PREPARATION AND CHARACTERIZATION OF IRON OXIDE MAGNETIC NANOPARTICLES COATEDWITH PEG OR PVA AND 5-FLUOROURACIL FOR DRUG DELIVERY SYSTEM

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Abstract: Two nanocarriers were prepared by the co-precipitation of iron salts in ammonia solution followed by coating separately with polyvinyl alcohol (PVA) or polyethylene glycol (PEG) to form PVAMNPs and PEGMNPs nanoparticles, respectively. They were then loaded with 5-fluorouracil (5F) at different pH from 4 to 9. Physico-chemical characterizations were accomplished via X-ray diffraction, high-performance liquid chromatography (HPLC) and particle size analysis (PSA). X-ray diffraction results showed that both nanocarriershave the cubic inverse spinal structure. HPLC analysis indicates thatthe increase in pH and the use of PEG as the stabilizer markedly increased the drug loading. Particle size analysis (PSA)revealed that at high pH and with PEG as the stabilizer resulted in smaller particle size.

Keywords: Nano drug delivery, Layered double hydroxide, Iron oxide, 5-fluorouracil.

I. INTRODUCTION

Nanomedicine is an advanced field of medical studies where nanomaterials are designed and synthesised for various biomedical applications. Lately, nanomedicine is widely getting attention for theranostics applications i.e. simulatneous disease diagnosis and treatment. In addition, the use of magnetic nanomaterials is highly sought-after for nanomedicine applications particularly for targeted delivery, hyperthermia and biosensors. As important biomedical nanomaterials, magnetic nanomaterials need to have (1) superparamagnetism property which prevents residual magnetism induced aggregation; (2) sufficient magnetic responsiveness, which ensures the feasibility for external magnetic field induced separation and delivery; (3) monodispersion in size, which is critical for the electrical and magnetic properties of any nanoparticles due to their fundamental size dependent properties;(4) easily functionalizable surfaces, which are important for further functionalization, such as the linkage of recognition molecules. Core–shell structural superparamagnetic iron oxide hybrid nanoparticles are exceptionally promising materials. Coatings could stabilize magnetic nanoparticles, lead to better dispersion and biocompatibility, and could also be further modified with functional molecules of various descriptions for diverse applications. This paper will describe the development of theranostic nanoparticles by exploitation of their superparamagnetic core–shell structures.

II. DETAILS EXPERIMENTAL

2.1. Materials and Procedures

Distilled deionized water ($18.2 M\Omega cm^{-1}$) was used in all experiments. Iron (II) chloride tetrahydrate ($FeCl_2 \cdot 4H_2O \geq 99\%$), iron (III) chloride hexahydrate ($FeCl_3.6H_2O$, 99%) were purchased from Merck, Germany. Polyvinyl alcohol (99-100% degree of hydrolysis) and polyethylene glycol, average M.W. 6000 were purchased as a raw material from Acros Organics. Ammonia solution (25%) was obtained from Scharlau. Aluminium nitrate($Al(NO_3)_3.9H_2O$) with 98.5% purity and magnesium nitrate ($Mg(NO_3)_2 \cdot 6H_2O$) with 99%puritywere supplied by ChemAR. The drug used in this study is 5-fluorouracil($C_4H_3FN_2O_2 \geq$ 98%) was obtained from AKSci.Dimethyl sulfoxide ($(CH_3)_2SO \geq 99\%$) was purchased from Sigma Aldrich, Merck.

2.2 Experimental

In order to prepare magnetite iron oxide coated with polyethylene glycol and polyvinyl alcohol (FPEG/FPVA), the mixture of 2.43 g ferrous chloride tetrahydrate ($FeCl_2 \cdot 4H_2O$), 0.99 g ferric chloride hexahydrate ($FeCl_3 \cdot 6H_2O$), and 80mL deionized water in the presence of 6mL ammonia hydroxide (25% by mass) was exposed to ultrasonic irradiation for 1 h. The precipitates were centrifuged and washed 3 times and then the washed precipitates were dispersed in 100mL deionized water and mixed with 2% PEG or 2% PVA. Then the nanoparticles were placed in an autoclave at 200 ^oC for 24 h. The black precipitates were then collected by a permanent magnet and washed three times to remove the excess PEG or PVA which does not participate in the coating process. The washed precipitates were re-dispersed in 50 mL ethanol and added dropwise into a layered double hydroxides solution (Mg/Al) by stirring the mixture until the pH decreased to about 7. Then the core-shell were centrifuged at 5000 rpm.The 3% of drug, 5F [4, 21] which was dissolved in dimethyl sulfoxide, was added into the composite

