Synthesis of high-potential polymer-coated cobalt ferrite magnetic nanoparticles for biomedical applications

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INTRODUCTION

Chemotherapy is one of the most significant and broadly used methods of cancer treatment. Doxorubicin (DOX) is a chemotherapy drug that is used in treatment of numerous types of cancers [1]. DOX has severe side effects of this drug such as hair loss [2], heart damage [3], allergic reactions [4] and tissue inflammation [5]. Furthermore, short period of circulation in blood and uncontrolled release are other problems of using this drug [6]. Therefore, designing and manufacturing nanocarriers to increase efficiency and reduce side effects of this type of drug is one of the challenges in field of chemotherapy. Organic-inorganic nanocomposites were extensively studied in the last decades due to their interchangeable physical and chemical properties, which are related to the properties of both components. In particular, polymer/magnetic composites because of their wide spread [7]applications in various fields, ranging from technology to medicine, such as magnetic resonance imaging (MRI), intelligent drug delivery, Hyperthermia and photothermal. The use of this types of nanocomposites can help to solve the problems of DOX side effects and also create multifunctional nanocarriers to enhance the healing process. This reasons has provided a very good basis for researchers [8].

As a magnetic agent, there are lots of researches on Fe3O4 nanoparticles and nanocomposites because of biocompatibility. Among the other types of magnetic nanoparticles, cobalt ferrite (CoFe2O4) with inverted spinel structure is an important spinel ferrite, due to its unique properties such as high Curie temperature TC (520 °C), moderate saturation magnetization and high anisotropy constant, photomagnetic properties, high strain rate Exposure to magnetic field, electrical insulation, and chemical [7]. These properties make CoFe2O4 a good candidate as a hard magnetic material for a range of applications, especially for targeted drug delivery [9].

Coating of cobalt ferrite magnetic nanoparticles with polymeric materials provides advantages, including preventing agglomeration by creating a polymer layer between magnetic nanoparticles that prevents magnetic interaction and also active sites for the conjugation of biomolecules, receptors and drugs, providing high chemical stability and high biocompatibility in biological environments so it prevents from being identified and eliminated by the immune system [10]. Therefore, two types of biopolymers, Polyethylene glycol (PEG) and Polyaniline (PANI), have been selected for coating cobalt ferrite magnetic nanoparticles.

polyethylene glycol has been selected due to its different applications in various industrial, commercial and its medical sectors and having unique properties such as high biocompatibility, non-toxic and non-flammable [11]. Recently, new approaches appeared in designing and coating of magnetic nanocomposites with conductive polymers. conductive polymers such as polyaniline have received special attention due to its unique π conjugated structures, which lead to the environmental stability, high electrical stability and photothermal effect for tumor ablation. In addition, high biocompatibility, morphology and controllable particle size with changes in synthesis conditions are the reasons why this type of polymer was chosen [12].

In this study, we designed and fabricated a new ternary multifunctional biocompatible nanocomposite with high potential of targeted and controlled drug delivery, Hyperthermia and photothermal therapy.

OBJECTIVES

Designing the nanocarriers can be used as a novel multifunctional and synergistic platform for delivering different types of anti-cancer drugs and other biomedical applications, especially in cancer therapy.

MATERIALS and METHODS

Materials

All chemical reagents used in this study were used without further purification, except for aniline. Iron (III) chloride hexahydrate (FeCl3.6H2O, 99%), Cobalt (II) chloride hexahydrate (CoCl2.6H2O, 98%), sodium hydroxide (NaOH), aniline, ammonium persulfate and hydrochloric acid and polyethylene glycol (MW=1500) were purchased from Merck. Deionized water was used as a solvent.

Synthesize of CFO

According to E. Puscasu et al [13] briefly, stochiometric amount of Iron (III) chloride hexahydrate (FeCl3.6H2O, 99%) and Cobalt (II) chloride hexahydrate (CoCl2.6H2O, 98%) were used to a facile coprecipitation synthesize method of CoFe2O4 in an aqueous solution. Nucleation of cobalt ferrite nanoparticles in 90 ºC and magnetically stirring were started by drop-wise addition of NaOH until pH reached 12. The resulting suspension was aged for 1 hour. Finally, magnetic nanoparticles were separated by the magnet and were washed with deionized water and ethanol to remove formed NaCl.

Preparation of CFO/PEG

The synthesis steps were the same as for the CFO sample, only from the beginning PEG was poured into distilled water with a 3 times cobalt ferrite ratio and the rest of the steps were performed in the order given.

