STRUCTURAL AND PHYSICAL PROPERTIES OF NANOPARTICLE SYSTEMS $Zn_xFe_{3-x}O_4$ FOR BIOMEDICAL PURPOSE

©Yevgen Levitin[1], Iryna Vedernikova[1], Alla Koval[1], Larisa Olkhovik[2], Nathalie Borisova[2], Zynaida Sizova[2], Alina Fatalieva[1]

[1]National University of Pharmacy
[2]Kharkiv National University named after V.N. Karazin
Correspondence should be addressed to Iryna Vedernikova; irina.vedernicova@rambler.ru

The developed technology provides obtaining finely-dispersed ferrite powders $ZnxFe_3$-xO_4 (x=0-0.5), which meet the requirements to magnetic nanoagents used in the biomedical field such as biochemical purity, nanometric particle size, rather high magnetization and superparamagnetic state in the therapeutic range of temperatures. The average particle sizes have been determined by the methods of X-ray diffraction analysis and electron microscopy. The dependence of the crystalline lattice constants on the zinc ions concentration has been determined. Magnetic measurements at 300 K have demonstrated the increase of magnetization as a result of replacement of iron ions with zinc ions and the size effect – the superparamagnetic state of the powder particles has been found.
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1.Introduction

Currently finely-dispersed ferrite powders are actively studied due to the possibility of their application in innovative biomedical technologies. Such applications of magnetic nanoparticles as targeted drug delivery to the disease sites with the help of magnetic field, hyperthermia for treating oncological diseases, usage in radiopaque fluids in the rentgenological study are considered.

The main requirements to both individual magnetic nanoagents and powder materials are: biocompatibility, the particle size at the level of the cell size (10-100 nm), proteins (5-50 nm) or genes (2-10 nm), rather high magnetization and magnetic susceptibility, close to the critical for superparamagnetic particle volume.

Besides, the finely-dispersed ferrite particles are of interest as an object of research to detect and study size effects. For ferrites of the spinel structural type the change of the magnetic state of particles, stipulated by the size effect in relation to the temperature and magnetic strength, is the most extensively studied area [1,2].

In the biomedical field the magnetite particles (Fe3O4) are widely used as magnetocontrollable particles because of good biocompatibility of magnetite [3-12]. For a macroanalog of the given ferrite, it is known that its magnetization can be increased by partial substitution of Fe^{2+} ions with Zn^{2+} ions [1].

The aim of this work was to obtain the system of nanoparticles of zinc-substituted magnetite with different concentration of zinc ions and to study the effect of the size factor on magnetic and structural parameters.

2. Material and Methods

2.1. Samples and Chemicals. To obtain a finely-dispersed ferrite powders with the composition $Zn_xFe_{3-x}O_4$ with the concentration of zinc x = 0; 0.1, 0.2, 0.3, 0.4, 0.5, the method of chemical condensation of ferrite-forming components from aqueous solutions of salts in the alkaline medium has been used. The corresponding equation for the chemical reaction is:

$$2FeCl_3+xZnSO_4+(1-x)FeSO_4+8NaOH\rightarrow Zn_xFe_{3-x}O_4 + 6\ NaCl+ Na_2SO_4. + 4H_2O$$

It has been experimentally confirmed that for proceeding the reaction and forming a black precipitate, which is characteristic to magnetite, it is sufficient to keep the mixture, obtained as the result of the reaction on the water bath for approximately two hours at T = 80° C, constantly stirring. Then the mixture is kept up to 2 days for complete "maturation" of the precipitate, after that it is repeatedly washed by distilled water to pH = 7.5 - 8.0. To prevent a possible aggregation of ferrite particles the obtained water suspension is placed to the ultrasonic disperser for 2-3 min.

2.2. Analytical Methods. X-ray and electron microscopic research of the synthesized powder.

2.2.1. X-ray analysis. The X-ray research of the samples was conducted on the automated X-ray diffractometer DRON-4 with the source of monochromated Co-radiation. The spectra were processed by the modified Rietveld method using applied programs [13, 14].

Fig. 1 presents diffraction patterns of the powder samples under research. The diffraction patterns character testifies the powders single phase and indicates the fact that the synthesized crystals have a cubic structure of the ferrite spinel type belonging to Fd3m(227) space group. From diffraction patterns using Selyakov formula ($D= K\beta/\lambda\cos\theta$) the average particle sizes were determined for all the studied compositions. The obtained values were in the range of 5.8-9.2 nm.

