

OBTAINING OF Ag@Fe₃O₄ MAGNETIC NANOCOMPOSITE WITH THE “CORE-SHELL” STRUCTURE FOR MEDICAL PURPOSE

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ABSTRACT

PURPOSE: The method of one-pot synthesis of Ag@Fe₃O₄ nanoparticles consisting of a spherical core of magnetite and silver islet shell has been developed. Formation of Ag@Fe₃O₄ composite structures such as “core-shell” will allow combining magnetic controllability of the magnetite core with bactericidal and bacteriostatic properties of the silver shell. This effect is very interesting from the perspective of using particles with the “core-shell” structure in pharmacy and medicine to create new medicines.

MATERIALS AND METHODS: The study subject is magnetite with the islet silver coating obtained by the original single-phase method of chemical co-precipitation with the temperature increasing up to 60–70°C. The studies were conducted by the following methods: X-ray analysis, semi-quantitative phase analysis using the program Match!, scanning electron microscopy. The specific surface area of the samples was determined by thermal desorption of argon, magnetic characteristics were also determined.

RESULTS AND CONCLUSIONS: In the diffraction pattern the silver peaks at 44.6°, 52° and 76.65° were registered, while magnetite peaks did not disappear. It may indicate the islet surface of the magnetic cores. The ratio of the phases is confirmed by the data of the semi-quantitative phase analysis. According to the data of scanning electron microscopy the average particle sizes of the samples obtained were determined. The particle sizes of Fe₃O₄ were 60 nm and for Ag@Fe₃O₄ they were 23 nm. Ag@Fe₃O₄ compared to the Fe₃O₄ one has a slightly larger specific surface area. Magnetization of saturation for the sample of an uncoated magnetite is 67.5 emu/g, for the sample with a silver coating it is 62.5 emu/g.

Keywords: synthetic modified magnetite, nanoparticles, composite magnet system, silver shell

INTRODUCTION

At the stage of intensive development of modern pharmacy, biology and medicine the technologies for obtaining nanoparticles are actively investigated and the magnetic properties of nanosystems finding a variety of applications are studied (1). Advances in nanotechnology is the basis for development of interdisciplinary fields of nanoscience. Physical and chemical effects that occur in the nanoobjects are underlying determinants for nanopharmacy, nanobiology, nanochemistry,

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nanomedicine, nanophysics, nanoelectronics, nanotechnology-based photonics, etc. This is due to the fact that obtaining and studying such small objects is possible only when combining achievements and methods of different scientific disciplines.

In recent years a substantial progress has been made in obtaining micro- and nanoparticles, both monocomponents (2) and composites on their basis with predetermined size, shape and sometimes structure, for a wide range of compositions of composites with the complex structure (3), or by the “core-shell” type (4). An advantage of the latest is increase of the thermal and chemical stability, decrease of cytotoxicity, the possibility of addition of other molecules and functional groups, and the shell itself prevents oxidation of the basic material (5).

In order to produce magnetic nanoparticles with new properties their surface is modified with organic or inorganic materials (polymers, biomolecules, silica, metals, etc.) giving nanocomposites of the “core-shell” type (6,7).

By modifying the surface of nanoparticles with a shell having active functional groups, they can be linked up to different biological objects (8). Introduction of composites of this type is a crucial task, which allows to solve a number of conceptual problems associated with diagnosing of cancer (9–11), obtaining magnetically controlled containers for targeted drug delivery to target cells (12–16), creating medical nanorobots that are capable to eliminate defects in the body of a sick person (17–19), developing biocompatible nanomaterials of a wide range of application, materials with antimicrobial, antiviral and anti-inflammatory activity (20,21), X-ray contrast agents for MRT (22), etc.

The preparative methods of synthesis of magnetite particles with Au-shell (23), and formation of colloidal silver particles (24) are known from the literature, but considerable attention is drawn to similar composite particles partially or completely covered with silver.

Modification of the surface of the magnetite by silver results in appearing bactericidal and bacteriostatic properties of the system and allows to avoid the use of a stabilizer (25) because it is the role of the silver coating. The ability to promote the regeneration of damaged tissues, destruction of old and can-

cer cells, normalization of inflammatory processes, destruction of bacteria (26), viruses, fungi, etc. (27), is due to the advantage of silver over many modern chemotherapeutic agents.

