Synthesis and Characterization of Super Magnetic Nanocomposites to be used as Doxorubicin Carrier for Liver Cancer Treatment

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Liver cancer remains a leading cause of cancer-related death universally, claiming the lives of millions of people. Statistically, there are about 9.1% cancer deaths globally with 782,000 new cases diagnosed in 2012. Drug-loaded nanoparticles have allured extraordinary consideration in the field of medicine. These nanocomposites not only improve specific drug delivery and its circulation time, but also can minimize chemotherapy side effects. Henceforth, the objective of the study was to fabricate dextran and Pluronic F127 stabilized magnetic iron oxide nanoparticles (Dex-SPIONs and F127-SPIONs) through a solvothermal method. Doxorubicin (DOX) will further be uploaded on these nanocomposites to be delivered on targeted liver cancer cells. Furthermore, different characterization techniques such as TEM, CryoTEM, XRD, FTIR, TGA, XPS, XANES, EXAFS, SANS, and SAXS were utilized to further analyze the properties of the synthesized nanocarriers. The XRD patterns showed that the synthesized nanoparticles had a crystal structure with a diffraction peak of at $2\theta = 35.44°$ which corresponded to that of magnetite (Fe_3O_4) (311) while the XANES spectra of the Fe atom in the different samples displayed an absorbance feature (Fe = 7112 eV) of a *1s* to *3d* transition. The SANS spectra was used to investigate any changes in the core-shell structure of dextran/Pluronic F127 micelles as a function of increasing DOX and polymer concentrations hence to predict the drug loading and release mechanisms. Concerning the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay, there was no observed cell cytotoxicity amongst the cells (293T, HepG2 and Huh7) treated with varrying concentrations of IONPs, DIONs, and PIONPs. This study established a multidisciplinary work to fabricate new formulation of DOX in treatment of liver cancer with improved treatment. DIONs and PIONPs based drug delivery system would be a potential tool to increase targeting delivery of conventional chemotherapeutic drugs and MRI imaging.

Keywords: Drug delivery, Magnetic iron oxide nanoparticles, Dextran/Pluronic F127, Doxorubicin, Liver cancer, TEM, XANES/EXAFS.

1. Introduction

Nanomaterials have recently evolved in the research fields of chemistry, biotechnology, and biomedicine. Inorganic nanomaterials (INMs) have attracted much attention in bio imaging, targeted drug delivery and cancer therapies [1,2]. Nanomaterials usage have facilitated its fabrication into vesicles, inestimable nanocarriers have been established for bioimaging/diagnosis and delivery of drugs and different therapeutic agents into specific targets [3]. Drugs are usually incorporated in nanocarriers through encapsulation, surface entrapping, which changes the drug pharmacokinetics in vivo. The development of synthesis techniques, involving the ability to generate molecules and supramolecular structures for proposed functions, has recently encouraged the usage of engineered nanopartices. This has led to the emergence of new DDSs based on inorganic nanoparticles [4]. Amongst these inorganic nanomaterials, iron oxide nanoparticles have been one of the potential nanoparticles for biomedical applications. These magnetic nanomaterials are highly biocompatible, biodegradable and non-cytotoxic and also show fascinating properties, suchlike super-paramagnetism, irreversibility of high field magnetization, high photo thermal effect. Moreover, super-paramagnetic nanoparticles based on Fe_3O_4 have been approved as high-performance contrast agents in magnetic resonance imaging (MRI). Fe_3O_4 nanoparticles can be utilized as a contrast agent which will enhance the contrast and imaging effect of MRI [5].

