

Синтез і характеристика наночастинок супермагнітного оксиду заліза (SPION), покритих аminosіланом

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Наночастинки супермагнітного оксиду заліза (SPION) широко вивчаються останніми роками з огляду на їх унікальні, залежні від розміру властивості і потенційне застосування в органічному синтезі, біотехнології і медицині. Їх широке медичне застосування у таких сферах, як контрольована система постачання лікарських засобів (DDS), магнітний резонанс (MRI), магнітно-рідинна гіпертермія (MFH) і лікування раку є найбільш істотними.

Магнітні частки нанорозміру мають тенденцію збиратися в більш об'ємні групи, втрачаючи специфічні властивості, пов'язані з їх маленькими нанометричними вимірами. Утворення оболонки довкола магнітного ядра запобігає такому скупченню ядер та гарантує дисперсію і стабільність цих наночастинок в різних розчинниках при одночасному збереженні їх властивостей. Крім того, це збільшує біологічну сумісність і забезпечує розташування функціональних груп на поверхні магнітних наночастинок (MNP) для подальшої дериватизації.

Для утворення оболонки довкола магнітних ядер часто використовується кварц (SiO₂), як матеріал, який відзначається чудовою біологічною сумісністю, хімічною інертністю, оптичною прозорістю і некоагуляційним характером.

У цьому дослідженні описано утворення гідрофобних залізних оксидних наночастинок з їх наступним покриттям (3-амінопропіл) триметоксисіланом (TMOSNH₂) і/або тетраетоксисіланом (TEOS) для утворення добре дисперсованих магнітних кварцевих наносфер.

Отримані дані підтвердили утворення наночастинок супермагнітного оксиду заліза (SPION), покритих аminosіланом з різною товщиною кварцового шару і відносно везьким розподілом. Проведено аналіз залежності властивостей MNP (наприклад, дисперсія, стійкість до хімічних реактивів, норма міграції під зовнішнім магнітним полем) від товщини оболонки. Результати цього дослідження цінні для оцінки майбутнього використання цих магнітнокварцевих наносфер в біомедицині.

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Synthesis and characterization of aminosilane-coated superparamagnetic iron oxide nanoparticles (SPIONs)

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Magnetic nanoparticles coated with diverse aminosilane shells were synthesized. The size, structure and chemical composition of the nanoparticles were determined by various techniques, including transmission electron microscopy (TEM), Fourier transform infrared spectroscopy (FTIR) and differential scanning calorimetry (DSC). These results are valuable for assessing the future applications of such magnetic silica nanospheres in biomedicine.

Keywords – magnetic nanoparticles, superparamagnetism, core-shell structure, surface coating, aminosilane.

I. Introduction

Superparamagnetic iron oxide nanoparticles (SPIONs) have been widely studied in recent years due to their unique, size-dependent properties [1] and potential applications in organic synthesis [2], biotechnology [3] and medicine. Medicinal applications, including controlled drug delivery systems (DDS) [4], magnetic resonance imaging (MRI) [5], magnetic fluid hyperthermia (MFH) [6] and cancer therapy [7] are particularly significant.

The prevailing factors that determine medical applications of SPIONs are their shape, size and size distribution. *In vivo* biomedical applications require homogeneous particles for uniform physical and chemical properties. The shape, dimensions and size distribution of resulting nanoparticles can be adjusted by applying a strict control of the reaction conditions (time, temperature, pH, concentration of reactants and added surfactants, stirring rate). The most common methods used to synthesize iron oxide nanoparticles are: coprecipitation of the corresponding salts from solution [9-11], high-temperature decomposition of organic precursors [12, 13] or microemulsions [14, 15].

Nanometer-sized magnetic nanoparticles tend to aggregate into larger clusters losing the specific properties connected with their small nanometer dimensions. [1] For medical purposes it is desirable that particles remain well dispersed in the medium. It can be achieved by surrounding of magnetic cores by homogeneous shell wall. In addition, shell of coating material:

- prevents the formation of large aggregates,
- provides biocompatibility and resistance to physiological conditions such as pH or enzymes,

- o delivers functional groups at the surface of MNPs for further derivatization,
- o ensures stability of these nanoparticles in various solvents.

Magnetic nanoparticles may be coated by organic (usually polymeric [16]) or inorganic (e.g. metallic [17] or silica [18-20]) materials. The shells may be either biocompatible in itself (such as dextran or PEG), or may possess active groups which can be used to connect biologically active compounds as drugs, proteins, nucleic acids etc. Preparation of coating requires highly controlled and sensitive synthesis conditions to ensure complete coverage of core particles with the shell mate.

Silica (SiO₂) is a material frequently used to form shells around magnetic cores because of its excellent biocompatibility, chemical inertness, optical transparency and non-coagulating nature [8]. Silica-coated SPIONs are redispersible and stable in aqueous solutions with a wide range of pH values [21-23]. In addition, hydrophilic negatively charged silica coating provides an ideal platform for covalent binding. Process of silanization is rather complex. It involves a few mechanism and many various intermediates are possible [24-25]. Size of silica-coated iron oxide MNP may be amended depending on the parameters of their synthesis, but the development of monodispersed solution often encounters difficulties.