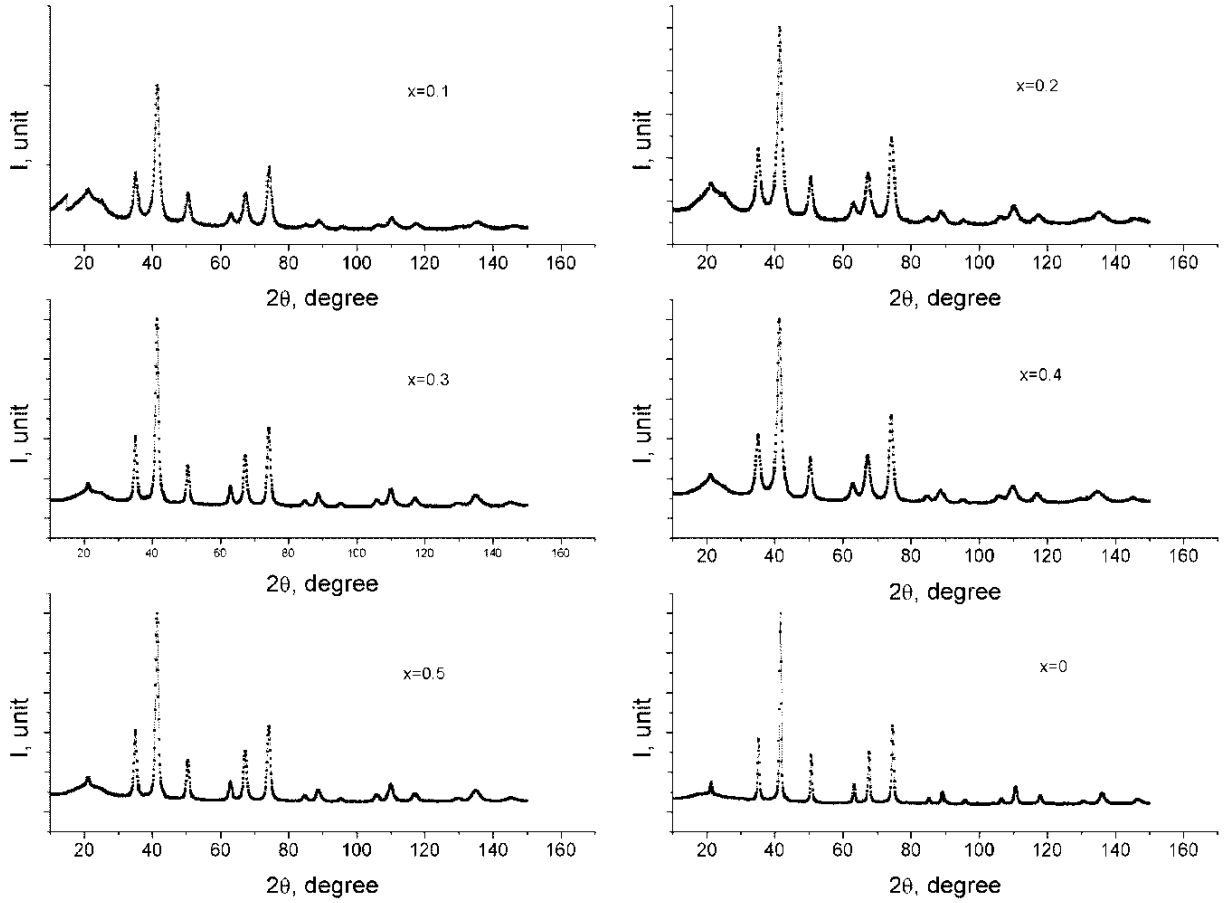

Figure 1. X-ray spectra of the synthesized nanopowder with $Zn_xFe_{3-x}O_4$ composition

2.2.2. Electron microscopic research. The method of electron microscopy was used in order to determine the distribution of particles by size, which is necessary, in particular to identify their magnetic state. Fig. 2 as an example presents the electronic picture of the powder particles for the composition with the zinc concentration of x=0.4 and their distribution by size obtained with statistics of ~400 particles. Distribution is close to symmetrical, the range of values is D=3-13 nm, the mean <D>

