Study on the polymeric nanosphere with imaging functionality

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ABSTRACT

The aim of this research was to develop a novel contrast agent with magnetic resonance (MR) imaging, fluorescent imaging and drug encapsulation functionalities. This multifunctional vehicle was composed of amphiphilic chitosan (ACD), ZnO and Fe_3O_4 nanoparticles. The structure and magnetic property of the proposed vehicle was characterized via using transmission electron microscopy (TEM), high-resolution transmission electron microscopy (HR-TEM), X-ray diffraction (XRD), superconducting quantum interference device (SQUID).

The ACD-Fe_3O_4 /ZnO polymeric nanospheres could provide valuable to support the design and fabrication of multimodal-image-guided drug carriers.

Keywords: contrast function, drug carriers, drug delivery systems (DDSs), magnetic resonance (MR), fluorescence

1 INTRODUCTION

Many drug delivery systems (DDSs) associating with different functions (i.e., magnetic resonance image-guided delivery, optical image-guided delivery) are developed to diagnose diseases, deliver therapeutic agents and label cell for cancer treatment [1-2].

Recently, there has been focused on multifunctional system or drug vehicles that exhibit multi-functions and applications in their properties [3-5], such as optical, magnetic, electrical and drug-encapsulated. The drug vehicles also can be cell -labeling and anticancer therapies.

Zinc oxide (ZnO) can be effectively used in many important areas, such as ceramic, chemical, electronic, optical, biological and textile [6]. In recent years, many studies have found that ZnO can be used on cell labeling. Zinc oxide has not only a larger excitation energy bands (exciton the binding energy: 60 meV) at room temperature with strong and stable emission but also various advantages such as low toxicity [7,8]. It is expected to be quantum dots (QDs) in different light emission through the adjustment of the QDs size. Many studies also found that zinc oxide demonstrated ability to kill the cancer cells. They show that ZnO have great potential of caner treatment in the biomedical field. [9-11].

The objective of this study is to investigate the image functionality of the ZnO and Fe3O4 polymeric nanospheres. The polymeric nanospheres was developed to encapsulate hydrophobic and hydrophilic agent, exhibit dual-modal imaging functionality. The size of polymeric nanospheres are about 50~200 nm.

2 EXPERIMENTAL METHODS

2.1 Materials

Zinc acetylacetonate, ($Zn(acac)_2$), Iron(III) acetylacetonate ($Fe(acac)_2$), ethanol, hexane and dichloromethane(99%), were used as received. Phenyl ether (99%), benzyl ether (99%), 1,2-hexadecanediol (97%), oleic acid (90%), oleylamine (>70%).

2.2 Synthesis of zinc oxide and iron oxide nanoparticles

The process of zinc oxide (ZnO) nanoparticles synthesis was developed by Liu et al [12]. Zinc oxide nanoparticles were prepared by thermal decomposition methods. The amount of $Zn(acac)_2$ in oleylamine (molar ratio of 1: 100) was heat up to 205℃ with stirring for 1h and cooling to room temperature. The white nanoparticles were washed and centrifuged several times with excess alcohol.

Same as ZnO, superparamagnetic iron oxide were prepared by thermal decomposition methods [13]. The process was developed by Sun et al. $Fe(acac)_2$ (2 mmol) and 1,2-hexadecanediol (10 mmol) were mixed with oleylamine (6 mmol), oleic acid (6 mmol) and phenyl ether (20 ml) was heat up to 245℃ for another 30 min.

2.3 Preparation ACD-Fe_3O_4 /ZnO polymeric nanospheres

Polymeric nanospheres were prepared by sonicating ACD aqueous solution. The amphiphilic chitosan derivative (ACD) was conjugated with folic acid (FA) molecules. Fe_3O_4 and ZnO suspensions were added to ACD solution and sonicated with a probe-type sonicator (XL2000, Misonix Inc., USA) at the interface for few minutes. Subsequently, the ACD-based nanospheres containing ZnO and Fe_3O_4 nanoparticles (AZF nanosphere) were prepared.

3 RESULTS AND DISCUSSION

The structure of ZnO nanoparticles were observed via transition electronic microscope (TEM) and high resolution TEM (HR-TEM). As shown in Figures 1(A)-(B), the average size of ZnO nanoparticles were about 5~10 nm. Nanoparticles could be identified as ZnO because the lattice fringe of 0.285 nm assigned to the (100) planes of ZnO was clearly observed. Same as ZnO, The structure of Fe3O4 nanoparticles were observed via transition electronic microscope (TEM) and high resolution TEM (HR-TEM). As shown in Figures 1(C)-(D), the average size of Fe_3O_4 nanoparticles was about 5 nm. Nanoparticles could be identified as Fe_3O_4 because the lattice fringe of 0.2545 nm assigned to the (311) planes of Fe_3O_4 was clearly observed. The structure of the ACD polymeric nanospheres were observed via TEM. As shown in Figures 1(E), the diameter of the polymeric nanospheres was about 50~200 nm.

