Synthesis and Characterization of Biocompatible Magnetic Iron Oxide-Silica nanoparticles as Nanocarriers for the delivering of Doxorubicin against liver cancer

Maria Janina Carrera Espinoza[1](尹珍妮), Kuen-Song Lin[1,*](林錕松), Meng-Tzu Weng (翁孟慈)[2], Chun-Ming Wu (吳浚銘)[3], Jyh-Fu Lee (李志甫)[3]

[1]Department of Chemical Engineering and Materials Science/Environmental Technology Research Center, Yuan Ze University, Taoyuan, Taiwan

[2]Department of Internal Medicine, National Taiwan University Hospital, Taipei 100, Taiwan

[3]National Synchrotron Radiation Research Center, 101 Hsin-Ann Road, Hsinchu Science Park, Hsinchu, Taiwan

kslin@saturn.yzu.edu.tw

The present research has the objective of the synthetization and characterization of silica modified magnetic iron oxide nanocomposites (Fe_3O_4-SiO_2) through solvothermal method. The final nanoparticles will perform as carriers of doxorubicin (DOX) drug against liver cancer. Spherical shaped nanoparticles with final size of around 20-50 nm in diameter were obtained using the cryo-TEM. Besides, the results of XRD patterns demonstrated the crystallization of the synthetized nanoparticles with diffraction peak of at $2\theta = 35.44°$ agreed to that of magnetite (Fe_3O_4) (311). The XANES spectra of the iron atom in the various samples demonstrated an absorbance feature (Fe = 7112 eV) of a 1s to 3d transition. The successful coating of SiO_2 on the surface of IONPs was demonstrated by the presence of the characteristic bands between 1625, 1091, and 460 cm^{-1} which corresponds to the stretching vibration bends of Si-O bonds. EXAFS structure parameters of quartz and stishovite were obtained and shown to be in good agreement with the X-ray structures. Si in sixfold and fourfold coordination can be distinguished precisely from SiK- and Siledge XANES features and SiK-edge. The cell cytotoxicity test detected that there was no significant cell toxicity perceived among the HEK293T and HepG2 cells incubated using various concentrations of IONPs and IONP-SIO_2. Remarkably, MTT test presented that after DOX encapsulation, the Fe_3O_4-SiO_2-DOX complex was able to induce more cell apoptosis. This study offers an interdisciplinary work to generate new a way of DOX delivery against liver cancer with consequential advanced treatment.

Keywords: Magnetic iron oxide nanoparticles, Silica (SiO_2), Doxorubicin (DOX), XANES/ EXAFS.

Introduction

Liver cancer is one of the most common cancer around the globe which claimed millions of lives. As sourced from a World Health Organization (WHO), liver cancer has been reported to be the fifth most typical cancer and the third cause of death globally with over 850,000 new cases yearly. Unfortunately, current pharmacotherapies have serious side effects and poor efficacy against cancer. These treatments are limited due to their inability to differentiate between tumor and ordinary cells.

Nowadays many research groups have been working to find a new methodology using novel drug delivery systems (DDSs) by means of non-toxic and biocompatible materials that can reduce the limitations of chemotherapy. Nanomedicine has recently received more attention due to all the successful results through the utilization of nanotechnology. The size of these nanocomposites allow them to penetrate across the cell membrane via cellular endocytosis mechanism [1,2]. Additionally, magnetic iron oxide nanoparticles (IONPs), have been investigated due to their biocompatibility and non-toxic nature. Hence, introducing a silica layer on the surface of IONPs can play a vital role in mitigating the aggregation, enhance stability, and reduce any possible cytotoxic effects of IONPs [3]. Moreover, DOX has remained a drug of choice in several targeted delivery research works due to its multifunctional application in different types of cancers. The DOX functions through disruption of gene expression. Thus, in this research we synthesized a multifunctional nanocarriers which may overcome the existing side effects of DOX and can deliver the drug by targeting the affected cells for liver cancer treatment.

Experiments

2.1. Synthesis of IONPs-SiO_2

The IONPs-SiO_2 nanoparticles were synthesized by solvohermal method, briefly, 100 mg of Fe_3O_4 were diluted in a dilution of alcohol and deionized water (1:10 w/v) the resulting solution was stirred for 30 min. Then 2.5 mL of ammonia and 4 mL of TEOS were added into the previous solution. The final precipitates were collected by centrifugation, washed with dH_2O and absolute ethanol, then dried in a hot air oven at 60 °C for 10 h. Finally, the particles were grinding and sieving to get an optimum size.

2.2 Formulation of the DOX-encapsulated IONP-SiO2 core-shell

Doxorubicin loaded IONPs were prepared by dissolving 5 mg of nanoparticles mixed with different DOX concentrations into 5 mL Acetone. The samples were then dried at 70°C and rehydrated with 5 mL phosphate-buffered saline (PBS) at 80°C. After 30 min of incubation, the drug encapsulated IONP-SiO_2 core-shell were centrifuged at 19,000 rpm for 15 min.