The known methods for obtaining nanosystems of the “core-shell” type have some drawbacks (28–30): the use of little accessible and relatively expensive polymers, time-consuming synthesis and its multistaging. The loss of magnetic properties due to stabilization and full cover significantly reduces the prospects of further use of the product as a magneto-carrier (31,32).

The aim of the work was to optimize the process for the synthesis of Ag@Fe₃O₄ magnetic nanocomposite of the “core-shell” type with the islet cover with preservation of the magnetic properties.

MATERIALS AND METHODS

Such reagents as iron (II) sulfate FeSO₄·7H₂O, iron (III) chloride FeCl₃·6H₂O, 25% aqueous ammonia, argentum nitrate AgNO₃ were used in our study. Glucose was chemically pure.

The X-ray analysis was performed for identification of substances, qualitative phase analysis and determination of the composition of the surface layer. Diffraction patterns were recorded on a DRON-UM1 diffractometer in CoK α radiation of the anode line with a graphite monochromator in the reflected beam with Bragg-Brentano geometry in the angular range of 10-80 degrees in increments of 0.05.

The semi-quantitative phase analysis was performed using the Match! program, version 1.9a.

The average particle size of Ag@Fe₃O₄ nanocomposite was determined by scanning electron microscopy (Tescan Mira 3 LMU), magnification – 500 000 times.

The specific surface area of the samples was determined by thermal desorption of argon (33). Many scientists have already proven that particles with a large specific surface become owners of such unique properties as increased chemical and biochemical activity (34).

To study the magnetic properties a VMP 3000 vibration magnetometer (the membrane oscillation frequency is 70 Hz) at constant magnetic fields with the strength up to 150 kA/m was used. Based on the data obtained cyclic dependencies of magnetization

values on the applied external magnetic field were plotted.

Experimental part

The object of the study is magnetite with the islet silver coating obtained by the original single-phase method of chemical co-precipitation with the temperature increasing up to 60–70°C.

Magnetite nanoparticles coated with the silver islet layer are obtained as follows.

I. Preparation of solutions.

Solution 1. Dissolve the mixture of 13.89 g (0.05 mol) of $\text{FeSO}_4 \times 7\text{H}_2\text{O}$ and 26.90 g (0.1 mol) of $\text{FeCl}_3 \times 6\text{H}_2\text{O}$ in distilled water and dilute to 1 l.

Solution 2. Dissolve the calculated mass of AgNO_3 in distilled water to obtain a solution with the mass fraction of 0.1%.

Solution 3. Glucose solution with the mass fraction of 10%, in the amount required for complete reduction of AgNO_3 (Solution 2).

II. Carrying out the synthesis (the method modified by Elmore (35)).

To 1 l of Solution 1 quickly add 25% aqueous ammonia solution with a thin jet while stirring vigorously with a mechanical stirrer, it is needed for formation of Fe_3O_4 and creation of pH in the range of 10–12 (92.32 ml) and subsequent application of the silver coating (476.91 ml). A black precipitate of Fe_3O_4 is formed.

To apply the silver coating in 10–15 min add successively Solutions 2 and 3 to the solution obtained that is preheated to 40°C while stirring vigorously with a mechanical stirrer. Gradually increase the temperature to 60–70°C, keeping the reaction mixture for 40 min. The change of a black color of the precipitate to light brown indicates completion of the reaction. Keep the resulting solution in a constant magnetic field for 24 h, wash with distilled water to pH = 9–10, filter on a Buchner funnel and dry in the air at room temperature.

RESULTS AND DISCUSSION

The synthetic method proposed provides formation of a colloidal black solution of composite nanoparticles, from which in a few minutes the precipitate of Ag appears on magnetite, and the solution becomes brown. Complete bleaching of the solution over the precipitate when keeping in a constant mag-

netic field within 24 hours was not observed, indicating the formation of a colloidal solution of the silvered magnetic nanoparticles. Along with the adsorption of silver on the surface of Fe_3O_4 , its slight amount remains in the free state in the form of droplets of about 40 nm. The ability of magnetite to behave as a “single drop” (36) provides preservation of all silver introduced in the sample.

To develop an effective method of synthesis the complex of physical and chemical studies was carried out; on their basis the main parameters of the resulting nanocomposite were determined.

