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Synthesis and Surface modification of Iron Oxide Nanoparticles for Drug Delivery

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Abstract

Surface functionalized magnetic iron oxide nanoparticles (NPs) are a kind of novel functional materials, which have been widely used in the biomedical applications such as drug delivery [1]. In order to implement the practical application, the particles must have combined properties of high magnetic saturation, stability, biocompatibility, and interactive functions at the surface. Moreover, the surface of iron oxide NPs could be modified by organic materials or inorganic materials, such as polymers, biomolecules, silica, metals, etc. In this paper we focused on synthesis of iron nanoparticles and coating of them with PVP,SiO_2 and Au to combine drug (theophylline) and apply in drug delivery. The FT-IR, XRD, TEM and SEM and EDX indicated correctly the synthetic nanoparticles and showed drug well loaded on iron oxide nanoparticles surface.
Keywords: Iron oxide nanoparticles, PVP, silica, gold, drug delivery, theophylline

Contents

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1. Introduction

For biological and biomedical applications, magnetic iron oxide nanoparticles are the primary choice because of their biocompatibility and chemical stability. They also need to bind to a range of drugs, proteins, enzymes, antibodies, or other molecular targets. Magnetic drug delivery systemusing magnetic nanoparticle carriers targeted by an external magnetic field is a promising alternative to avoid the problems associated with conventional chemotherapy [2-3]. In magnetically targeted drug delivery, carriers comprising of coated magnetic nanoparticles loadedwith anti- asthmatic drug are injected into the patient body via the human circulatory system. An external magnetic fieldis used to localize the drug loaded carriers at the site and the drugcan then be released from the carriers either via enzymatic activity orchanges in physiological conditions such as pH or temperature. Many synthesis methods have been explored for magnetic iron oxide nanoparticles. These include organic solvent heating method, polyol method, and co-precipitation method [4-6]. The co-precipitation method is the most effective technique for preparing aqueous dispersions of iron oxide nanoparticles because the synthesis is conducted in water. For this report, we studied several biological materials as surface coatings to achieve biocompatibility such as poly

ethylene pyrrolidone(PVP), SiO_2 and gold (Au). These materials were used to control the particle size, to prevent the nanoparticles from aggregation, and to achieve biocompatibility. After modification of surface of nanoparticles, theophylline as drug was loaded them surfaces on. Theophylline had been used worldwide for the treatment of asthma for several decades and acts as anti-asthmatic agent.

2. Materials and Methods

All chemicals were of analytical grade and used withoutfurther purification. Ferric chloride ($FeCl_3$. $6H_2O$), ferrous chloride($FeCl_2$. $4H_2O$), sodium hydroxide (NaOH),Polly vinyl alcohol(PVP),anhydrous ethanol(C_2H_5OH), TEOS, Iso-Butanol, sodium borohydride($NaBH_4$) and $HAuCl_4$wereall purchased from MERCK.Theophylline anhydrous was procured from Sigma, USA.Deionized water was used throughout the experiment.

2.1 Synthesis of nanoparticles

Iron oxide nanoparticles were synthesized by a modified co-precipitation method. The precipitation method is the simplest chemical pathway to obtain SPIONS .Ferric chloride ($FeCl_3.6H_2O$-1.09 g) and ferrous chloride ($FeCl_2.4H_2O$, 0.394 g) at a ratio of 2 to 1 were dissolved in 100 mL deionizedwater, which was then stirred at room temprature. The solution was bubbled with N_2gas to prevent unwanted oxidation. Subsequently, 0.64 gr NaOH solution was injected and the reaction continued at that room temperature for 30 minutes before the flask was removed from stirring.

$$Fe^{2+} + 2Fe^{3+} + 8OH^- \rightarrow Fe_3O_4 + 4H_2O$$

2.2 Surface coatings with PVP

iron oxides are not very stable, and are not soluble in water. Stabilization of SPIONS is essential to prevent against aggregation and oxidization. After synthesis, the black precipitates werecollected, washed with DI water, three times, and acetone, tow times.