Preparation of CFO/PEG/PANI

Polyaniline (PANI) Coated CoFe2O4/PEG was prepared by in-situ chemical oxidative polymerization technique of aniline in presence of CoFe2O4/PEG nanoparticles. In a conventional procedure [14], 0.7 ml aniline was dissolved in 12.5 ml HCl (1M), 1 g of CFO-PEG was added and the solution was placed in an ultrasonic bath for 15 min and then mechanically stirring for 30 min. Then 12.5 ml of HCl (1M) in which 1.7115 g of ammonium persulfate was dissolved was added to the first solution and polymerization process was performed in ice water bath for 6 hours. After separation, it was washed with HCl (0.1M), distilled water and alcohol several times respectively and dried for 24 hours at 60 ° C. The different steps for the fabrication of CFO/PEG/PANI was shown in Fig.1.

Characterization

X-Ray Diffraction (XRD) Analysis

The phase identification of the samples was investigated by X-ray Diffraction (XRD) at room temperature using a Philips PW-3170 with Cu-Kα radiation (λ=0.15406) in a 2θ range between 20 to 100º and step size of 0.02º.

Fourier Transform Infrared (FTIR) Spectroscopy Analysis

Fourier transform infrared spectroscopy (FTIR) studies were carried out on compressed films containing KBr pellets and samples using a FTIR spectrophotometer. FTIR spectra of synthesized samples were obtained with FTIR spectrometer in the wavenumber range 4000 to 400 cm-1. FTIR investigations were carried out to confirm the polymerization of aniline monomer and interactions between elements in the coating process of CFO with polyaniline and polyethylene glycol during the synthesis.

Morphology and microstructure analysis

The morphology, microstructure and chemical composition of the synthesized samples were evaluated using field emission scanning electron microscopy (FESEM) equipped with Energy dispersive X-ray (EDS). The average diameters of nanoparticles were calculated by ImageJ (US National Institute of Health, Bethesda, MD).

RESULTS

XRD analysis

Fig.1 shows the XRD patterns of CoFe2O4, CoFe2O4/Polyethylene glycol and CoFe2O4/Polyethylene glycol/Polyaniline. Analysis of the XRD pattern of CFO confirms that all the detected peaks at 2θ= 18.36º, 30.20º, 35.60º, 37.23º, 43.26º, 53.56º, 57.20º, 62.60º, 71.14º, 74.28º and 79.05º are well matched with the cubic structure cobalt ferrite spinel phase having Fd-3m space group (ICCD No.96-153-3164) [15]. As can be seen, the main ferrite peaks are seen in the diffraction pattern of both PEG and PEG/PANI coated CFO based nanoparticles, indicating the presence of CoFe2O4 crystalline structure without any degradation or damage. Reducing the intensity of the peaks could be a sign that, coating has been created on the cobalt ferrite.

FT-IR analysis

The chemical characteristics of nanoparticles and interactions between their elements were determined using Fourier-transform infrared spectroscopy (FTIR). FTIR results were shown in fig.2 Cobalt ferrite has two main peaks related to metal-oxygen bonds. The absorption peaks with wavenumber 478 and 613 are related to the M-O bond in octahedral and tetrahedral locations [11]. The characteristic and main adsorption bands for polyethylene glycol are 1098 and 2850-2920, which belong to C-O-C and CH2 groups, respectively [16]. The absorption bands 840 and 1464 correspond to C-C. The FTIR spectrum of polyaniline has the adsorption bands at 3230, 1562 and 1480 related to the NH, C=C and C=N bonds [17].

For CFO/PEG, the absorption bands 445 and 643 correspond to the vibration of metal-oxygen bonds at tetrahedral and octahedral locations. Bands 1633 and 3453 represent the OH group. The partial band in the range 2921 belongs to the methylene (CH2) group and the 1060 band belongs to the C-O-C. The ferrite absorption band has shifted from 613 to 643, which is indicating an interaction between the metal and the polymer[18].

The spectrum of PANI shows two peaks in 1292 and 1240 corresponding to the strong aromatic C-N stretching vibration. The absorption band in 1110 belongs to the group N=Q=N (Q represents the quinoid ring). Absorption band 787 indicates the presence of Cl and its vibration in the structure, which demonstrates successful doping of the Cl atoms and proved conductivity of synthesized polyaniline [19].

In the CFO/PEG /PANI nanocomposite, Absorption bands 508 and 621 represent cobalt ferrite. 1134 corresponds to N=Q=N. Bands 1247 and 1303 represent the C-N group. 1293 and 1575 are also related to C=C and C=N. A short peak 2924 also shows CH2 and 3447 bands related to the vibration of OH and NH groups. The vibration peak around 1100 is sharper and also shifts to higher frequencies than in the PANI and PEG specimens, which is due to the formation of C-O-M bonds [20]. The shift to higher frequencies of the 1292 peak than the polyaniline is related to CNH bonds. Also, the 1570 band has been changed in both intensity and frequency due to the formation of CONH bonds between polyaniline and polyethylene glycol. In addition, the intensity ratio of the two peaks at 1493 and 1575 has been changed and the 1575 band has become sharper than the 1493, which is another reason for the interaction between the two polymers[21].

