STUDY OF MAGNETICALLY CONTROLLED NANOTEMPLES FOR APPLICATION IN PHARMACY AND MEDICINE

Kryskiv O. S., Koval A. O., Antonenko O. V., Kolisnyk S.V.
National University of Pharmacy,
Kharkiv, Ukraine

One of the areas of nanotechnology development in pharmacy is the use of magnetic material nanoparticles to create pharmaceuticals with magnetically controlled properties, which can be considered a good example of improving non-magnetic pharmaceutical objects.

At the Department of General Chemistry of NUPh, highly dispersed particles of ferrite materials of different composition $M^{II}Fe^{II}Fe^{III}{}_2O_4$ (M^{II} = Zn, Ba, Mn, Fe, Co, Ni, Cu) were synthesized, and their physicochemical and biopharmaceutical properties were determined. Using magnetite Fe_3O_4 and barium hexaferrite $BaFe_{12}O_{19}$, medicinal and diagnostic products of various compositions were developed. There were created ointments with magnetite for the treatment of purulent and inflammatory diseases, a soft medical form for use in otolaryngology, and a diagnostic radiopaque contrast agent with barium hexaferrite suitable for radiological examination of hollow organs of the gastrointestinal tract. There were found new ways of using the created drugs with the use of external magnetic field sources.

A nanodispersed powder of zinc-substituted magnetite has been synthesized, the main functional parameters of which (biocompatibility, dispersion, magnetic state, etc.) allow us to recommend it for testing in biomedical technologies. There was determined the dependence of the magnetic properties of ferrites on the content of zinc cation for the synthesized particles of partially substituted magnetite with zinc cations of variable composition $Zn_xFe_{3-x}O_4$. The X-ray phase analysis of the experimental samples allowed us to establish the single-phase nature of all samples and confirm the crystallographic parameters of the spinel structure.

Microbiological studies of zinc ferrite (Mechnikov Institute of Microbiology and Immunology of the National Academy of Medical Sciences of Ukraine) *in vitro* experiments revealed its mild activity against gram-positive, gram-negative bacteria and fungi of the genus *Candida*.

A comprehensive study of changes in the functional parameters of nanoparticle systems in aggressive environments of the gastrointestinal tract was carried out, which allows predicting the magnetic behavior of an oral dosage form and assessing its ability to be magnetically controlled. There was studied the kinetics of ferrite particles dissolution of different structure and size in the environment corresponding to the conditions of the gastrointestinal tract. Also changes in the elemental composition of the surface layer of particles and inter-particle magnetic interaction under these conditions were analyzed. There were determined changes in the structural and functional parameters of nanoparticles. It was found that the influence of the stomach aggressive acidic environment leads to the erosion of the structurally defective surface layer of particles and does not cause changes in the physicochemical state of their bulk fraction. The dissolution is a function of the particle size and the type of ferrite lattice and is associated with a violation of the stoichiometry of the structural composition and exchange interactions of Fe–O–Fe bonds on the surface and in adjacent layers.

For the first time, systematic data of the influence of synthesis conditions on the structure of modified particles were obtained, the optimal ratio of nanocomposite components and temperature regime were determined, and a one-reactor synthesis method for magnetically controlled Ag@Fe_3O_4 nanoparticles with a spherical core and a silver island shell was developed. A method for quantitative determination of the composition of the magnetic nanocomposite Ag@Fe_3O_4 has been developed, which can be used to determine argentum and ferrous (III) in one sample and can be recommended for use in the development of methods for quality control of Ag@Fe_3O_4. Information on the chemical composition of the surface was obtained and the full elemental composition of the Ag@Fe_3O_4 sample was determined. An express optical method for determining the size of the obtained nanoparticles of the synthesized Ag@Fe_3O_4 composite was proposed. A number of its advantages over common methods have been established: simplicity, low complexity, and relatively low time spent on measurements and calculations. It has been theoretically substantiated and practically proved that the methods of modern mathematical signal processing of the obtained optical characteristics are in good agreement with the previously obtained data using instrumental methods and make it possible to determine the necessary parameters of the composite nanoparticles.

The average size of the nanoparticles of the synthesized composite was determined, and the island type of the coating was confirmed. It is shown that silver on the surface is in the form of flat clusters (200 atoms). The stabilizing effect of the coating on the formation of the composite nanoparticles was confirmed.

The surface state of the synthesized Ag@Fe_3O_4 sample was studied by SEM with EDX and PPR and it was confirmed that silver is in the form of islands on the Fe_3O_4 surface and consists of clusters of atomic silver with a size of 20–100 atoms. An increase in the specific surface area of the sample by 25% (compared to pure magnetite) was found, which increases the likelihood of contact of silvered particles with bacteria or viruses, significantly improving their bactericidal effect. The optimum magnetic characteristics of the Ag@Fe_3O_4 sample selected for further research were determined. It was found that silver in the form of islands does not significantly affect the decrease in the magnetic properties of the synthesized product.

Microbiological studies of Ag@Fe_3O_4 samples with different ratios of components have shown that the sample with the ratio of Ag : Fe_3O_4 – 0.5 : 1 has optimal antimicrobial properties. Magnetically controlled soft medical forms based on the Ag@Fe_3O_4 composite – an ointment composition with magnetically controlled and thermally conductive functions to improve the method of removing skin tumors and an ointment for their treatment – were created. It has been established that the ointment composition provides deep and complete tissue freezing without damaging healthy skin, the Ag@Fe_3O_4 ointment exhibits bactericidal, bacteriostatic and wound healing properties, and its use significantly reduces the time of cryodestruction and subsequent rehabilitation.