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Advanced composite materials based on hydrogels and ferrites for potential biomedical applications

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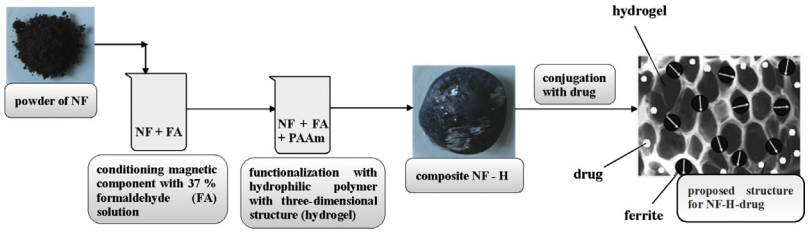
HIGHLIGHTS

- $NiFe_2O_4$ was obtained by sol–gel autocombustion method.
- The hydrogels were obtained by the polymerization-crosslinking simultaneous method.
- The composites were obtained by the polymerization/crosslinking method.
- The as-obtained composites were used for attaching of active principles.
- The microbiological activities were determined by the *Staphylococcus aureus* test strain.

GRAPHICAL ABSTRACT

Synthesis protocol for NF–H–drug.



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ABSTRACT

The paper discusses the synthesis, characterization and microbiological testing of a nanostructured nickel ferrite embedded within polyacrylamide based hydrogels matrix. Nickel ferrite was obtained by the sol–gel autocombustion method using citric acid as chelating/fuel agent, while the hydrogels and the ferrite–hydrogel composites were prepared by an original polymerization-crosslinking simultaneous method using a monofunctional crosslinking agent. The as-obtained samples were characterized by IR spectroscopy, XRD, SEM, being subsequently used for the attachment of active principles (ampicillin). The microbiological activities of composites were determined against the *Staphylococcus aureus* test strain. Kinetic studies of drug delivery were performed.

The antibiotic was progressively delivered both by the ferrite–hydrogel–drug and ferrite–hydrogel with gelatin–drug systems for a longer time.

1. Introduction

Nanoscience is one of the most important research and development frontiers in modern science. Synthesis of nanostructured materials offers several advantages due to their suitable structural and physical properties, which permits their use in biomedical areas [1].

Studies developed in the last decade have shown a high interest for using magnetic nanoparticles in biomedical field for hyperthermia tumor treatment, targeted and pulsed release of active principles, or as contrast agents for diagnosis and magnetic guided devices. Magnetic nanoparticles are able to "carry" active (antibiotics, antitumor, antifungal) principles on their surface or within

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their core, and to target them directly at the site disease. Magnetic nanoparticles are interesting due to their high chemical (oxidation resistance) and thermal stability [2]. Application of magnetic nanoparticles in biomedical areas is based on their ability to combine properties like appropriate saturation of magnetization, surface interactive functions, biocompatibility, known as contributing to reducing side effects, concomitantly with increasing drug efficacy. In the absence of a "shell", nanoparticles tend to agglomerate and to absorb plasma proteins on their surface. Consequently, they are swallowed by macrophages before arriving at the disease site, which reduces treatment's efficiency [3].

The solution often employed to eliminate these disadvantages is "dressing" nanoparticles with hydrophilic polymers, such as poly-ε-caprolactone, dextran, polyethylene glycol, hydrogels [4]. Hydrogels, porous polymeric materials with a three-dimensional structure, high hypersorption capacity and sensitivity to external stimuli (temperature, pH, humidity, light, electrical fields), aroused the interest of researchers as early as 1960, when Wichterle and Lim found out the excellent optical properties of poly (2-hydroxyethyl methacrylate), a polymer used as a basic component for soft contact lenses [5,6]. Due to their excellent mechanical and diffusion properties, capacity to absorb a large among of water (up to 95% by weight of polymer), high biocompatibility with human tissues and the capacity to mimic living tissues, hydrogels are used in the most various areas, namely pharmaceuticals [6], cosmetic industries, medicine [7], tissue engineering, electrophoresis and chromatography, food, agriculture, electronics and electrotechnics, photographic technique, etc. [8,9].

Polyacryalmide-based hydrogels are used for biomedical, pharmaceutical or agricultural applications such drugs containing hydrogels (5%) and hydrogen peroxide (95%) in plastic surgery, as coating agents of drugs for protecting the active principles and masking of unpleasant taste and odor, as well as for controlled and targeted release of drugs, mechanical protector for iris, corneal endothelium and retina, in sandy soil stabilization, etc. [10,11].

