Magnetic core-shell structures as potential carriers in drug delivery system

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Abstract: *Magnetic core-shell structures have a high potential for promising application in biomedicine as drug carriers. In this paper, magnetic core-shell structure obtained by the sol-gel method was presented. In order to provide the protective coating of magnetic MnFe2O4 nanoparticles, amorphous silica was used. It has been shown that magnetic core was successfully encapsulated in SiO2 matrix and that the received core-shell material had magnetic properties.*

Keywords: magnetic nanoparticles, silica matrix, core-shell structure, drug delivery

1. Introduction

Magnetic nanoparticles are of a great interest in biomedicine applications. For instance, such magnetic nanomaterials can be used in drug delivery as drug carriers. However, it is important to develop protection strategies using biocompatible coatings. Coating layer, like polymer or silica, isolates the magnetic core against the environment and can be additionally used for further functionalization with other molecules [1].

In this work, the method of exemplary magnetic core-shell structure preparation was presented. The role of magnetic core performed $MnFe_2O_4$ nanoparticles, whereas amorphous silica acted as a protecting shell. The sol-gel technique was used to produce the core-shell material. As reported in this article, the sol-gel method enabled the successful coating of magnetic particles with SiO_2 layer. It has been also observed that the encapsulation of magnetic nanoparticles inside the non-magnetic silica matrix influences on a decrease of the saturation magnetization. Such obtained powder still has a potential suitable for use as a drug carrier.

2. Theory

In general, drug delivery system (DDS) is defined as a formulation or device that enables the introduction of pharmaceutical agents into the body to achieve a therapeutic effect. This process concerns not only the transportation of the active drug to the right place in the organism but also the controlled release of medicinal substances. The main objective of drug administration is to reduce the dosage by more efficient and localized targeting of the drug [1-3]. Figure 1 shows a graph presenting the comparison of conventional and controlled drug release concept. As demonstrated, controlled drug delivery provides a steady-state level that is therapeutically effective and nontoxic for an extended period of time, whereas traditional dosage is characterized by immediate release and repeated dosing of the drug which might lead to the risk of dose fluctuation and additional side effects [4,5].

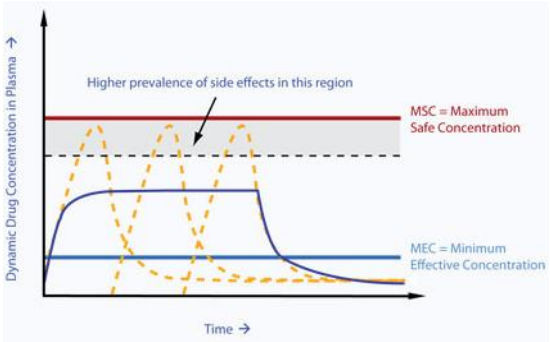

Fig. 1. Plasma drug concentration profiles for conventional (- - -) and controlled release dosage formulations (—) [4]

In recent years, several drug delivery systems have been developed including cyclodextrins, microemulsion, organogels or colloidal carriers (e.g. nanoparticles or liposomes) [6]. There is a lot of attention being given to magnetic nanoparticles as drug carriers. It is connected with their nano-scale dimensions, magnetic properties and possibilities of using them for carrying active molecules [7]. The concept of magnetic drug targeting system relies on the intravascular injection of magnetic nanoparticles with attached drug molecules (e.g. antitumoral agents) and their transportation by the blood

circulation to a chosen location (tumor) by using the magnetic field gradients (Fig. 2). These particles are being concentrated in the selected site with the aid of a magnetic field until the therapy is completed, and subsequently they are removed from the body [1,8,9].

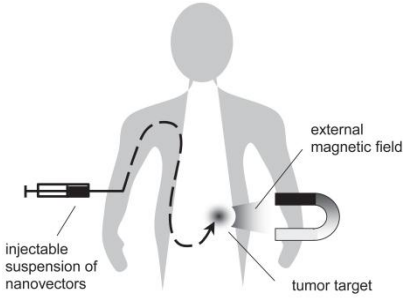

Fig. 2. The principle of magnetic-field guided drug delivery [9]

In terms of magnetic nanoparticles that can be used in DDS the most commonly are quoted iron oxides, like magnetite (Fe_3O_4) or maghemite (γ-Fe_2O_3). However, also other metal and metal oxide nanoparticles are frequently mentioned as potential drug carriers. The most promising transport agents for biomedical applications are especially nanoparticles that exhibit superparamagnetic behaviour. Superparamagnetism is a type of magnetism that occurs in sufficiently small ferromagnetic or ferrimagnetic nanoparticles that have single-domain, i.e. they are composed of a single magnetic domain. These molecules are attracted to a magnetic field but after the removal of this field they do not retain residual magnetism [8,10-12].

