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The Preparation and Characterization of Meso-Silica Based Nano-Composite

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***Abstract*—In recent years, cancer has become the one of the most serious threats to human health on the global scale, which cause increasing mortality rate in hospital. Chemotherapy is still the first line strategy in cancer therapy despite high its serious side effect towards normal tissues. Therefore, we designed a novel meso-silica based nano-composites (MSNCs) to solve the above issues for efficient drug delivery in cancer treatment. The as prepared MSNCs can achieve effective delivery of anti-cancer drug to tumor tissues with prolonged blood circulation time, effective accumulation in tumor sites, and controlled drug release in tumor cells due to their stimuli-responsive structure, excellent biocompatible, and high drug loading. In this work, a pH-sensitive MSNCs was prepared, and the chemo-physical properties of the MSNCs were characterized. Based on the experimental results, the as prepared MSNCs can achieve good dispersity in water, charge switch property, and high drug release rate, which can be used as a promising drug carrier for cancer therapy.**

***Index Terms*— meso-silica, composites, pH-sensitive, drug delivery.**

INTRODUCTION

In recent years, meso-silica nano-composites (MSNCs), as a presentative inorganic material, have been widely used for drug delivery system (DDS) due to its excellent biocompatibility, structural stability, and high drug loading capacity.[1-3] However, the MSNCs based DDS is still challenging by its low water-dispersity, high aggregation, and non-functionality, which has greatly impeded the practical application in clinic.[4,5] Therefore, functional coating materials are supposed to modify the MSNCs to solve the above problems.[6-8] 2,3-dimethylmaleic anhydride (DMA) is a kind of pH-liable compound, which has a detachable structure under the tumor acidic microenvironment.[9-11] In this regard the DMA can be modified onto the MSNCs based DDS for stimuli-responsive drug delivery to decrease the side effect. However, to our best knowledge the DMA modified MSNCs based DDS has scarcely studied so far.

Herein, a smart pH-responsive MSNCs based DDS in prepared for controlled drug release. DMA was used to modify MSNCs as a coating material in order to response the acidic condition around the tumor tissue. The as prepared MSNCs can achieve effective drug delivery, prolonged blood circulation time, and controlled drug release in tumor cells, which can potentially used as the drug vehicle in treatment of cancer.

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EXPERIMENTAL

Materials

Hexadecyl trimethyl ammonium bromide (CTAB, A.R.), NaOH (A.R.), 2,3-dimethylmaleic anhydride (A.R.), Methylene Blue (A.R.), DOX (98%, A.R.), Tetraethyl orthosilicate (TEOS, A.R.), alcohol (A.R.), (3-aminopropyl)triethoxysilane (ATPES, A.R.), 4,4,13,13-tetraethoxy-3,14-dioxa-8,9-dithia-4,13-disil (ATPES, A.R.) The organic solvents were used after purified. The other chemicals were used as received.

Synthesis of meso-silica nanoparticles (MSNs)

Firstly, the ethanol, deionized water, CTAB, and NaOH were added into a 150 mL single mouth flask with magnetic stirring for 1 hour. The TEOS was then dropwisely added into the flask with magnetic stirring for 6 hours. The above mixture solution was then centrifuged, and the supernatant was removed. The raw product was vacuum dried to obtain a white powder. *Modification of MSNs*

Firstly, the as prepared MSNs and ethanol were added into the round bottom flask with vigorous stirring for 30 min. APTES and ammonia were dropwisely added into the round bottom flask with vigorous stirring for 24 hours. The raw product *MSNs-NH_2* was obtained by centrifuging, and then dried in oven. The *MSNs-NH_2* and ethanol were added into the round bottom flask with vigorous stirring for 30 min. DMA was dropwisely added into the round bottom flask, and the pH of the mixture solution was adjusted to 10 with magnetically stirring for 24 hours. After centrifuging, the supernatant was removed, and the precipitate was washed for several times. The product was obtained by oven dried for 24 hours.

Preparation of MSNCs

The as prepared MSNs and ethanol were added into the round bottom flask with vigorous stirring for 30 min. The MB and DOX were added into the round bottom flask with stirring for 30 min by exclusion of light. After centrifuging, the supernatant was removed, and the precipitate was washed for several times. The final product was obtained by by oven dried for 24 hours.

RESULTS AND DISCUSSION

Synthesis and characterization of the MSNCs

FTIR spectra were used to investigate the chemical structure of the as prepared MSNCs. The representative FTIR spectra were shown in Figure 1. The peaks at 1123 cm^{-1} belonged to the Si-O vibration. The peaks at 1253 cm^{-1} and 687 cm^{-1} identified the existence of S-C bond in the MSNCs, which indicated the successful synthesis of the MSNCs. The peaks at around 1710 cm^{-1} can be assigned to

the C=O vibration, which suggested the successful modification of DMA.