In the diffraction pattern (Fig. 1) of the magnetite sample without the shell (curve 1) the peaks at 2θ : 21.3°, 35.2°, 41.55°, 50.75°, 63.2°, 67.65°, 74.5° were registered; for the magnetite covered with a silver coating (curve 2) there were the corresponding peaks at 44.6°, 52° and 76.65°, while magnetite peaks did not disappear. It may indicate the islet surface, and is consistent with the literature data (28,37,38).

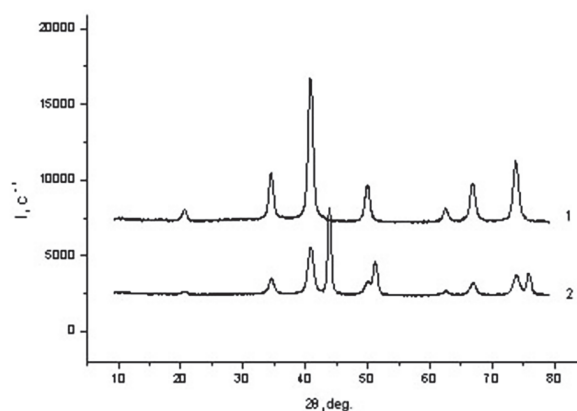


Fig. 1. Diffraction samples Fe_3O_4 (1) and $\text{Ag@Fe}_3\text{O}_4$ (2).

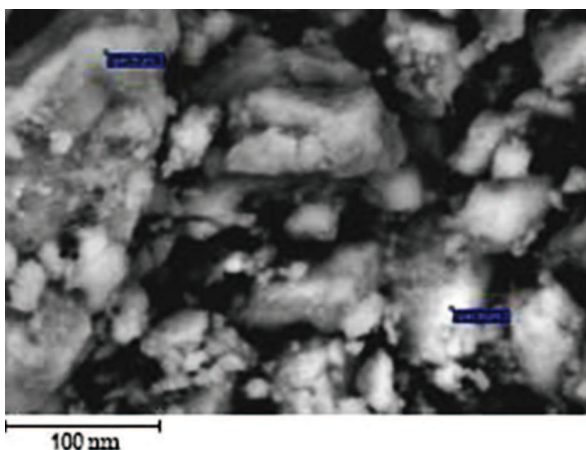
The ratio of the phases is confirmed by the data of the semi-quantitative phase analysis (Table 1).

Table 1. The results of semi-quantitative phase analysis

Sample	Phase composition	Phase content, mass%
Fe_3O_4	Fe_3O_4 JCPDS#88-315	100
$\text{Ag@Fe}_3\text{O}_4$	Fe_3O_4 JCPDS#88-315	67
	Ag JCPDS#87-717	33

According to the data of scanning electron microscopy the average particle sizes of the samples ob-

tained were determined. In the dried sample of Fe₃O₄ the average agglomerate size was 3.2 μm. In the case of the magnetite with a silver coating the desired product was formed immediately as a fine powder with the average particle size of 23 nm. It indicates the absence of agglomeration since the silver coating acts as a stabilizer.



Magnetization of saturation for the sample of an uncoated magnetite (Fig. 3, curve 1) is 67.5 emu/g, for the sample with a silver coating it is 62.5 emu/g (Fig. 3, curve 1). This small difference may be due to a small area of the covered surface, which changes the magnetic parameters.

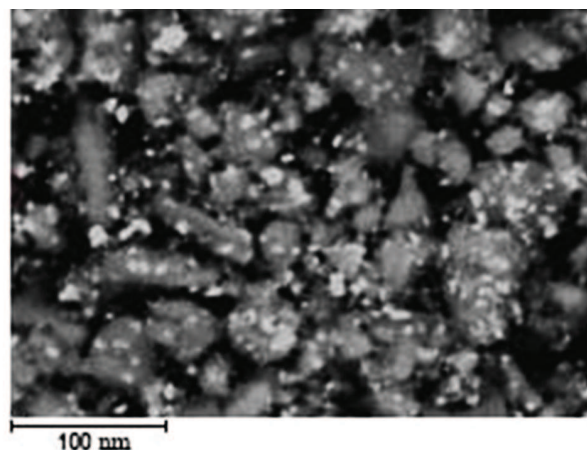


Fig. 2. Microphotography of Fe₃O₄ (a) and Ag@Fe₃O₄ (b).