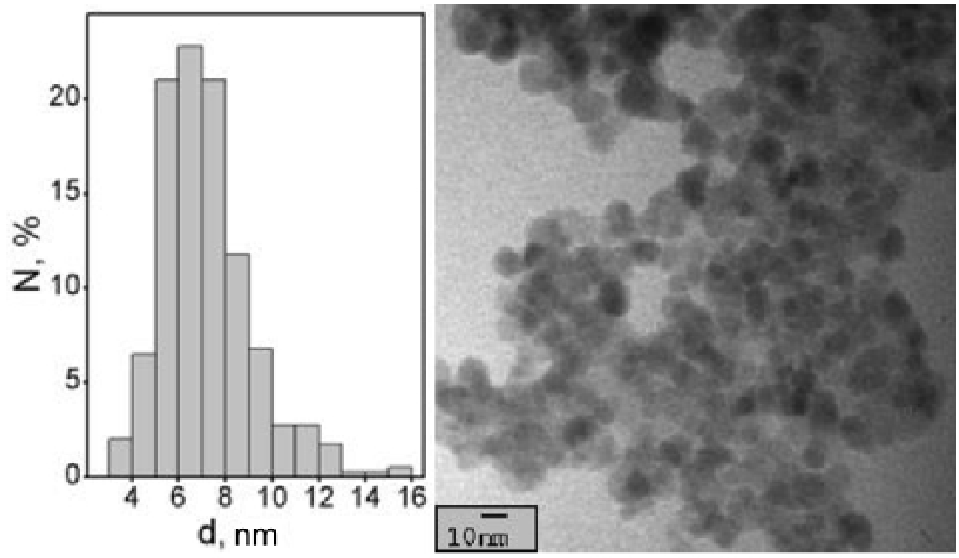

Figure 2. Electronic picture of powder particles with the composition x=0.4 and their distribution by size.

value is ~ 6.5 nm. At the same time approximately 80 % of particles have the size of 5.0-9.0 nm, and it is consistent with the result obtained by the X-ray diffraction method.

Thus, the single-phase ferrite powders with the obtained compositions with rather narrow distribution of particles by size at the lower limit of the nanoscale can be classified as model systems intended for solving fundamental tasks.

3. Results and Discussion

3.1. Structural size effect. For finely-dispersed powder materials it is known that the structural size effect can be revealed in the change of syngony and the constant of the crystalline lattice [15, 16]. In this case the crystal symmetry is not changed for all the studied compositions. Therefore, only the change of the lattice constant might be expected.

The value of the lattice parameters were calculated from diffraction patterns with an accuracy of (3-4)·10^{-4}Å. Fig. 3 shows the dependence of the crystalline lattice a on the Zn^{2+} ions concentration comparing to the linear dependence supposed for macroanalogs. It is obvious that for all studied compositions the values of the lattice parameter are less than for the corresponding macroanalogs. The observed difference exceeds the experimental error by an order and changes from 0.25% to 0.20 % with increase of the zinc concentration in the range of x = 0.1-0.5. It should be noted that the greater deviation for magnetite (0.45 %) can be associated with the supplementary reasons with the exception the size factor, namely with the presence of iron

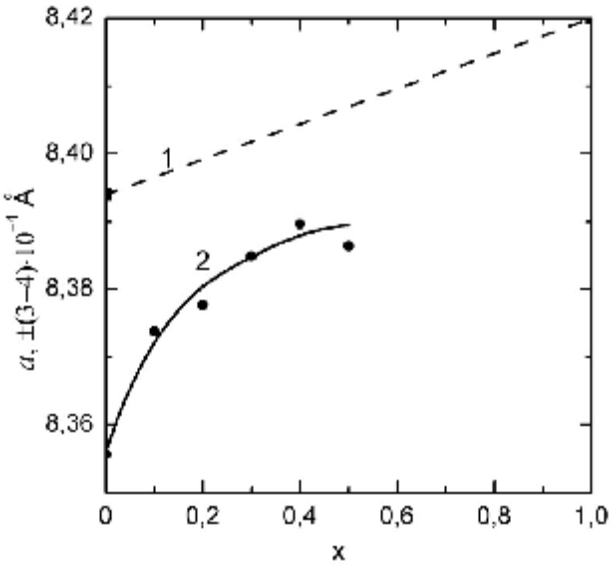

Figure 3. The dependence of the crystalline lattice of zinc-substituted magnetite $Zn_xFe_{3-x}O_4$ on the zinc ions concentration: 1 – macroscopic analog, 2 – nanodispersed powder-based samples.

oxide γ-Fe_2O_3 on the surface of magnetite particles, as referred in the paper [17].

