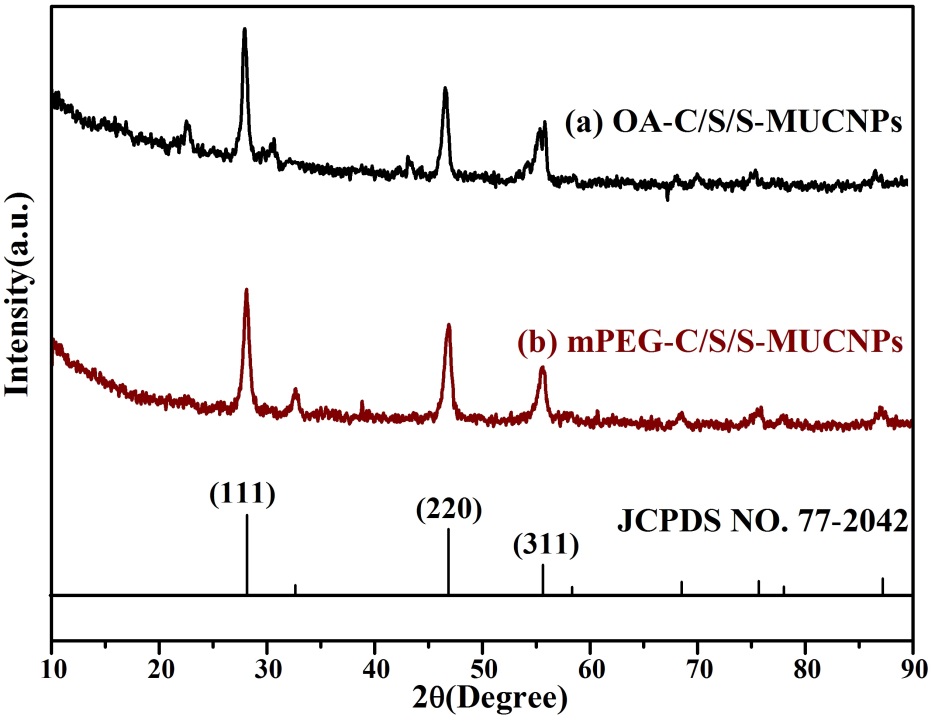
**Scheme S1.** Proposed synthetic mechanism for the formation of Fe3O4@NaYF4 NPs.

**Figure S1**

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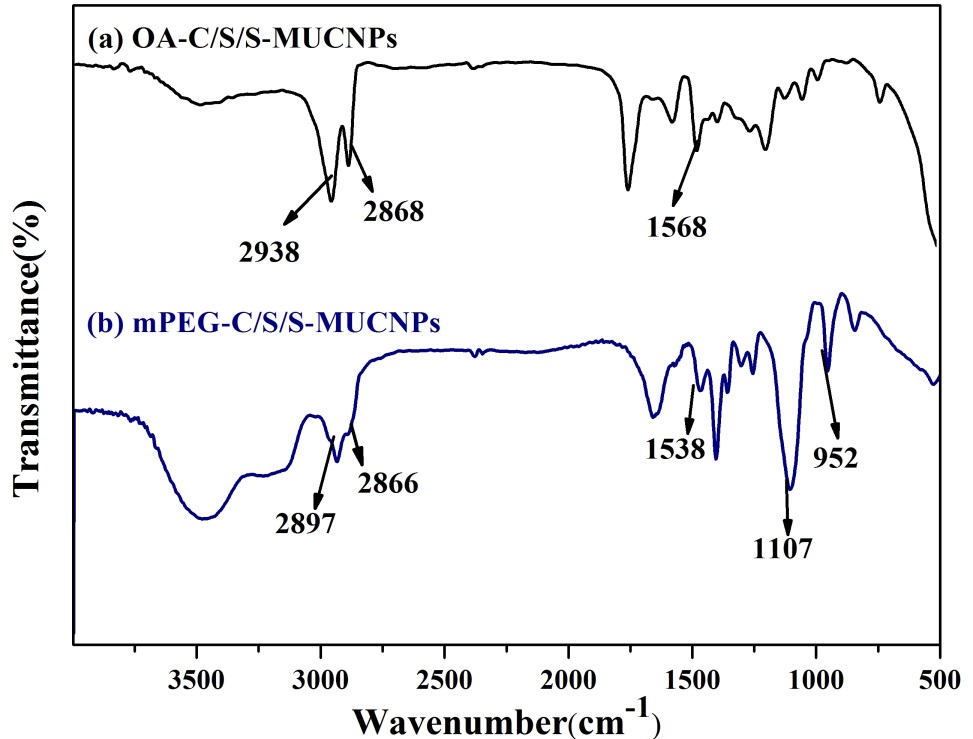
**Figure S1.** XPS spectra of Fe3O4 NPs treated by hydrothermal process in the presence of NaF.