To coating of IO nanoparticles with PVP, the 10% of PVP solution(50 ml) in distilled water was sonicated 20 min to remove oxygen. Then the black precipitation was added to PVP solution slowly, washed with water and dried with oven at 35^0C.

2.3 Surface coating with SiO_2

In this step, 0.08 gr of IO nanoparticles was dispersed in 20 ml iso-butanol and 0.5 ml NH_3, 1ml TEOS, 4 ml of H_2O was added the solution and stirred 8 h. then the precipitation washed with ethanol tow times and dried with oven at 35^0C.

2.4 Surface coating with Au

0.02 gr of synthesis nanoparticles at previous step was dispersed in water and 100 ml of 0.01×10^{-4} M of $HAuCl_4$ and 0.01 M $NaBH_4$ as reducing agent was added to the solution. Then stirred 8 h and washed with water and dried with oven.

2.5 Drug loading

In this step, 0.01 gr of nanoparticles synthesizing previous step was dispersed in water/alcohol and added 0.01gr theophylline. Stirred of the solution for 8h and washed with water and dried with oven. In this step, the drug was loaded on nanoparticle surfaces.

3. Results and Discussion

The functional groups of the surface modified iron oxide nanoparticles were confirmed by FT-IR spectra. Fig.1 shows FT-IR spectra of PVP and Fe3O4-PVP. The FT-IR spectrum of iron oxide exhibits strong bands in the low-frequency region (1000-500cm-1) due to the iron oxide skeleton. This pattern is consistent with the magnetite (Fe_3O_4) spectrum (band between 570-580cm^{-1}) .The characteristic band of Fe-O at 572 cm^{-1} shows that the particles consist mainly of Fe_3O_4.

The shift of the vibrational band of the carbonyl group from 1659 cm-1 to 1634 cm-1 in the nanocrystal samples, suggests that PVP is modified on the surface of the Fe3O4 nanocrystals via coordination interaction through its carbonyl group. But no change has been observed for the peak of N-OH (at 1291cm-1) which was weakened greatly. These changes of intensity can be attributed to the coordination between NOH and iron oxide nanoparticles. The broad intense absorption peak at around 564 cm-1 can be attributed tolattice absorption of the Fe3O4 particles.The FT-IR spectra of Fe_3O_4-PVP-$SiO_2$and coated with Au and theophylline are shown in Fig.2. The peaks of Si-O-Si(447,1097cm^{-1}) , Si-OH(802,945cm^{-1})are for IO-PVP-SiO_2 and CN(1189cm^{-1}), CH(1447cm^{-1}), C=C(1565cm^{-1}),C=O(1568,1716 cm^{-1}) , NH(3431cm^{-1}) for theophylline. From FT-IR spectra we demonstrated that Au and Theophylline located on IO-PVP-SiO_2. The crystal structure was verified using x-ray diffraction (XRD); The XRD patterns of PVP, $SiO_2$1bv modified magnetite nanoparticles, Fe3O4 compared to neat Fe3O4 molecules are shown in Fig. 3. The peaks observed in this pattern were consistent with those of standard XRD pattern of Fe3O4 (reference JCPDS No. 82-1533) and confirm crystallinity of Fe3O4 nanoparticles. The crystalline size of Fe3O4 at the characteristic peak was calculated by Scherrer formula as follows:

$D = K\lambda/\beta\ 1/2\ \cos\theta$

where D is the average crystal size, K is a constant (here chosen as 1); λ is the wavelength of X-ray radiation (1.54056 A), β 1/2 is the half width of the diffraction peak and θ (°) is Bragg angle. The results of D values, using 311 plane for the sample were 8 nm. While the absence of (210) and (300) peaks in this recorded XRD pattern show that separate maghemite (γ-Fe2O3) is not present in the samples.