However, the magnetic nanoparticles should be covered by a biocompatible coating. The applied coating research directions are divided into two major groups: coating with organic shells, including polymers and coating with inorganic components such as silica or carbon. Materials which consist of thin layer deposited on magnetic core are also called magnetic core-shell structures (Fig. 3). The coating performs the role of a protective shield for the surrounding environment and can be additionally functionalized to link other molecules (e.g. drug, fluorescent dye or targeting ligand) [3,8,13]. The use of a nonmagnetic shell has other tasks as well. It protects magnetic core against air oxidation and prevents metal nanoparticles from aggregates forming [8].

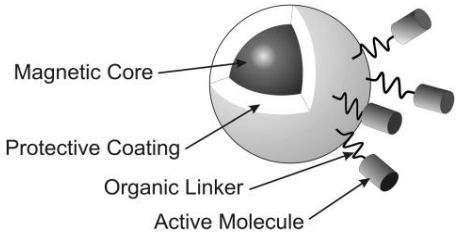

Fig. 3. Schematic diagram of a magnetic core-shell structure for drug delivery [7]

Amorphous silica as a coating of nanomaterials has the advantages of high biocompatibility, lack of toxicity, facile surface modification and chemical stability [14]. SiO_2 also prevents the direct contact of the magnetic core with additional agents linked to the surface of silica shell thus avoiding undesirable interactions [1,15]. Silica encapsulation of magnetic nanomaterials can be attained by a simple sol-gel approach. This method involves the hydrolysis and condensation of silica precursor in alcoholic medium in the presence of ammonia solution as catalyst. Such obtained magnetic core-shell structures have a huge possibility to be applicable in medical drug targeting [16,17].

3. Materials and characterization methods

3.1. Sample synthesis

Magnetic core-shell structure consisting of commercially available magnetic manganese iron oxide (Aldrich) nanoparticles and amorphous silica coating was obtained according to the modified sol-gel Stöber method. The flow chart for the preparation of this material is shown in Figure 4. All reagents were of analytical grade and used as received without further purification.

Silica substrate was prepared by the hydrolysis and condensation of tetraethoxysilane (TEOS, Alfa Aesar, 98%) in a mixture with methanol (POCH, 99.8%) and distilled water, using aqueous ammonia solution (POCH, 25%) as a catalyst to initiate the reaction.

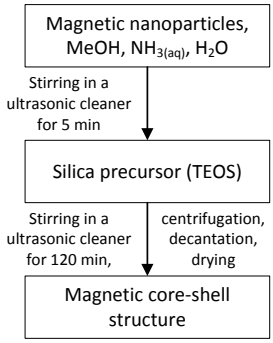

Fig. 4. Chart for the preparation of magnetic core-shell structure

$MnFe_2O_4$ nanoparticles were added to the solution before the addition of silica precursor in order to encapsulate the magnetic dopants in SiO_2 matrix. The sol was continuous stirred for 2 hours in an ultrasonic cleaner at room temperature. The obtained particles were centrifuged, decanted and afterwards dried in a natural air circulation laboratory heating oven at 55 ºC. As a result, magnetic core-shell structure, hereinafter referred to as $MnFe_2O_4/SiO_2$, was obtained.

3.2. Characterization

The morphology of magnetic core-shell structure was determined by a transmission electron microscope (FEI Tecnai G^2 20 X-TWIN). The structure of the received material was confirmed by Rigaku Ultima IV X-ray powder diffractometer equipped with a Cu radiation source. Magnetic properties of $MnFe_2O_4/SiO_2$ and $MnFe_2O_4$ powders were investigated by Quantum Design VersaLab Vibrating Sample Magnetometer. XRD measurements were made in Sol-Gel Materials and Nanotechnology Laboratory of Lower Silesian Center for Advanced Technologies, while magnetic measurements were performed in Multifunctional Amorphous and Crystalline Materials Laboratory.

4. Results

Magnetic core-shell structure $MnFe_2O_4/SiO_2$ was successfully obtained according to the preparation process presented in subsection 3.1. TEM images of the prepared particles are shown in Figure 5. As can be seen, manganese iron oxide nanoparticles are effectively entrapped in silica grains. There is also no visible tendency to nano-sized magnetic particles occurrence on the surface of SiO_2 shell. Therefore, the above presented method of core-shell structure preparation is efficient.