The phase of the nanoparticles was identified by XRD pattern as shown in Fig. 2, the major characteristic peak of iron oxide nanoparticles were observed at 2θ~ 29.7°,35.0°, 42.6°, 56.3°and 61.8°. According to the JSPDS No. 89-0951 databases, those peaks can be assigned to the planes (220), (311), (400), (511) and (440) of Fe_3O_4. The major characteristic peak of zinc oxide nanoparticles were observed at 2θ~ 31.7°, 34.4°, 36.2°, 47.5°, 56.5°, 62.8° and 67.9°. According to the JCPDS No. 96-1451 databases, these peaks can be assigned to the planes (100), (002), (101), (110), (103) of ZnO, respectively. As it can be seen, the phase of the polymeric nanospheres was identified as ZnO and Fe_3O_4. These results suggested that the composite polymeric nanospheres were composed of ZnO and Fe3O4 nanoparticles.

The photoluminescence characteristic was shown in Figure 3. As it can be seen, the ZnO nanoparticles and the AZF nanospheres without conjugated FA both exhibit an emission peak 410 nm under excitation at 350 nm by fluorescence spectrometer (FL). The emission peak of FA-AZF nanospheres shifted to 450 nm, which was probably due to the fact that FA exhibits an emission peak (280 nm) under the same excitation.

FA-AZF nanospheres were expected to demonstrate MR T_2 image contrast. This was supported by Figure 4, which shows that in vitro MR T_2 images of FA-AZF nanosphere increased with increasing concentration. The FA-AZF nanosphere with fluorescence property could be comfirmed by confocal microscopy, as shown in Figures 5, suggesting that it could be applied not only for the MR contrast agent but also acted as a cell labeling due to their fluorescence.

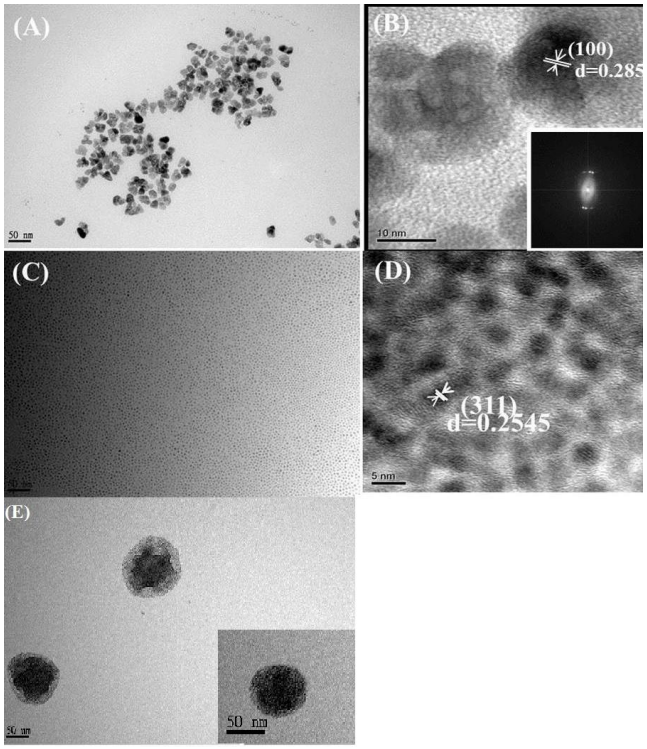


Figure 1. TEM images HR-TEM images of (a), (b) ZnO nanoparticles; (c), (d) Fe_3O_4 nanoparticles; (e) TEM images of FA-AZF nanospheres.

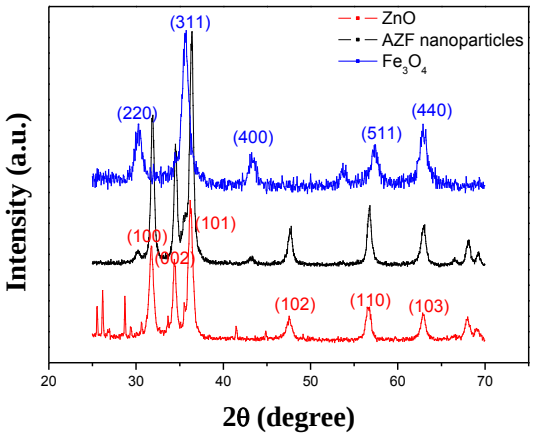


Figure 2 XRD patterns of ZnO , SPIO and FA-AZF nanospheres.