Results

The final nanocomposites presented a spherical sized between 20-50 nm reported by TEM. XRD results showed the crystal lattice with diffraction peak of at 2θ = 35.44° agreed to that of magnetite (Fe_3O_4) (311). The diffraction peaks for Fe_3O_4-SiO_2 were stablished and catalogued as regular spinel structure and consistent with JCPDS-ICDD. The EXAFS parameters indicate that the bond length of the first layer of Fe_3O for Fe-O is 1.95 ± 0.01 Å, and the coordination number is 3.38; in the case of the synthesized Fe_3O_4-SiO_2 the first layer structure for Fe-O bond length is 1.94 ± 0.01 Å, and its coordination number is 3.75. The normalized XANES for at the Fe K-edge and its first derivative spectra displayed same values for the pre-edge peaks of Fe_3O_4 and Fe_3O_4-SiO_2 in different concentrations. The results of Fe_3O_4-SiO_2 presented a strong pre-edge absorbance peak of Fe = 7113 eV, which is of Fe^{3+} cations feature. Such pre-edge peak is dedicated to 1s → 3d electronic shift. As the 1s and 3d positions are outwardly symmetric, the shift likelihood ought to be low and the shift strength is sensitive to the coordination symmetry [36]. Upon comparison of the absorption edge to that of other already known iron standards, it was proven that the prepared nanoparticles are similar to Fe_3O_4.

Discussion

EXAFS patterns reported different values for the sample this may be due to the fact that the position of the Fe in the Fe_3O_4 structure and its position are complicated, causing a difference in the coordination number, bond length and layer structure. The bond length of the first layer structure Fe-O is within the error range, so it can be judged that Fe_3O_4-SiO_2 and Fe_3O_4 have the same reverse spinel structure. In addition, the XANES regions and pre-edge of the absorption spectrum are crucial due to both enclose on the immediate environment electronic information of the absorbing atom. The pre-edge intensity is also valence-dependent since the electronic configuration has to be factored in when associating the target atom intensities with different valences. These peaks are valuable because their intensities and sites are sensitive to the immediate symmetry of the metal. The results show the magnetic hysteresis curves of Fe_3O_4 and Fe_3O_4-SiO2 nanoparticles studied at room temperature. Both of tested samples display superparamagnetic character with high saturation magnetization of 15.70 and 14.06 emu/g for Fe_3O_4 and Fe_3O_4-SiO_2 samples, respectively. The Fe_3O_4-SiO_2 had lower magnetization when compared to Fe_3O_4 due to the silica coating on the surface of the iron, nevertheless both particles remained magnetic. Such magnetism is essential for target delivery since it can help direct the nanoparticles to the targeted cells using and external magenta force.

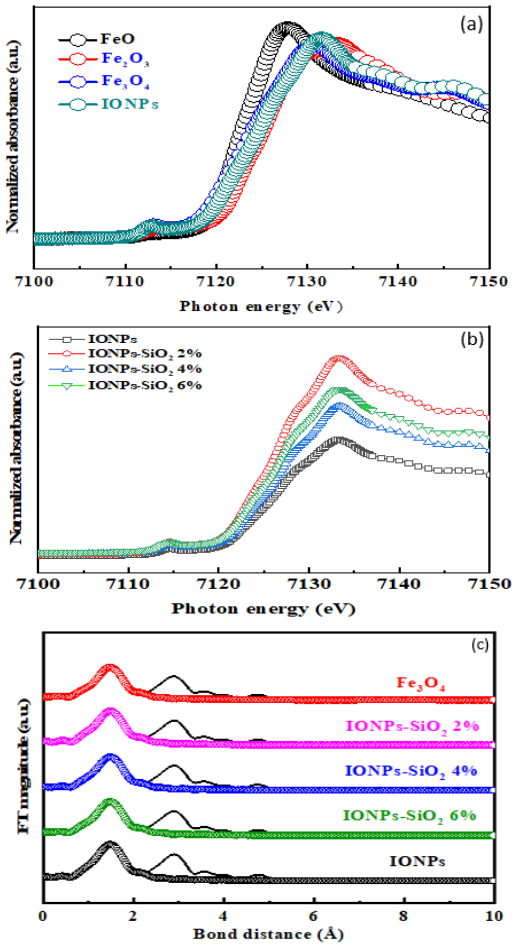

Fig. 1. Fe K–edge derivative XANES spectra of (a-b) Fe_3O_4-SiO_2 and iron standards. EXAFS spectra of (c) Fe_3O_4-SiO_2 at different concentrations.

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