In this work we describe the preparation of magnetic nanoparticles coated with single and double aminosilane layer and their characterization by transmission electron microscopy (TEM), Fourier transform infrared spectroscopy (FTIR) and differential scanning calorimetry (DSC).

II. Preparation and characterization of aminosilane-coated MNPs

Hydrophobic iron oxide nanoparticles were synthesized according to the well-known modification of Massart's method [25]. This process, based on a particle coprecipitation from a mixture of hydrated ferrous and ferric chloride in an alkaline environment, is commonly used to produce water-based magnetic nanoparticles at low temperatures. Employment of oleic acid (OA) as a surfactant facilitates controlling of the size, distribution and shape of the particles. Subsequently, on the surface of obtained magnetic cores, formation of silica coatings has been carried out. Magnetic nanoparticles were treated with tetraethoxysilane (TEOS) and/or (3-aminopropyl) trimethoxysilane (TMOS-NH₂) to deposit the amino-terminated silica on their surface. Two types of magnetic silica nanospheres were obtained: monolayered Fe₃O₄@TMOS-NH₂ and double layered Fe₃O₄@TEOS@TMOS-NH₂. The overall surface modification procedures are shown in Fig. 1

Magnetic nanoparticles surrounded by a different thicknesses of the aminosilica shells were received in reactions of equal amounts of oleic acid-stabilized MNPs with varying volumes of TMOS-NH₂ (Table 1).

The Fe₃O₄@TEOS@TMOS-NH₂ nanospheres were prepared in two-step synthesis. Initially, MNPs were modified with TEOS leading to insertion of silanol (Si-

OH) and ethoxysilane (Si-OEt) groups at the surface of the magnetic nanoparticles. These functional groups, were subsequently treated with TMOS-NH₂ creating second, amine-terminated silica layer around magnetic cores.

Table 1

Reaction volumes of tmos-nh₂ used to synthesize the silica shells of different thicknesses

Sample name	Volume of added TMOS-NH ₂ [mL]	Mass increase [mg]	Shell thickness [nm]
Fe ₃ O ₄ @TMOS-NH ₂ 1	0.1	50	1-3
Fe ₃ O ₄ @TMOS-NH ₂ 2	0.4	255	3-6
Fe ₃ O ₄ @TMOS-NH ₂ 3	0.8	395	5-8

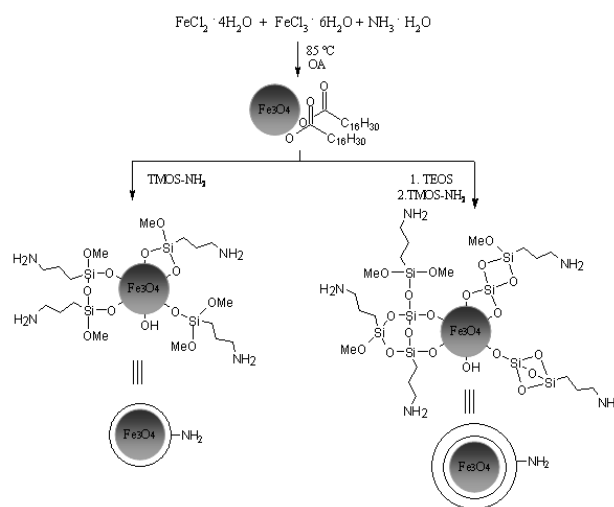


Fig. 1. Synthesis and a surface modification of SPIONs.

The obtained, silica-coated SPIO nanoparticles exhibit higher stability compared to the uncoated nanospheres. In the case of Fe₃O₄@TMOS-NH₂, depending on the thickness of the silane coating, MNPs show different properties in solution. The rate of aggregation and the rate of migration of nanoparticles under external magnetic field decrease with an increase of the thickness of the silane coating. Nanospheres with double silica coating form aggregates that do not undergo dispersion after sonication.

The formed nanostructures have been analyzed using TEM. Figure 2 shows representative TEM images of synthesized magnetic nanoparticles before and after silica coating. It was found that uncoated magnetite nanoparticles (Fig. 2 (A)) show a relatively narrow size distribution and the average size over 100 particles is 10 nm. It is noticeable that uncoated MNPs tend to aggregate in loose clusters. The Fe₃O₄@TMOS-NH₂ nanoparticles (Fig. 2. (B)) are more dispersed than the uncoated one, suggesting successful silanization process. The dependence of shell thickness on volume of added (3-aminopropyl)trimethoxysilane is summarized in Table 1. Isolated particle (Fig 2.(C)) with light contrast shell, presumably due to the silica, and dark contrast core of Fe₃O₄ is easily observed. Particles with double silica

coating (Fig. 2(D)) instead of monodispersed core-shell nanostructures turn out to form bulk composites, thus they are useless for medical purposes.