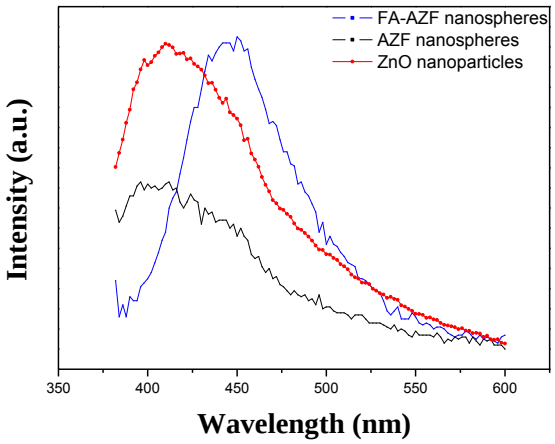


Figure 3. Fluorescence property of ZnO nanoparticles, AZF nanospheres and FA-AZF nanospheres.

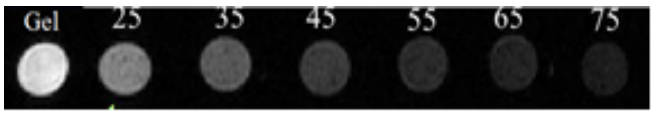
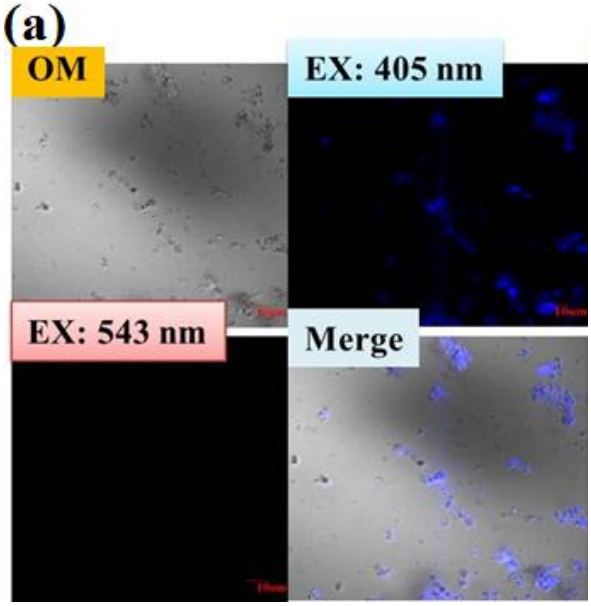


Figure 4. T_2 -weighted images of FA-AZF nanospheres increased with increasing concentration.



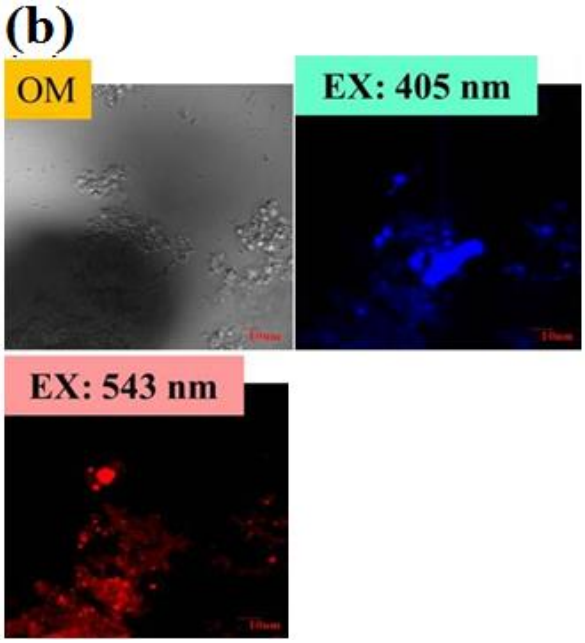


Figure 5. (a) Confocal images of ZnO nanoparticles (b) FA-AZF nanospheres encapsulated nile red.

4 CONCLUSION

We successfully fabricated a novel folic acid-conjugated drug vehicle to demonstrate dual modal imaging functionality (fluorescence and MR imaging) and encapsulate hydrophobic drug. Hence, FA-AZF nanospheres could be assessed as an anti-cancer drug delivery vehicle to specifically target the folic acid receptor overexpressing tumor cells.

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