2. Experiments

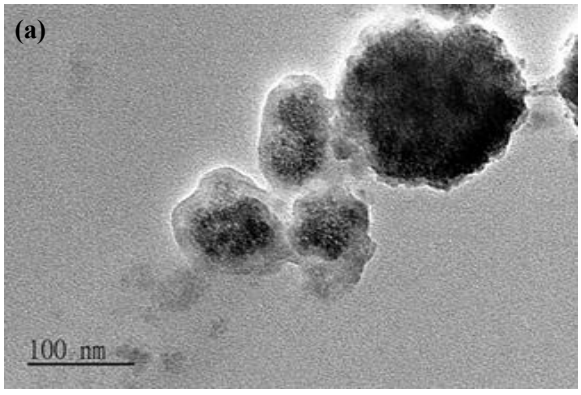
Iron oxide nanoparticles were synthesized via solvothermal method whereby 1.08 g of $FeCl_3.6H_2O$, 0.25g of trisodium citrate and 1.6 g of sodium acetate were dissolved in a mixture of EG (40 mL) and DEG (10 mL) under vigorous stirring for 30 min. The solution was then transferred into a Teflon- lined stainless-steel autoclave and heated for 10 h at 200℃, and then coated with different dextran and pluronic F127 concentrations.

3. Results

Spherical iron oxide nanoparticles with an obvious polymer coating on its surface was demonstrated in TEM **Fig. 1(a)**. The XANES spectra was performed to provide information about on-site symmetry, chemical species and oxidation state of the absorbing atom. XANES spectra for iron oxide nanoparticles and dextran coated iron oxide nanoparticles were recorded. As illustrated in **Fig. 1(b)**, the XANES spectra for iron oxides indicate that they are Fe_3O_4 nanoparticles. This is because the main peak of the magnetic nanocarrier is located between Fe^2 and Fe^3 iron with the curve fitting more to Fe_3O_4. Standard Fe–O bond distance was investigated using EXAFS spectra in IONP and Dex–IONP samples and was 1.95 Å, with co-ordination numbers, 3.71, 3.90, 4.08, 4.13 and 3.72 respectively (**Fig. 1(c)**.

4. Discussion

The obtained results indicate that the magnetic nanocarriers were synthesized properly as there have a spherical morphology as indicated by TEM in **Fig 1 (a)**. XRD patterns also confirmed the crystallinity of the prepared nanocarriers demonstrated by the presence of the characteristic peak (311) for magnetite nanoparticles. The ellipsoid shape of nanoparticles also indicated by SANS spectra is important for efficient drug loading and long half-life of the magnetic nanocarriers in the circulation, thus delivering enough drug to the cancerous cells in the targeted side. The magnetite iron oxide nanoparticles coated with different concentrations of dextran and pluronic F127 also displayed no cell toxicity. Overall the attained data illustrated that the magnetic nanocarriers are appropriate to be used as drug delivery vehicles specific targets without causing injury to normal cells.



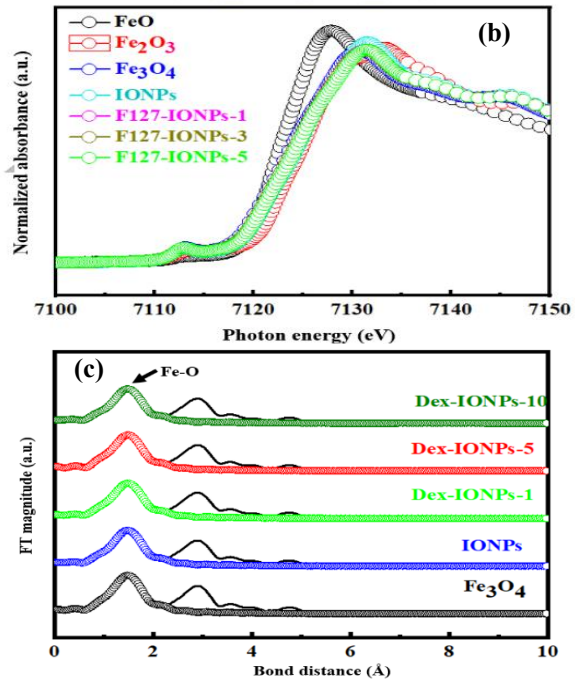


Fig. 1. (a) TEM image of Dex-IONPs (b) Fe K–edge derivative XANES spectra of F127–IONPs samples and iron standards. (c) EXAFS spectra of Dex-IONPs at different polymeric concentrations.

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