Increase of the concentration of zinc leads to increase of the lattice constant, which can be explained as follows. Unlike replaceable Fe^{2+} ions located in octahedral interstitial sites, substituting Zn^{2+} ions are prone to the tetrahedral surrounding, i.e. after substitution the regular decrease of degree of ferrite structure conversion is expected. The ion radii of Zn^{2+}(0.82Å) and Fe^{2+}(0.83Å) are practically the same. However, the interstitial site both for Fe_3O_4 (0.55Å) and for $ZnFe_2O_4$ (0.65Å) has smaller size than the octahedral one (0.75Å and 0.70Å, respectively). In this regard localization of Zn^{2+} ions in tetrahedral interstitial sites leads to increase of the lattice constant. The nonlinear character of the observed dependence $\alpha(x)$ can be associated with the fact that Zn^{2+} ions take partially octahedral sites.

3.2. Development of the size effect on magnetic properties. It is known that decrease of particle sizes to the nanoscale is accompanied by decrease of magnetization for all oxide ferrimagnets [17]. For the test powder with the composition of x=0.5 the specific magnetization value in the field H=17 κOe equals σ = 75 emu·g^{-1} (fig. 4); it is twice less than for macroanalog. However, it is important that it exceeds the value of σ =67 emu·g^{-1} for the magnetite nanopowder (x=0).

Substitution with zinc ions allowed increasing the powder magnetization, and in combination with the small particle size it corresponds to the requirements to magnetic nanoagents used in the biomedical field. It is desirable the particles to be in the superparamagnetic state, which is characterized by a high magnetic susceptibility and, thus, by a good magnetic control.

The comparison of the real volumes of zinc-substituted magnetite particles with the critical superparamagnetic volume allowed predicting the superparamagnetic state even for the largest particles of the researched powders in the therapeutic range of temperatures. This forecast was confirmed by the results of studying the processes of magnetization and demagnetization in the fields sufficient for saturation of a macroscopic analog. It has been shown that the curves of magnetization and demagnetization coincide, i.e. the anhysteretic character of the magnetization process is observed: residual magnetization equals zero, the coercive force is absent (Fig. 4); therefore, it shows the superparamagnetic state of the samples of all compositions under research.

4. Conclusions

The given method for obtaining nanodispersed powder-based samples of the zinc-substituted magnetite system provides the chemical homogeneity of the powder, small particle sizes (at

