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Core–shell hybrid nanomaterials based on $CoFe_2O_4$ particles coated with PVP or PEG biopolymers for applications in biomedicine

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ABSTRACT

Monodisperse core–shell hybrid nanoparticles based on cobalt ferrite ($CoFe_2O_4$) particles coated with polyvinylpyrrolidone (PVP) or polyethylene glycol (PEG) biopolymers were obtained employing a two-step procedure: the $CoFe_2O_4$ of 21 nm mean particle size were first synthesized by coprecipitation method assisted by PVP soft template and then were coated by PVP or PEG biopolymers. The effect of the thermal treatment upon the phase evolution of the obtained precursor from the coprecipitation step was monitored by X-ray diffraction (XRD) and Fourier transform infrared spectroscopy (FTIR) analyses. The FTIR spectra also indicated the interaction between the cobalt ferrite particles and the two polymers were used as biocompatible coatings. Transmission electron microscopy (TEM) and Selected Area Electron Diffraction (SAED) analyses revealed the formation of approximately 22 nm $CoFe_2O_4$-PVP and $CoFe_2O_4$-PEG hybrid nanoparticles. The magnetic measurements indicated that all synthesized hybrids were appropriate for applying in biomedical field. Testing the bioeffect of the uncoated cobalt ferrite nanoparticles and corresponding hybrids on *Bacillus subtilis*, *Pseudomonas aeruginosa*, *Escherichia coli*, *Salmonella enterica serovar typhimurium* bacteria and *Candida scotti* yeast it was clear that no significant toxic activity was obtained. Moreover, all the prepared nanohybrids and their components possess antioxidant activity.

1. Introduction

Finding new therapies in the field of medicine is always one of the most important challenges. The development of new tools such as magnetic hybrid nanomaterials consisting of cobalt ferrite nanoparticles coated by biopolymers may have a crucial role in their implementation in cancer therapy since beneficial results would lead to the improvement of public health, increase of lifetime and decrease of mortality.

The cancer therapy applications of CoFe2O4 nanoparticles coated by biopolymers are sustained by the numerous properties of both components particularly by their special magnetic properties. For this reason there have been efforts made in the synthesis and characterization of CoFe2O4 to achieve their required features such as: narrow size distribution, high magnetization values and uniform shape. These cobalt ferrite nanoparticles are considered to have application in some fields of biomedicine like magnetic resonance imagining (MRI), hyperthermia and delivery drug consumption which implies the use of an external magnetic field to action them from the distance [1].

Until now various synthetic routes have been studied for the preparation of $CoFe_2O_4$ nanoparticles, such as hydrothermal [2], coprecipitation [3], microemulsion [4], forced hydrolysis [5], and reduction–oxidation routes [6] but the principal difficulty of these methods is that the as-prepared nanoparticles are extremely agglomerated, and have poor control of size and shape in most cases, thus restricting their applications [7]. A way to overcome these difficulties, for the preparation of size- and shape-controlled monodispersed $CoFe_2O_4$ nanoparticles is the coating of the magnetic nanoparticles with biopolymers [8,9]. Consequently we adopted a coprecipitation assisted with surfactant (e.g. as polymer) method to successfully synthesized the cobalt ferrite nanoparticles.

Coating the magnetic cobalt ferrite nanoparticles with polymers brings the following advantages: prevents their agglomeration by forming a steric barrier between them, provides biocompatibility, offers the possibility to link on the target zone and avoids the recognition and elimination from the human organism by reticuloendothelial system of the immune system [10–12]. Thus we chose two biopolymers for cobalt

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ferrite nanoparticle biocompatibilization: polyethylene glycol (PEG) and polyvinylpyrrolidone (PVP) (Fig. 1).

Choosing PEG polymer for cobalt ferrite nanoparticle coating is based on its following attributes: biocompatibility, low cost, nontoxicity, non-inflammability, easy to handle and its multiple medical uses such as: excipient in pharmaceutical, lubricant eye drops [13], basis in many skin creams, dispersant in toothpastes and vectors in gene therapy [14], and food additive used as anti-foaming agent [15] compound in monoclonal antibody production [16].

The second polymer PVP was selected for cobalt ferrite biocompatibilization taking into account the following reasons: is used as a binder for various pharmaceutical tablets [17], disinfectant in combination with iodine used in various products like Betadine [18] solutions, ointment, pessaries, liquid soaps and surgical scrubs. It is also used in the wine industry as a clearing agent for white wine or some beers.

The objective of this work is the facile and low cost approach to obtain core–shell nanostructured hybrids having suitable properties (such as: biocompatibility, special magnetic properties, no or low toxicity and antioxidant activity) for applying in biomedical field. Consequently, we proposed a synthesis strategy which involves two steps. In the first step we synthesized cobalt ferrite nanoparticles by nonconventional coprecipitation method assisted by PVP soft template. In a second stage we used the effective PEG and PVP polymers to coat the cobalt ferrite nanoparticles. The effects of various experimental conditions on the morphology of the prepared nanohybrids were investigated. Additionally, we report a comparison study of the influence of the PVP and PEG polymers used for the coating of the cobalt ferrite nanoparticles upon the morphology (size and agglomeration tendency) hybrids finally obtained.