(magnetite-PEG-LDH(Mg/Al) and the mixture was stirred for 24h. Finally, the coatedmagnetite was washed and dried in an oven. The same procedure was done to prepare magnetite iron oxide coated with polyvinyl alcohol.The co-precipitates were characterized by X-ray diffraction (XRD), high performance liquid chromatography (HPLC) and particle size analysis (PSA).

III. RESULTS AND DISCUSSION

3.1 X-Ray Diffraction

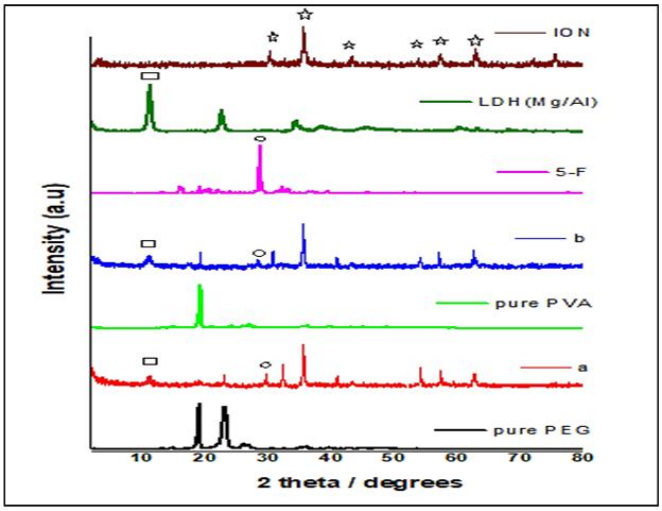

Fig. 1: XRD patterns of magnetite –PEG 2% -LDHs-drug (a), magnetite –PVA 2% -LDHs-drug (b)

Powder X-ray diffraction patterns of magnetite coated with PVA(PVAMNPs) and PEG (PEGMNPs), LDH(Mg/Al) and drug (5-FU) are presented in Figure 1(a) and (b), respectively. Pure PEG shows two main diffraction peaks with high intensity at $2\theta = 19.3^{o}$ and 23.5^{o} and a broad peak due to PVA at $2\theta = 19.5^{o}$. All iron oxide nanoparticles have six characteristic peaks at $2\theta = 30.16^{o}$, 35.95^{o}, 43.34^{o}, 54.17^{o}, 57.27^{o} and 62.98^{o}. From the XRD patterns, it has also been found that these six diffraction peaks correspond to the pure magnetite nanoparticles with a cubic inverse spinal structure (Reference JCPDS Number 82-1533). Owing to observing these characteristic peaks in two nanocomposites (Figures 1(a) and (b)) it is evident that the coating process did not result in a phase change of the iron oxide nanoparticles. In addition, the XRD also indicates that PEG or PVA was well loaded onto the iron oxide nanoparticles. The peaks belong to LDH and drugare also observed on both samples, which means that the combination of nanocomposite and drug are well integrated into the LDH.