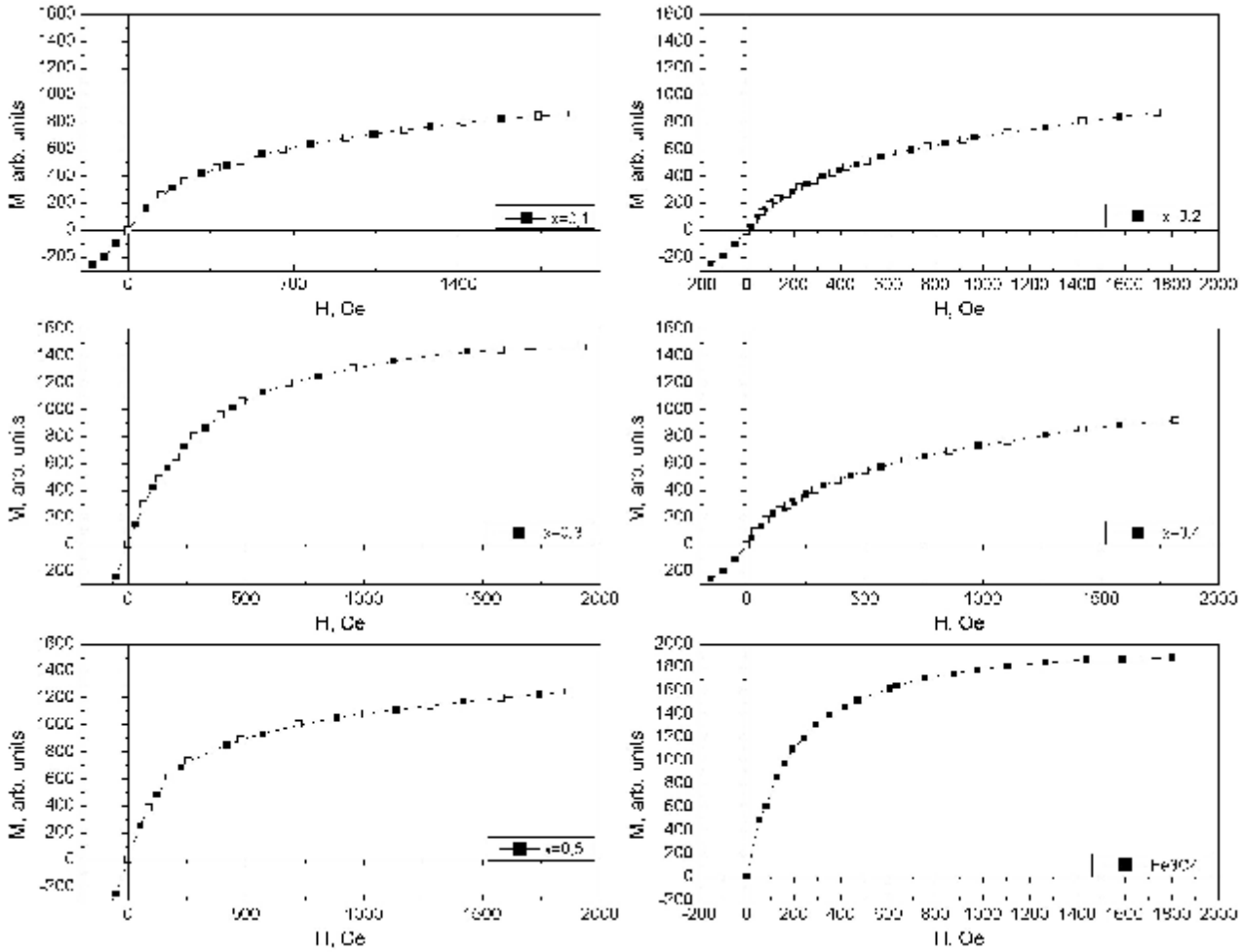

Figure 4. Illustration of the superparamagnetic state of the small particles systems of pure and zink-substituted magnetite.

the nanoscale lower limit), sufficient magnetization and the superparamagnetic state of particles in the therapeutic range of temperatures required for biomedical application. The size effect consisting in decrease of the array parameter with increase of the zinc concentration at constant syngony of the crystalline structure of ferrite has been found.

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References

1. Study of magnetically ordered structure formation in magnesium-zinc ferrites using Mossbauer method / B. Ostafiychuk, O. Kopayev, I. Gasyuk [et al.] // Functional materials. – 2001. – V. 8, № 3. – P. 502–506.
2. Effects of Interparticle Interactions upon the Magnetic Properties of $CoFe_2O_4$ and $MnFe_2O_4$ Nanocrystals / C. R. Vestal, Q. Song, Z. J. Zhang // Journal of Physical Chemistry B. – 2004. – V. 108, № 47 – P. 18222–18227.
3. Preparation of magnetite aqueous dispersion for magnetic fluid hyperthermia / T. Kikuchi, R. Kasuya, S. Endo [et al.] // Journal of Magnetism and Magnetic Materials. – 2011. – V. 323, № 10. – P. 1216-1222.
4. Kumar C. Nanomaterials for medical diagnosis and therapy / Kumar C. Darmstadt, Germany : Wiley VCH, 2009, 143 p.
5. Vizirianakis I. Nanomedicine and personalized medicine toward the application of pharmacotyping in clinical practice to improve drug-delivery outcomes / I. Vizirianakis // Nanomedicine. – 2011. – V. 10, № 7. – P. 11–17.
6. Zahn M. Magnetic ?uid and nanoparticle applications to nanotechnology / M. Zahn // Journal of Nanoparticle Research. – 2001. – V. 1, № 3. – P. 73–78.
7. Indira T. Magnetic nanoparticles / T. Indira, P. Lakshmi // International Journal of Pharmacy Scince and Nanotechnology – 2010. – V. 3, № 3. – P. 1035–1042.
8. Application of magnetic techniques in the fields of drug