FESEM and EDS analysis

FESEM and EDS analysis represent the surface morphology and chemical compositions of the nanoparticles. Fig.3(a) shows the CoFe2O4 magnetic nanoparticles (MNPs) that mostly have spherical morphology with a diameter range of 20-25nm. According to the EDS analysis, it is seen that the CFO (MNPs) only consisted of O, Fe and Co without any impurities. The FESEM images of CFO/PEG was displayed in Fig.3(b) to obtain a little change in size and morphology of CFO MNPs that confirm the creation of PEG coating and also the EDS analysis of CFO/PEG nanoparticles show the presence of C in the composition. It is observed In Fig.3(c) CFO/PEG/PANI composite nanoparticles is well disturbed and nearly spherical. The EDS spectrum of CFO/PEG/PANI indicate the presence of N, Cl and C, furthermore a sharp increase in peak C intensity, that confirms the formation of a polyaniline coating.

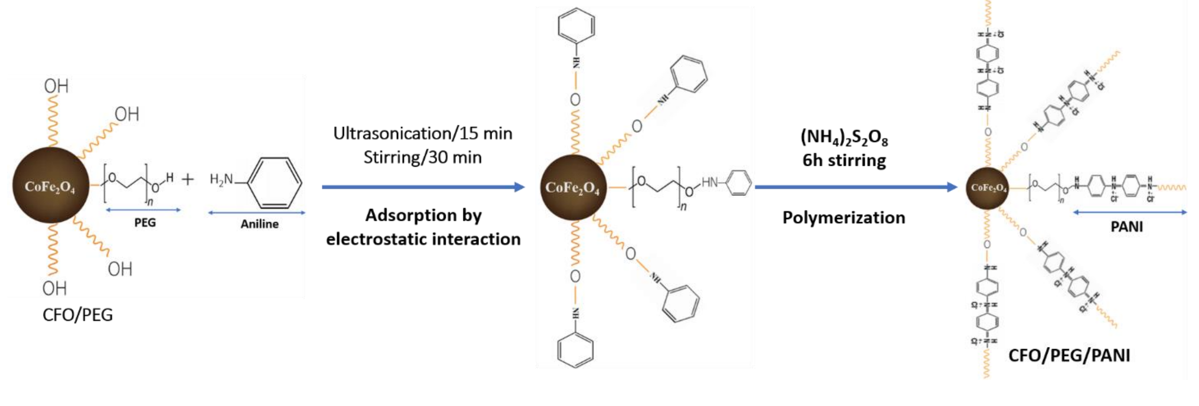

Figure 1: Schematic illustration of the fabrication of CFO/PEG/PANI.