**Figure S2**

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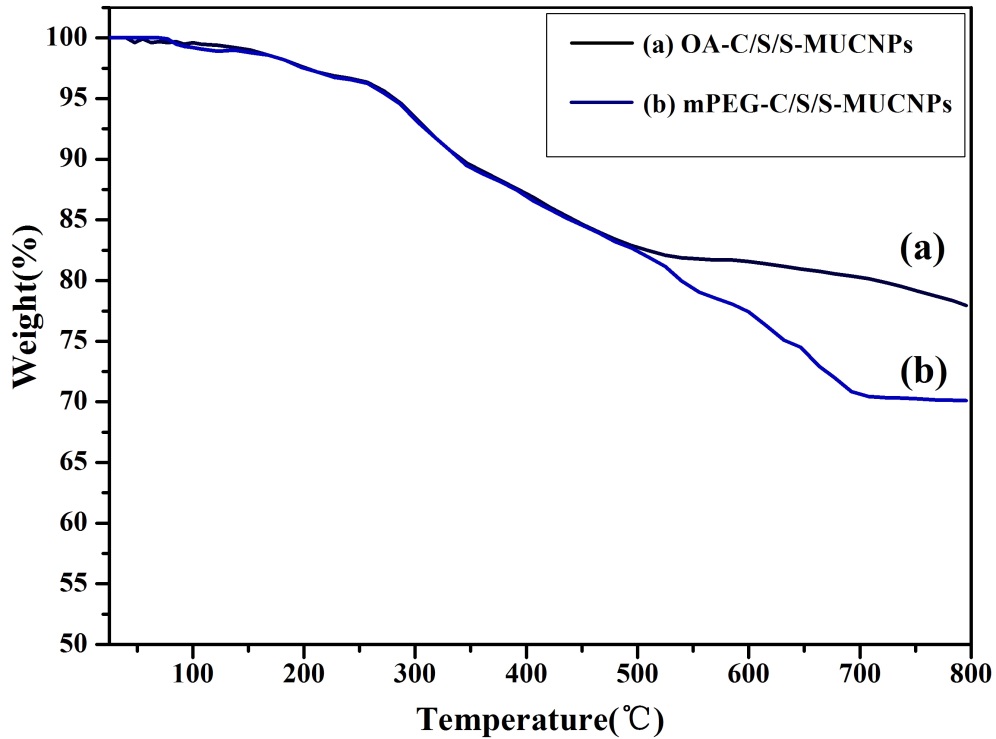
**Figure S2.** X-ray diffraction patterns of OA-C/S/S-MUCNPs (**a**) and mPEG-C/S/S-MUCNPs (**b**).

**Figure S3**

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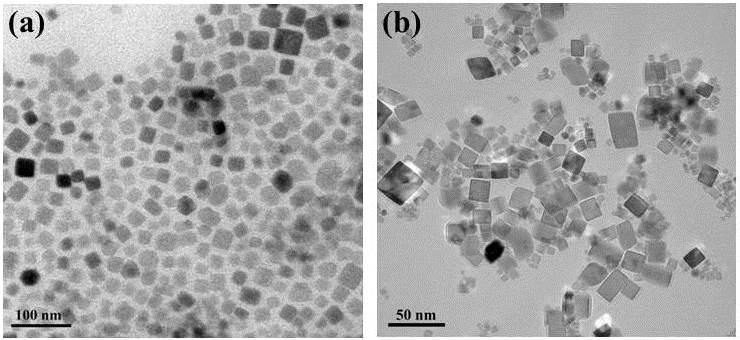
**Figure S3.** FTIR spectra of OA-C/S/S-MUCNPs (**a**) and mPEG-C/S/S-MUCNPs (**b**).

**Figure S4**

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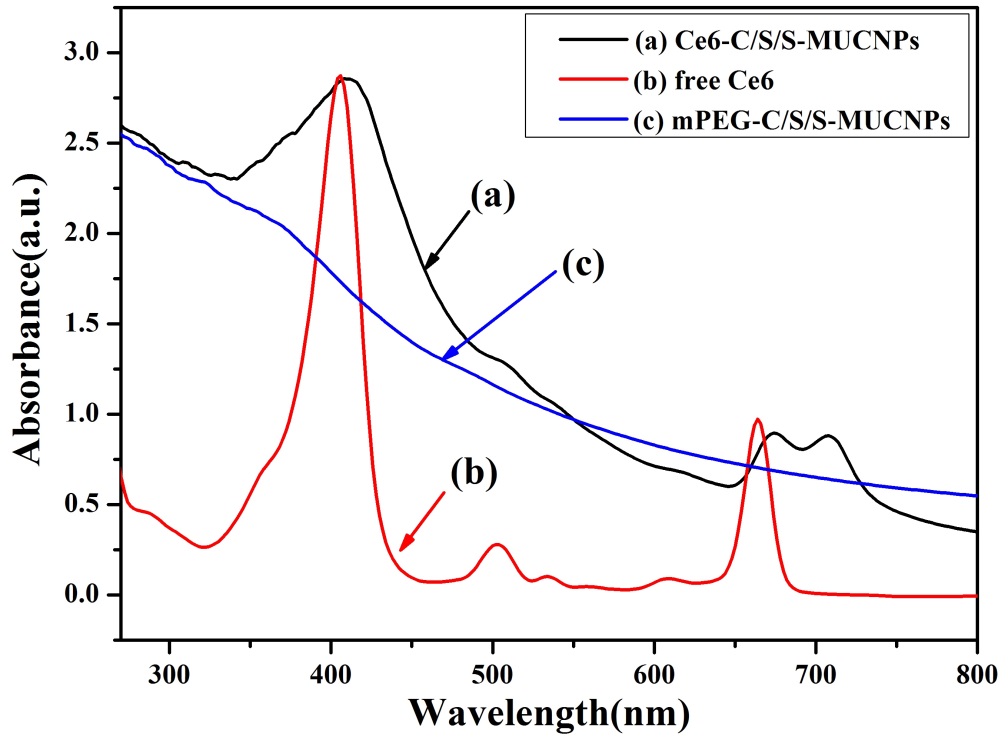
**Figure S4.** TGA curves of OA-C/S/S-MUCNPs (**a**) and mPEG-C/S/S-MUCNPs (**b**).

**Figure S5**

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**Figure S5.** TEM images of OA-C/S/S-MUCNPs (**a**) and mPEG-C/S/S-MUCNPs (**b**).

**Figure S6**



**Figure S6.** UV-Vis absorbance spectrum of Ce6-C/S/S-MUCNPs (**a**), Ce6 (**b**), and mPEG-C/S/S-MUCNPs (**c**).