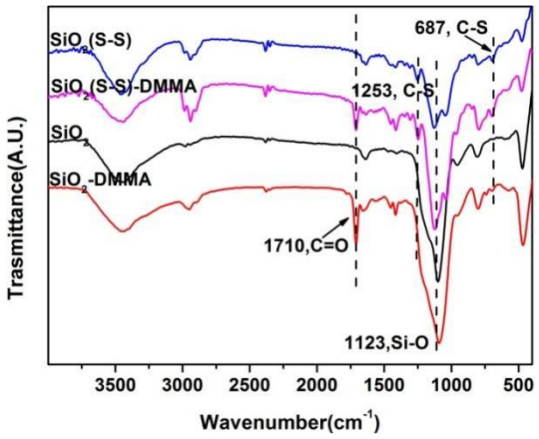

Figure 1. FI-IR comparison of different materials.

In order to further investigate the disulfide structure. Raman spectra was utilized to confirm the structure of the as prepared MSNCs. In Figure2, the absorbance at 508 nm can be assigned to the S-S bond in the MSNCs, however, the MSNCs without disulfide showed no such peaks in the Raman spectra, which indicated the successful synthesis of MSNCs.

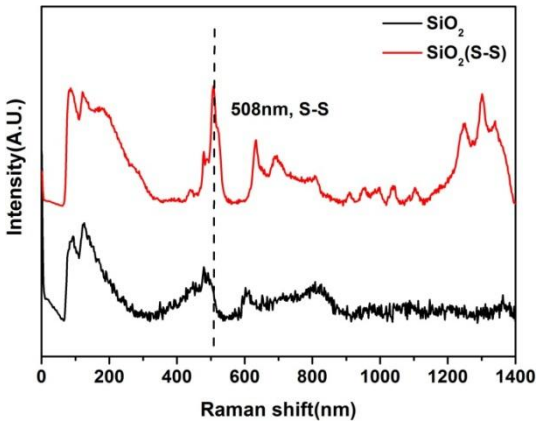

Figure 2 Raman comparison of different materials.

The TEM-EDS was used to investigate the morphology of the as prepared MSNCs. In Figure 3, the TEM photos of the as prepared MSNCs exhibited a sphere-like structure, and the nano-size of the composites was about 100 nm. The EDS spectra of the as prepared MSNCs demonstrated the existence of O, C, Si, and S elements, which demonstrated the successful preparation of MSNCs.

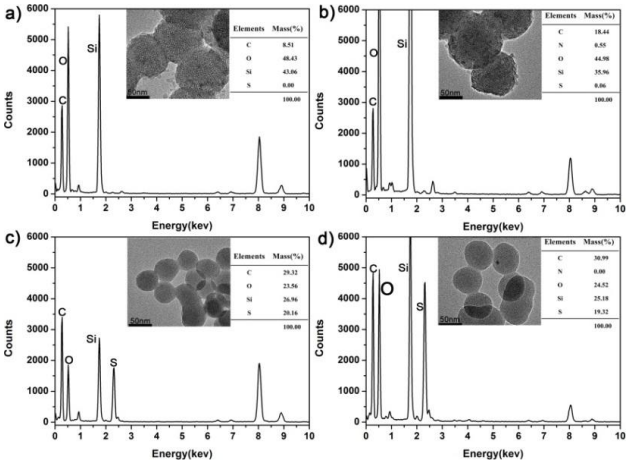

Figure 3 TEM-EDX spectrum scans of different samples.

, DLS was used to study nano-size of the as prepared MSNCs in water. In Figure 3, the nano-size of the MSNs, and MSNCs with or without disulfide was 162.15 nm, 121.85 nm, 189.12 nm, and 222.80 nm. The size increase from MSNs and MSNCs can be explained by the encapsulation of MB and DOX molecules.

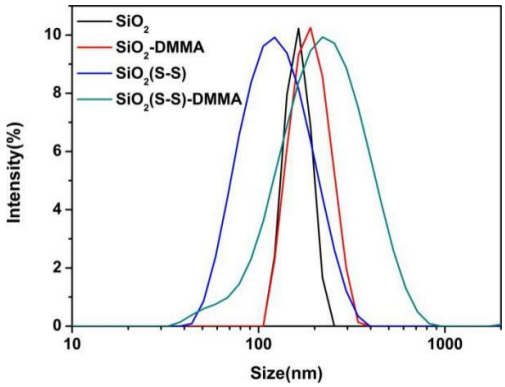

Figure 4 The particle size distribution of different materials.

CONCLUSION

In conclusion, we designed a novel meso-silica based nano-compositesto solve the above issues for efficient drug delivery in cancer treatment. The as prepared MSNCs possessed disulfide structure, and showed sphere-like micromorphology. The MSNCs exhibited good dispersity in water. The as prepared MSNCs were supposed to be a potential candidate for cancer treatment.

ACKNOWLEDGMENT

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