To justify the potential of applying them in biomedicine the two nanohybrids and the components that form them were characterized by magnetic measurement investigation, antioxidant activity tests and biologic activity analyses. It is known that the lack or low levels of antioxidants and the presence of reactive oxygen species (H_2O_2, $^{\bullet}OH$ e.g) in human body cause oxidative stress which appears to contribute to the occurrence of various human diseases such as cancer, Alzheimer's disease [19,20], Parkinson's disease [21], coronary heart disease, diabetes [22,23], and rheumatoid arthritis [24]. Therefore, the oxidative stress can be regarded as the cause and the consequence of some diseases. As a conclusion the antioxidants have been investigated for the prevention of the diseases caused by reactive oxygen species and used in dietary supplements. To the best of our knowledge, till now there is no report on the investigation of the antioxidant activity of the cobalt ferrite nanoparticles and their corresponding nanohybrids.

Also, from all magnetic oxide nanoparticle based hybrids with potential of applying in biomedical field, much attention was paid only to those based magnetite nanoparticles. Therefore, within present paper, the research is directed to the synthesis, characterization and investigation of properties useful for applying in biomedical field of other nanosized ferrite (cobalt ferrite) and its hybrids formed by coating it with PEG and PVP polymers.

2. Experimental section

The chemical reagents used in this study are ferric nitrate ($Fe(NO_3)_3 \cdot 9H_2O$), cobalt nitrate ($Co(NO_3)_2 \cdot 6H_2O$), ammonia solution 28%, polyvinylpyrrolidone (PVP), and polyethylene glycol (PEG). All reagents are from Sigma Aldrich and used without further purification. Manipulations and reactions were carried out in air without nitrogen or inert gas protection.

For antioxidant activity tests were used the following reagents: 1,10-phenantroline (Phen, 99%), 2,4,6-tris(2-pyridyl)-striazine (TPTZ, 99%) and neocuproine (Neo, 99%) were obtained from Sigma Aldrich, while acetic acid, hydrochloric acid, sodium acetate, iron (III) chloride hexahydrate ($FeCl_3 \cdot 6H_2O$), iron (II) sulfate heptahydrate ($FeSO_4 \cdot 7H_2O$), methanol (99,8%), acetone (99,5%), and copper (II) chloride ($CoCl_2 \cdot 6H_2O$) were obtained from Merck. Double distillated water was used for sample solution preparation.

The mixed solution containing 100 mL of 0.3 M $Co(NO_3)_2 \cdot 6H_2O$ and 0.6 M $Fe(NO_3)_3 \cdot 9H_2O$ (with Co:Fe ratio of 1:2) was arranged in distilled water. To this solution was added dropwise a volume of 1 M NaOH under strongly stirring till the pH value was 12. The reaction was kept at room temperature for 2 h. During the procedure, the color of solution changed from the initially brown to dark brown and precipitation occurred. The precipitate was filtered and carefully washed many times with distilled water and then was dried at 80 °C in air. The resulted powder was calcined at 200 and 400 °C respectively.

The single phase cobalt ferrite power obtained by calcination at 400 °C was used for the preparation of the two hybrids by dispersing 30% of cobalt ferrite in a solution of 20% PEG or 20% PVP. The nanohybrid powders ($CoFe_2O_4$-PVP, $CoFe_2O_4$-PEG) were separated by centrifugation and dried at room temperature.

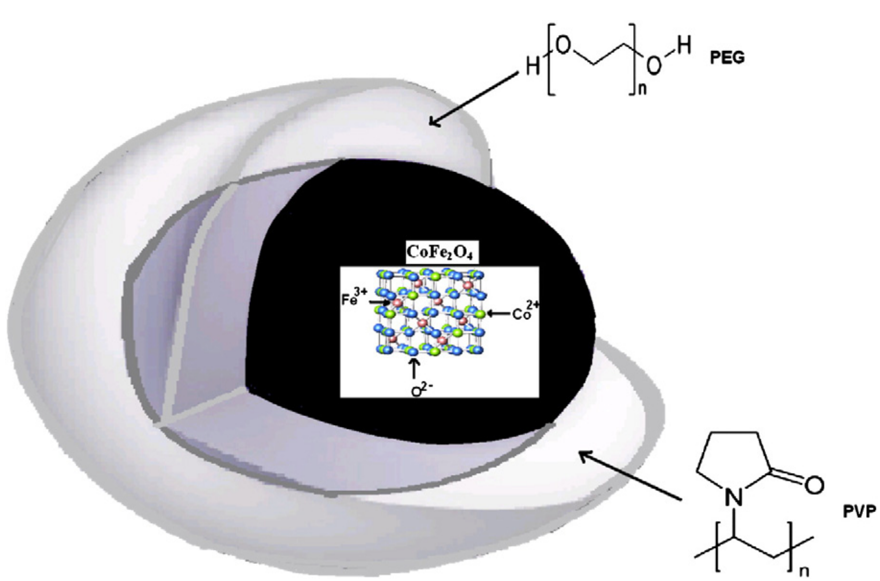

Fig. 1. The schematic representation of the core–shell hybrid materials containing the $CoFe_2O_4$ core and PEG or PVP shells proposed for investigation.