discovery and biomedicine / Z. Saiyed, S. Telang, C. Ramchand // Biomagnetic Research and Technology. – 2003. – V. 1, № 2 – P. 1021–1030.
9. Magnetic nanoparticles and targeted drug delivering / J. Chomoucka, J. Drbohlavova, D. Huska [et al.] // Pharmacutical Research – 2010. – V. 1, №. 62. – P. 144–149.
10. H. Yiu Engineering the multifunctional surface on magnetic nanoparticles for targeted biomedical applications: a chemical approach / Yiu H. // Nanomedicine – 2011. – V. 6, №. 8 – P. 1429–1446.
11. Synthesis and characterization of magnesium zinc ferrites as electromagnetic sourc / N. Yahya, A. Mohamad, H. Daud [et al.] // American Journal of Engineering and Applied Sciences – 2008. – V. 1, №. 1. – P. 54–57.
12. D. Yener Synthesis of pure and manganese-, nickel-, and zinc-doped ferrite particles in water-in oil microemulsion / Yener D. // Journal of the American Ceramic Society – 2001. – V. 84, №. 9. – P. 1987–1995.
13. E. Shelekhov Programs for x-ray analysis of polycrystals / Shelekhov E., Sviridova T. // Metal science and heat treatment – 2000. – V. 42, № 7. P. 309–313.
14. Application of Rietveld method of the structural characteristics of substituted copper ferrite compounds / I. Farag, M. Ahmed, S. Hammad [et al.] // Crystal Research and Technology – 2001. – V. 36, № 1. – P. 85–92.
15. Magnetic and structural properties of nickel zinc ferrite nanoparticles synthesized at room temperature / Morrison S., Cahill C., Carpenter E. // Journal of Applied Physics – 2011. – V. 95, № 11. – P. 6392–6395.
16. Physical and technological principles of creating biocompatible superparamagnetic particles / Levitin Ye., Koval A., Vedernikova I. [et al.] // Acta Poloniae Pharmaceutica – Drug Research – 2011. – V. 68, № 4. – P. 549–553.
17. Influence of crystallite size on the magnetic properties of acicular -Fe_2O_3 particles / Berkowitz A., Schuele W., Flanders P. // Journal of Applied Physics – 1968. – V. 39, №. 1. – P. 1261–1263.

СТРУКТУРНІ ТА ФІЗИЧНІ ВЛАСТИВОСТІ НАНОЧАСТИНОК СИСТЕМИ $Zn_xFE_{3-x}O4_3$ БІОМЕДИЧНОЮ МЕТОЮ

Є. Левітін[1], І. Ведернікова[1], А. Коваль[1], Л. Ольховік[2], Н. Борисова[2], З. Сизова[2], А. Фаталієва[1]

[1]Національний фармацевтичний університет,
[2]Харківський національний університет імені В. М. Каразіна

Резюме: розроблено технологію, яка забезпечує отримання дрібнодисперсних порошків феритів $Zn_xFe_{3-x}O_4$ (x=0-0,5), які відповідають вимогам до магнітних наночастинок, що використовуються в галузі біомедицини, таким як біохімічна чистота, розмір наночастинок, досить висока здатність намагнічуватись і суперпарамагнітний стан в терапевтичному діапазоні температур. Середній розмір частинок був визначений методами рентгенівської дифракції та електронної мікроскопії. Визначено залежність констант кристалічної решітки від концентрації іонів цинку. Магнітні вимірювання при 300 К показали збільшення здатності намагнічуватись в результаті заміни іонів заліза на іони цинку і розмірного ефекту – таким чином було визначено суперпарамагнітний стан частинок порошку.

Ключові слова: наночастинки, ферити, здатність намагнічуватись, суперпарамагнітний стан.

СТРУКТУРНЫЕ И ФИЗИЧЕСКИЕ СВОЙСТВА НАНОЧАСТИЦ СИСТЕМ $Zn_xFE_{3-x}O4_3$ В БИОМЕДИЦИНСКИХ ЦЕЛЯХ

Е. Левитин[1], И. Ведерникова[1], А. Коваль[1], Л. Ольховик[2], Н. Борисова[2], З. Сизова[2], А. Фаталиева[1]

[1]Национальный фармацевтический университет,
[2]Харьковский национальный университет имени В. Н. Каразина

Резюме: разработана технология, которая обеспечивает получение мелкодисперсных порошков ферритов $Zn_xFe_{3-x}O_4$ (x=0-0,5), отвечающих требованиям к магнитным наночастицам, которые используются в области биомедицины, таким как биохимическая чистота, размер наночастиц, достаточно высокая намагничеваемость и суперпарамагнитное состояние в терапевтическом диапазоне температур. Средний размер частиц был определен методами рентгеновской дифракции и электронной микроскопии. Определена зависимость констант кристаллической решетки от концентрации ионов цинка. Магнитные измерения при 300 К показали увеличение намагничеваемости в результате замены ионов железа на ионы цинка и размерного эффекта – таким образом было определено суперпарамагнитное состояние частиц порошка.

Ключевые слова: наночастицы, ферриты, намагничеваемость, суперпарамагнитное состояние.