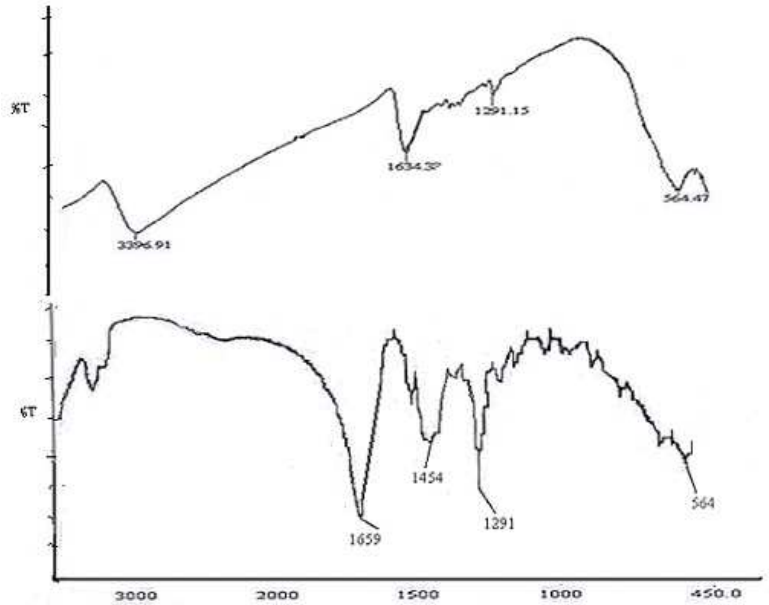

Fig.1 the **FT-IR** spectra of PVP- Fe_3O_4 (top) and PVP(botom)

The size and morphology of nanoparticles were studied by transmission electron microscopy (TEM); in Fig.4 was showed TEM of IO-PVP ,IO-PVP-SiO_2-Au and loading with drug. These images showed that nanoparticles are spherical and the size of them are about 10-12 nm. This value is in accordance with the particles size calculated hsingSherrer formula for Fe3O4 core. The surface images and surface morphology were studied by scanning electron microscopy(SEM). In Fig.5 SEM images of with and without drug of nanoparticles are shown .surface images of nanoparticles well defined loadind of drug.

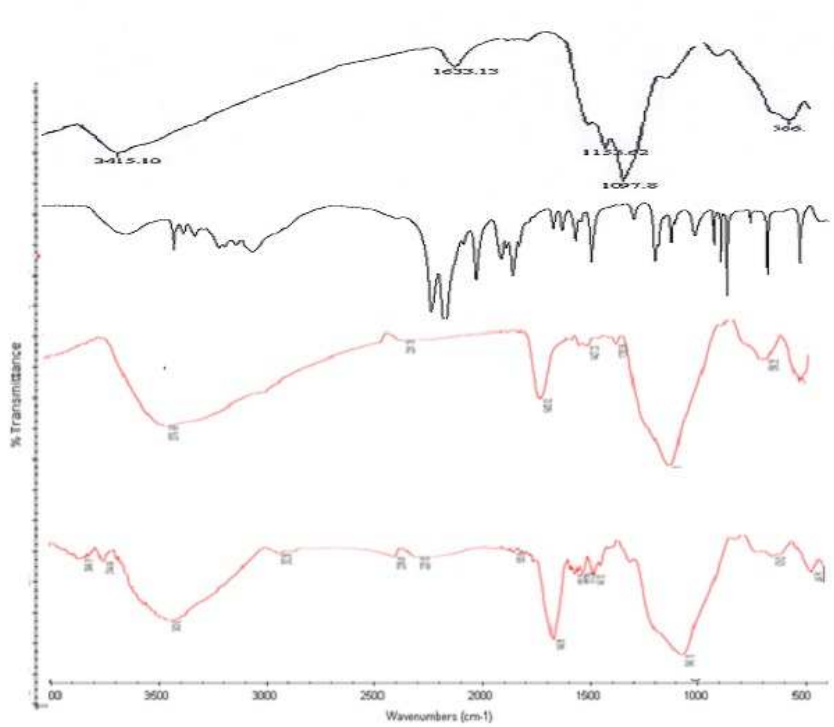

Fig .2 The **FT-IR** spectra of (from up to down), IO-PVP-SiO_2, IO-PVP-SiO_2-Au, IO-PVP-SiO_2-Au-Theophylline