Inserting magnetic nanostructured oxidic compounds within the polymeric three-dimensional network leads to materials with pre-established architectures, magnetic properties and high biocompatibility provided by the high water content. These composite materials can be used for immobilization of active principles, or as materials subsequently guided to the place of disease where the drug is slowly released. These composites have the effect of increasing the efficiency of the treatment, while avoid damage of the healthy tissue from the vicinity of the lesion [8].

The present paper discusses the synthesis, characterization and microbiological testing of composites of nanostructured nickel ferrite embedded within polyacrylamide-based hydrogels matrix.

2. Materials and methods

2.1. Synthesis of nanostructured nickel ferrite embedded within polyacrylamide based hydrogels matrix

Nickel ferrite ($NiFe_2O_4$) was obtained by the sol–gel autocombustion method using citric acid as chelating/fuel agent, according to the procedure described in a previous paper [12]. The sol–gel autocombustion method ensures stoichiometric control of the final product and allows obtaining of nanometer-size particles, extremely interesting for potential biomedical use. Nickel nitrate hexahydrate, $Ni(NO_3)_2{\cdot}6H_2O$ and ferric nitrate nonahydrate, $Fe(NO_3)_3{\cdot}9H_2O$, were used as cations sources. Atomic ratio of metal cations Ni^{2+}:Fe^{3+} is 1:2 and molar ratio ferrite:chelating/fuel agent is 1:3. The aqueous solutions containing $Ni(NO_3)_2{\cdot}6H_2O$, $Fe(NO_3)_3{\cdot}9H_2O$ and chelating/fuel agent was transformed into a brown colored gel, by heating over an water bath at 75 °C, under vigorous stirring. In order to obtain spinel monophase structure, the gel was subjected to three thermal treatments (at 500 °C, 700 °C and 900 °C, respectively), necessary for the removal of secondary phases and for obtaining high purity nanostructured ferrite of spinel type. After these treatments was obtained pure phase. This sample will be used to prepare the studied composites.

Hydrogels were synthesized by the original polymerization-crosslinking simultaneous method using a monofunctional crosslinking agent. Synthesis made use of acrylamide (AAm) (C_3H_5ON) as monomer, ammonium persulfate ($(NH_4)_2S_2O_8$) as initiator (I), formaldehyde (FA) (CH_2O) as crosslinking agent and gelatin (G) as inclusion polymer [13]. Introduction of gelatin into the polyacrylamide matrix helps to reduce the toxicity of biodegradation products and, consequently, to increase drug efficiency [14].

All chemicals used for synthesis were of analytical grade and were employed without further purification.

The following notations will be used: NF ($NiFe_2O_4$), H (monocomponent hydrogel), HG (hydrogel with gelatin as inclusion polymer), NF–H (composite ferrite – hydrogel), NF–HG (composite ferrite – hydrogel with gelatin).

Composites based on nanostructured nickel ferrite embedded within polyacrylamide (PAAm) based-hydrogel matrix were obtained according to the protocol illustrated in Fig. 1.

NF powder was conditioned in a 37% formaldehyde (FA) solution for 24 h, then the monomer, the initiator and the inclusion polymer, respectively, were added. The heterogeneous mixtures were transformed into gels by heating over a water bath at 50 °C for 5 h. The as-obtained gels were subjected to repeated washing procedures with distilled water in order to remove the unreacted monomer, the crosslinking agent and the linear polyacrylamide. The obtained composites were dried at 37 °C up to constant weight.

2.2. Synthesis of system composite – drug

The as-obtained NF–H and NF–HG composites were immersed in the drug aqueous solution (500 mg ampicillin in 5 ml distilled water), then dried at 37 °C.

The composite – drug systems were microbiological tested using *Staphylococcus aureus* ATCC (American Type Culture Collection) 25923, by the agar diffusion method (Difco).

2.3. Characterization

2.3.1. Characterization of ferrite

IR spectroscopy was used to monitor disappearance of the organic and inorganic phases and spinel structure formation. IR spectra were registered at ambient temperature in the mid infrared range (4000–300 cm^{-1}) using a Bruker spectrophotometer TENSORTM 27-type with Fourier transform (FTIR) and an ATR cell at a 2 cm^{-1} resolution.

The spinel-type structure and single phase formation was confirmed by the X-ray powder diffraction (XRD) technique. The XRD patterns were registered using a Shimadzu LabX 6000 diffractometer equipped with a graphite monochromator, with Cu K_α ($\lambda = 0.15405$ Å), for 2θ ranging between 20° and 80°, at a scanning speed of 0.02°/s.

The morphological characterization of powders was performed by scanning electron microscopy (SEM). Electron micrographs were registered with a Quanta 200 microscope and with an EDAX system of elemental analysis.