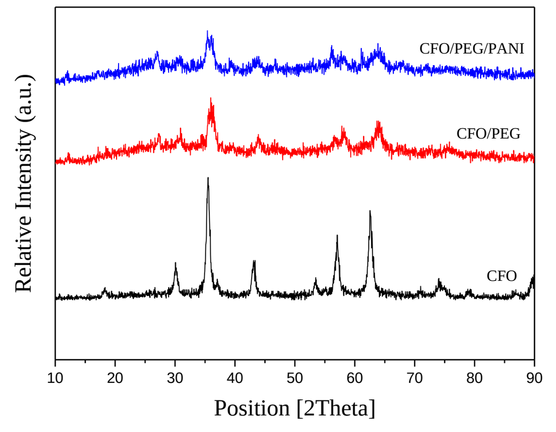

Figure 2: XRD patterns

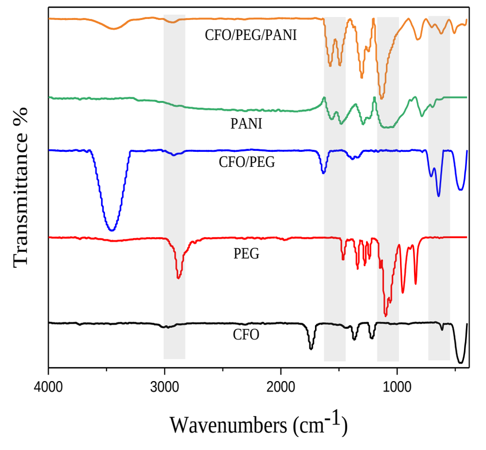

Figure 3: FT-IR results

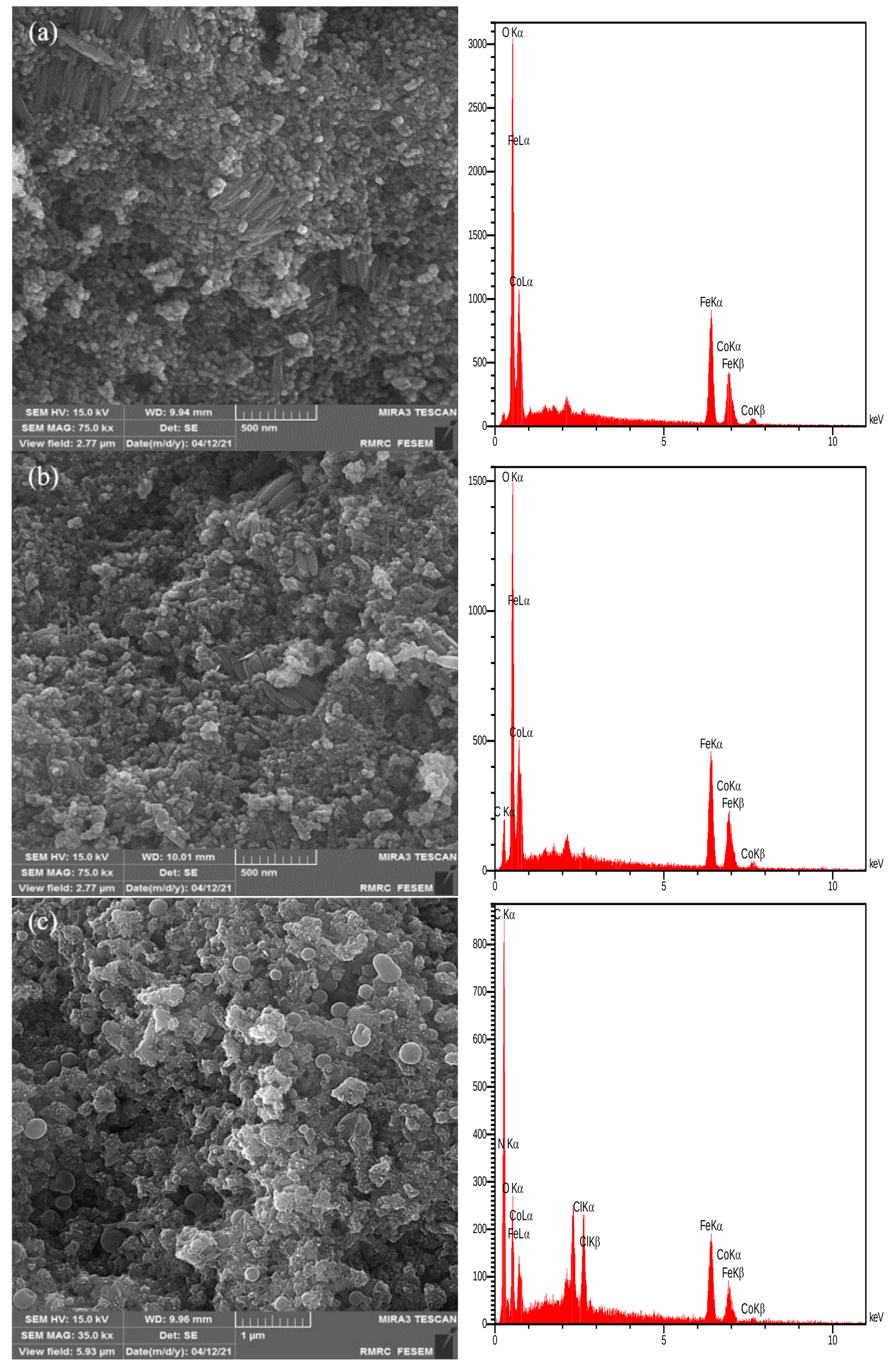

Figure 4: FESEM images and EDS spectra

CONCLUSION

Magnetically conductive nanoparticles have variety of applications, particularly in biomedicine. In this work, CoFe2O4/Polyethylene glycol/Polyaniline nanocomposite was fabricated by using a facile chemical technique. Nanocomposites were characterized by using XRD, FTIR, FESEM and EDS. CFO was used as a targeting agent and Hyperthermia because of good magnetically properties. PEG served as a coating polymer component that can enhance the biocompatibility and also, it was used as a primary coating to prevent the degradation of cobalt ferrite in hydrochloric acid solution. On the other hand, polyaniline coating gives the nanoparticles high drug loading capacity. This platform provides a unique drug carrier system for DOX due to the high number of functional groups and high surface to volume ratio. It can also have a high potential for photothermal therapy due to the presence of Cl-doped polyaniline. The main purpose of this research was to design a multifunctional nanocarrier for drug delivery, that was successfully completed.

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