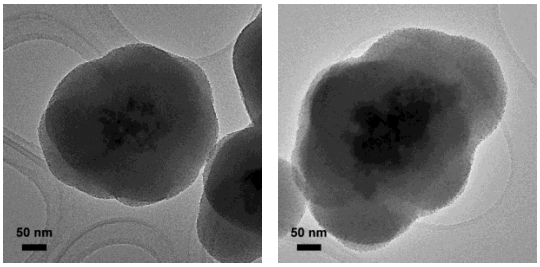

Fig. 5. TEM images presenting magnetic core-shell structure consisting of $MnFe_2O_4$ nanoparticles coated with amorphous silica

The x-ray diffraction pattern for $MnFe_2O_4/SiO_2$ is shown in Figure 6. The XRD pattern is characterized by a broad peak typical for amorphous silica at around 2θ = 23. Characteristic peaks representing the crystal structure of $MnFe_2O_4$ in the obtained powder are prominent at 2θ = 18, 30, 35, 43, 56 and 62. Diffraction pattern of $MnFe_2O_4$ was taken from ICSD database (Inorganic Crystal Structure Database).

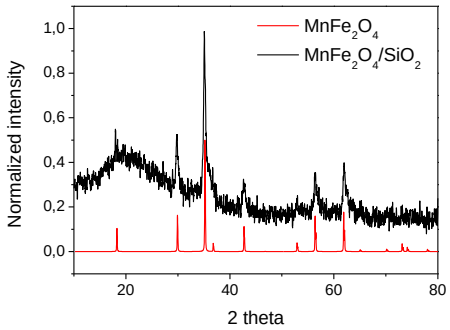

Fig. 6. XRD diffraction pattern of magnetic core-shell structure $MnFe_2O_4/SiO_2$

Figure 7 shows the magnetization with respect to the magnetic field applied (range from -15 to 15 kOe). The hysteresis loops of manganese iron oxide nanoparticles and magnetic core-shell structure were recorded at 300 K. The samples have reached the saturation magnetization (M_S) of 21.7 emu/g and 8.4 emu/g respectively. Encapsulation of magnetic nanoparticles inside non-magnetic silica grains causes a reduction of the saturation magnetization. The observed value of the saturation magnetization of $MnFe_2O_4/SiO_2$ structure was almost three times lower than the value recorded for $MnFe_2O_4$ nanoparticles.

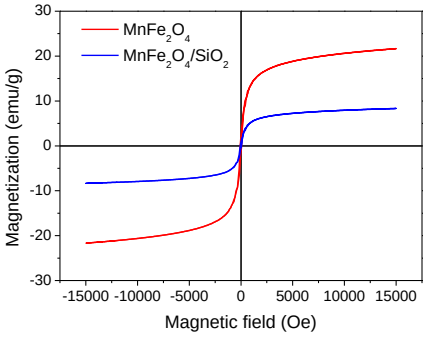

Fig. 7. Magnetic hysteresis loops of $MnFe_2O_4$ nanoparticles and magnetic core-shell structure $MnFe_2O_4/SiO_2$

The prepared core-shell material was dispersed in isopropyl alcohol, and when an external magnetic field was applied, particles immediately moved towards the neodymium magnet, as shown in Fig. 8.

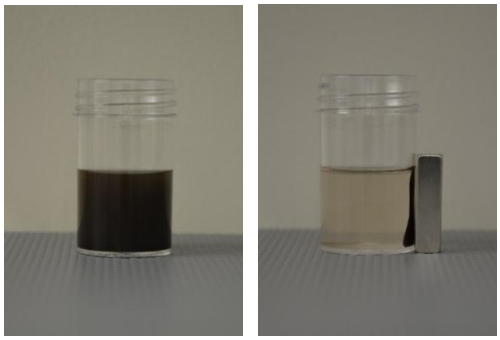

Fig. 8. Photos presenting $MnFe_2O_4/SiO_2$ powder behavior with the use of magnet

5. Conclusions

In summary, the method of magnetic core-shell structures obtainment was developed. The facile sol-gel technique was used for this purpose. Magnetic $MnFe_2O_4$ nanoparticles were effectively coated with amorphous silica. The silica shell acts as a protective barrier and isolates magnetic nanoparticles from reactive environment. Preliminary physicochemical and magnetic studies of the received materials shows it as a promising material for drug delivery system applications. Despite the encapsulation of magnetic core, the prepared structure retains magnetic properties. However, according to expectations the saturation magnetization of the powder decreases by the usage of silica coating. The value of M_S has been reduced from 21.7 to 8.4 emu/g. The silica-coated magnetic nanoparticles may potentially be useful in various biomedical fields such as diagnostics or therapeutic treatments as drug carriers. For this purpose, the SiO_2 shell should be further modified with functional groups (e.g. amine or thiol groups) to attach drugs or target antibodies to the carrier complex.

Acknowledgments

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