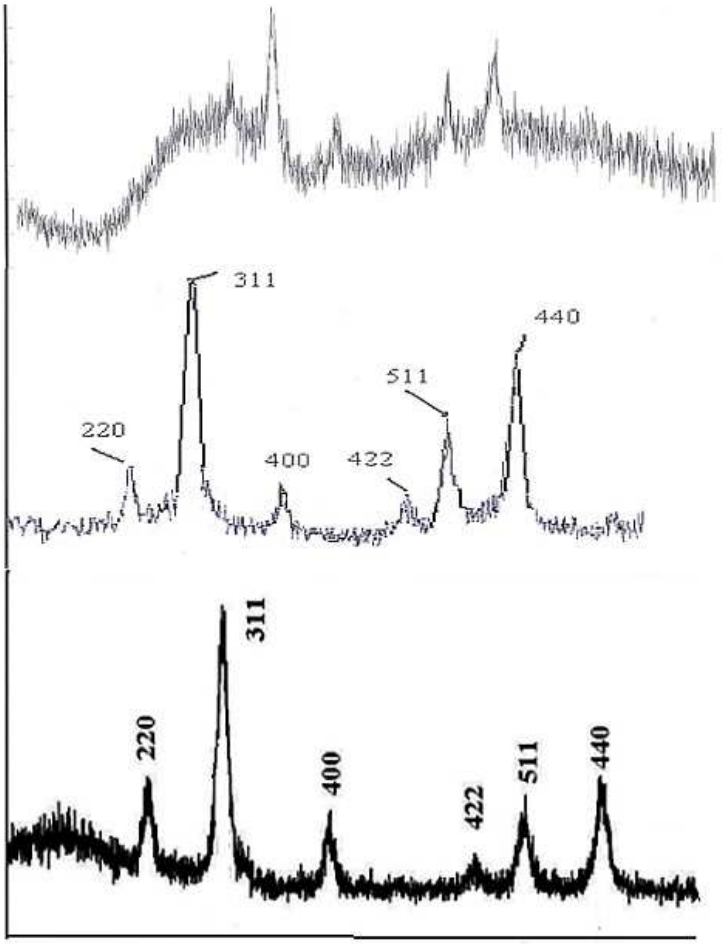

Figure 3. The XRD pattern of (from up to down) IO-PVP-SiO_2, IO-PVP, IO nanoparticles.

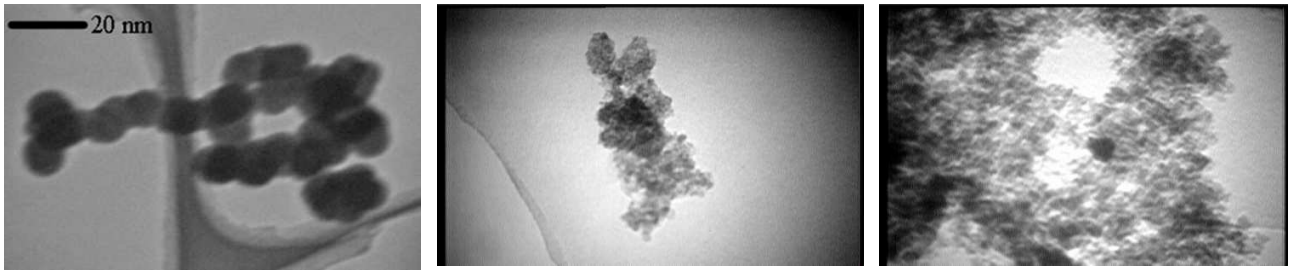

Figure 4 the TEM images of (from up to down) IO-PVP, IO-PVP-SiO_2-Au, IO-PVP-SiO_2-Au-drug