To avoid the possible agglomeration of Fe₃O₄ (Fig. 2a) at the stage of drying the magnetic fluids of Fe₃O₄ and Ag@Fe₃O₄ were obtained on the water base, after that the particle sizes of Fe₃O₄ (60 nm) and Ag@Fe₃O₄ (23 nm) were determined. It confirms the stabilizing effect of the silver coating in formation of colloidal magnetite particles (Fig. 2b).

Magnetite with the silver surface layer compared to the uncovered one has a slightly larger specific surface area (Table 2), and may indicate reduction of the particle size (39). The large specific surface area increases the area of contact of silvered particles with bacteria or viruses, greatly improving its bactericidal action (40).

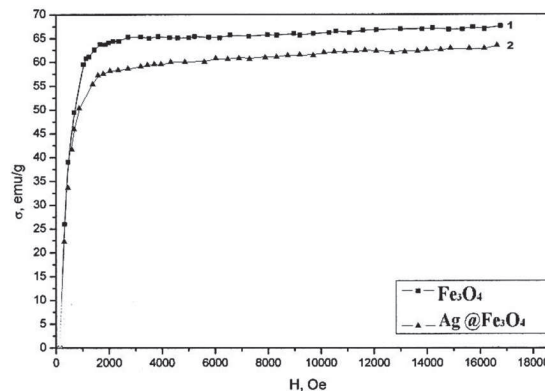


Fig. 3. Saturation magnetization of samples Fe₃O₄ (1) and Ag@Fe₃O₄ (2)

Table 2. Results of determination of specific surface

Sample	Sampleweight, mg	Surface Area	
		m ² /g	average, m ² /g
Fe ₃ O ₄	241.6	106	110
	194.0	111	
Ag@Fe ₃ O ₄	259.0	142	145
	218.5	151	

Thus, according to the results of the physical and chemical research it has been found that in Ag@Fe₃O₄ composite obtained by the method proposed silver is on the surface of the particles as an islet surface, and partially in the form of inclusions.

The resulting composite has high purity due to the shell, which prevents adsorption of ions affecting the magnetic properties from solution, and acting as a stabilizer makes it possible to avoid agglomeration of modified particles. Thanks to the dot coating of silver, the greatest advantage is the almost complete preservation of the magnetic properties of the desired product.

Formation of Ag@Fe₃O₄ composite structures of the “core-shell” type improved allows to combine the magnetic properties of the core with the bactericidal and bacteriostatic properties of the shell. The totality of these properties offers great opportunities for their further use in pharmacy and medicine.

The key advantages of the synthetic method proposed are as follows:

1. The use of ammonia hydrate as a precipitator allows precipitating magnetite more completely (the yield is 90 – 95%).
2. The synthesis of the magnetic carrier and its subsequent covering with the silver shell are carried out by the one-pot method.
3. The reaction occurs at a temperature of 60 – 70°C, and it makes possible to reduce the time of the experiment.
4. Coating thickness provides to preserve the magnetic properties while providing bactericidal and bacteriostatic properties.
5. The method proposed does not involve stabilization of magnetite, which affects the magnetic parameters of the desired product.
6. Keeping the sample in a constant magnetic field allows to precipitate particles quickly and to wash several times with distilled water.

CONCLUSIONS

1. The one-pot method of the synthesis of magnetically-operated Ag@Fe₃O₄ nanoparticles with a spherical core and silver islet shell has been developed; it allows to obtain modified particles of the required size.

2. For the first time the systematic data about the effect of conditions of the synthesis on the structure of the modified particles Ag@Fe₃O₄ have been obtained; the optimal ratio of the components of the nanocomposite and the temperature control for the single-phase synthesis have been determined.
3. It has been found that in this composite silver is on the surface of magnetic particles in the form of the islet layer and single inclusions.
4. The advantage of the method for obtaining Ag@Fe₃O₄ nanocomposite is to provide more precise control of the process and its simplicity, the possibility to obtain particles of the given sizes with high magnetic characteristics and reproducibility of results.

Formation of Ag@Fe₃O₄ composite structures of the “core-shell” type where the core is magnetite and the shell is a chemically inert biocompatible metal Ag allows combining the useful magnetic properties of the core with bactericidal and bacteriostatic properties of the shell, and it is promising for their further use in pharmacy and medicine.

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