3.2 Particle Distribution Measured by PSA

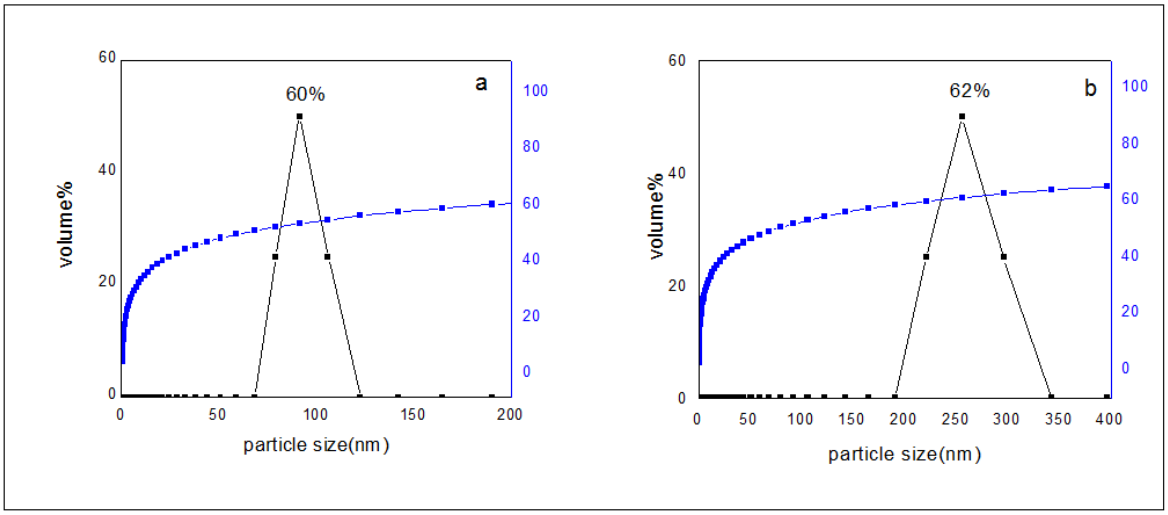

Fig. 2: Particles size distribution of magnetite –PEG 2% -LDHs-drug (a) , magnetite –PVA 2% -LDHs-drug (b)

The synthesized nanoparticles have a narrow size distribution when coated with PEG, and the average particle size is 87 nm with the size distribution in the range of 60 to 130nm. While the nanoparticles synthesized with PVA has larger average particle size. Nanoparticles with diameters of less than 100 nm can be easily passed

from the tissues of the blood vessels and rapidly collected in the liver cell, while nanoparticles with more than 150 nm are not. Therefore, the magnetite coated with PEG produces more appropriate particle size and useful for further studies.

3.3 Effect of PVP and PEG on drug loading percentage of 5-fluorouracil

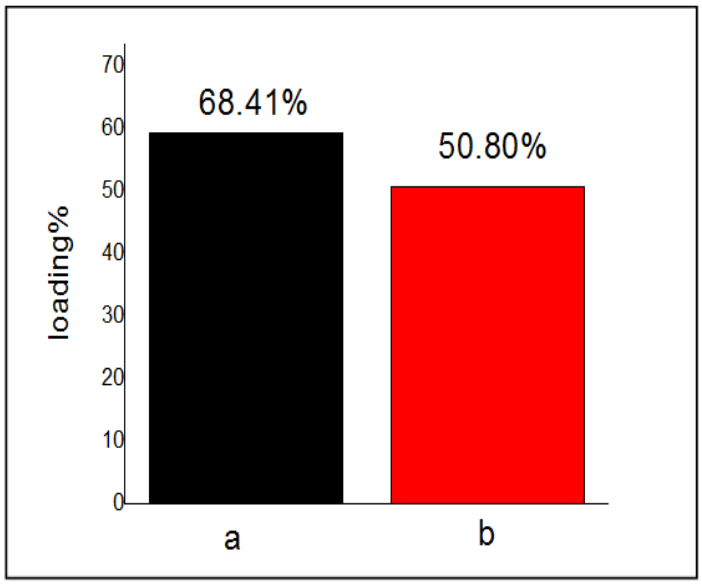

Fig. 3:Drug loading of the nanoparticles; magnetite –PEG 2% -LDHs-drug (a) and magnetite –PVA 2% -LDHs-drug (b) obtained by HPLC analysis.

Drug loading percentage of 5F is presented in Figure 3. The percentage of drug loading for magnetite–PEG 2% -LDHs-drugis higher than magnetite–PVA 2% -LDHs-drug, with 68.41 and 50.80% loading, respectively when thepH used is higher. Importantly, it was also observed that drug loading percentage in sample using PEG as the coating agent is higher than the one using PVA.

CONCLUSION

X-ray diffraction results showed that both nanoparticles with cubic inverse spinal structures were successfully prepared using the co-precipitation method. Highperformance liquid chromatography indicated that at high pHand the use of PEG as stabilizer resulted inmarkedly enhancedpercentage drug loading with smaller particle size and narrow size distribution.

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