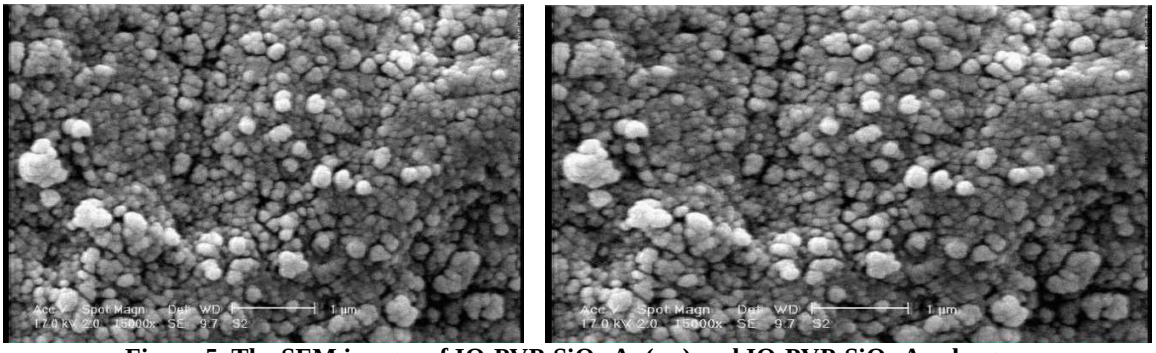

Figure 5. The SEM images of IO-PVP-SiO_2-Au(up) and IO-PVP-SiO_2-Au-drug

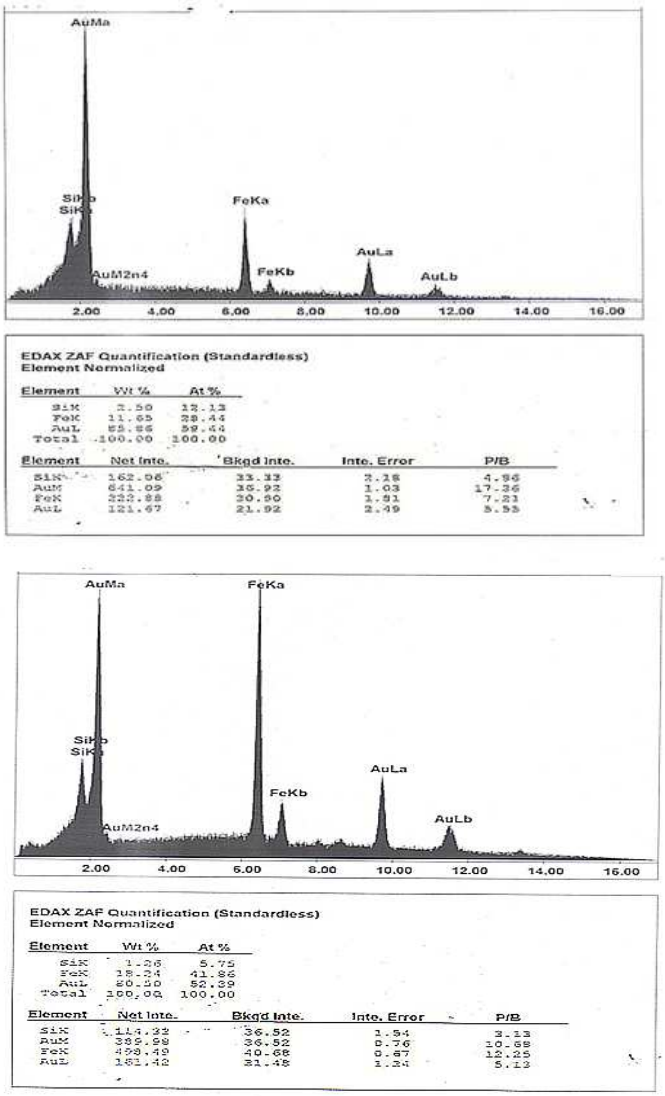

Figure 6 the EDX of IO-PVP-SiO_2-Au(top) and IO-PVP-SiO_2-Au-drug nanoparticles(bottom)

4. Conclusion

Following the investigation of the nano-sized magnetite particles, we assume that the resulted magnetic fluid based on multiple-layer coated nanoparticles obtained by co-precipitation method, could be used for biological applications. Manufacturing such type of nanomaterials, could be also useful in drug delivery.

5. Acknowledgement

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