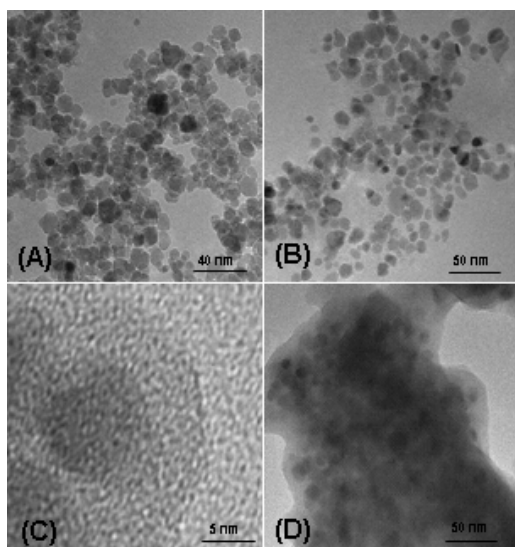


Fig. 2. TEM images of: (A) MNPs (B) $Fe_3O_4@TMOS-NH_2_2$ nanoparticles, (C) an isolated $Fe_3O_4@TMOS-NH_2_2$ nanoparticle and (D) $Fe_3O_4@TEOS@TMOS-NH_2$ structure

The FTIR spectra analysis was performed to confirm core-shell structure of $Fe_3O_4@TMOS-NH_2$ nanoparticles and different thickness of coating. Fig. 3 shows the FTIR spectra of magnetite nanoparticles before and after surface modification.

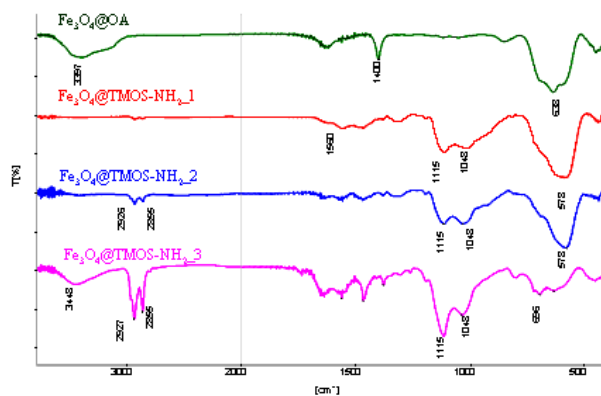


Fig 3. FTIR spectra of silica-modified SPIONs compared to OA-stabilized magnetite

The existence of magnetite nanoparticles stabilized with oleic acid is indicated by iron carboxylate bands around 1400 cm^{-1} and band at 638 cm^{-1} which corresponds to the Fe-O bond of bulk magnetite. Following spectra show new strong bands around 1115 , 1048 cm^{-1} which can be ascribed to the Si-O-H and Si-O-Si groups. The adsorption band of Fe-O-Si bonds cannot be seen in the FTIR spectrum because it appears at around 584 cm^{-1} and therefore overlaps with the Fe-O vibration of magnetite nanoparticles. Differences between the intensity of bands originating from the vibrations of Si-O-

H and Si-O-Si groups indicate changing of the shell thickness.

DSC analysis have been conducted to demonstrate thermal characteristics of MNPs. Differences in the shape of heating curves of uncoated and aminosilane-coated MNPs (Fig 4) confirm changes in the chemical nature of coating.

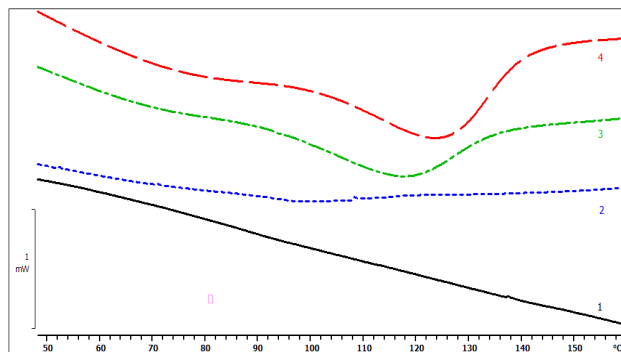


Fig. 4. DSC measurements of: oleic acid-stabilized MNPs (1) and $Fe_3O_4@TMOS-NH_2$ nanospheres of various shell thickness (2-4). Temperature range $50 - 160^\circ\text{C}$; heating rate 10 K/min .

Conclusion

In this study, diverse silica-coated magnetite nanoparticles were prepared with a relatively narrow-size distribution and dimensions in range required for clinical applications. TEM microscopy, DSC calorimetry and FTIR spectra analysis documented the formation of silica coating. The research have revealed that particles with double silica layer had formed large composites, thus they are useless for medical purposes. Therefore, studies focused on more promising monolayer coated MNPs. Obtaining of amino-terminated silane layers of various thickness around magnetic cores was confirmed by elemental analysis and the aforementioned techniques. It was found that thickness of shell affects properties of magnetic cores e.g. dispersion, tendency to agglomeration or resistance to chemical reagents. Influence on the rate of the migration under external magnetic field was also tested. The best properties in the context of potential medical applications exhibit $Fe_3O_4@TMOS-NH_2_2$ particles. The presence of amine group provides opportunity to attach compounds possessing biological activity e.g. drugs, proteins or nucleic acids. In the future, a further study on a biocompatibility and a cell toxicity of obtained aminosilane-coated MNPs will be developed.

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