DETERMINATION IN VIVO CONCENTRATION OF NANOMAGNETIC PARTICLES IN MEDICINE

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There are several areas of application of magnetic nanoparticles in medicine and pharmacy. The drug with magnetic properties solves the targeted delivery of the active substance, that allows to reduce the dose of the drug and, as a result, minimize the toxic reaction of the body, opens up new prospects for local conservative treatment with cryodestruction [1].

Taking into account that magnetic nanoparticles are able to be visualized, magnetic fluids are used as contrast agents in magnetic resonance imaging (MRI). Due to the fact that magnetic nanoparticles, in the therapeutic temperature range, are capable of heating in a magnetic field, magnetic hyperthermia as the treatment of cancer and diseases of the vascular system is developing rapidly.

The use of traditional medicinal substances acting on the central nervous system: narcotic analgesics, agents for the treatment of epilepsy, Alzheimer's disease, etc., requires overcoming the blood-brain barrier, which reduces the proportion of drugs delivered to the brain.

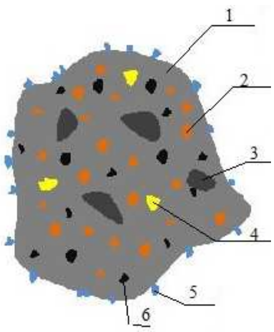
The nanotechnology development is tightly connected with high-tech valuable equipment, involving specialists from different areas. As world practice shows, a long and thorny path “from idea to development and further implementation into production” can be significantly reduced by cooperation in the framework of scientific programs and projects. Under the conditions of such cooperation, the contribution of biomedical and pharmaceutical nanotechnologies is projected to reach a high level in 2025-2035. The scientific direction of the development of modern nanofarmacia – the creation of magnetic drugs, certainly has the prospect of its development throughout the world. It is stated the tendency to development of regulatory framework for the use of nanoparticles.

For application in biological organisms, these particles have to be biocompatible. It could be shown that, generally, starch-coated magnetic iron oxide nanoparticles are tolerated quite well [1].

These particles show superparamagnetic properties and can be attracted by an external magnetic field. The solution of using magnetic nanoparticles in medicine, are directly related to determining in vivo the concentration of magnetic nanoparticles in a disease site in a short period of time.

The effectiveness of the usage of the previously proposed by I.S. Bondarenko and O.G. Avrunin [2] acoustomagnetic method of recording the number of magnetic nanoparticles, based on the simultaneous action of ultrasound and external direct magnetic field, exciting a secondary alternating magnetic field as a result of collective oscillations of magnetic nanoparticles in an environment of a colloidal liquid, oriented by external homogeneous field relative to the induction coil, measuring alternating field was tested. The viscosity of the mixture was chosen close to the viscosity of the blood.

The object of study was a colloidal solution of nanoparticles based on Fe_3O_4 (the granule scheme is shown in Fig. 1) in a mixture of oleic acid and kerosene.

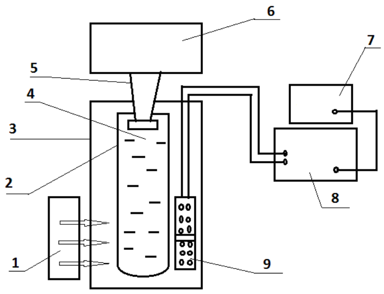


1-Polymer basis – styrene-acrylic copolymer binds together all the other components and promote the ability of the particles to acquire a charge; *2-The charge regulating additive* – for negative charge it is azo dyes and organic acids; for positive charge, quaternary salts and nigrosine dyes. *3-Magnetite (iron oxide)* – provides the magnetic properties of granules. *4-Pigments* – also magnetite; *5-Modifier* – wax, polypropylene, polyethylene, etc.; *6-Surface additives* – a polymer that provides the required characteristics of friction between particles.

Fig. 1. Scheme of the magnetic nanoparticle structure

The weight concentration of the powder containing nanoparticles was of 0.15%, that is comparable to the therapeutic dose used for vein injection [3].

The average particle size with magnetite was of 50-150 nm, Size of Fe_3O_4 was much less. Oleic acid prevents powder particles from sticking together in solution, and kerosene provides the necessary viscosity. The scheme of experimental installation is shown in Fig. 2.



1 – permanent magnet (⇨ - magnetic field line), 2 – test glass tube, 3 -copper screen, 4 – colloid solution, 5 – dispersant acoustic duct, 6 – ultrasound generator (disperser), 7 – oscillograph, 8 – microvoltmeter, 9- induction coil

Fig. 2. Diagram of the experimental installation.

The increase of the voltage on the induction coil proportionally to the intensity of the ultrasound confirmed the possibility of the magnetic particles registration using an acoustomagnetic method for measurement of the quantitative value of the magnetic particles concentration. It is worth noting that the magnitude of the magnetic field acting on a biological object of 0.1T was much less than the magnitude of the field in the MRI method.

Dependence of the voltage U at the induction coil on the intensity I of ultrasound can be described by the relation:

$$U = k\,N\,I, \qquad (1)$$

where the parameter k characterizes the magnetic field properties in the area of the coil, N number of the magnetic nanoparticles creating magnetic field when all the nanoparticles are oriented in the direction perpendicular to the plane of the coil by the direct magnetic field. Determination of the parameter k using the magnetic field properties in the area of the coil is presented in [4]. The value of the concentration (K) of the magnetic nanoparticles is equal to:

$$K = (NV\rho\,/m)\ 100\ \%\ , \qquad (2)$$

where V, ρ, m is, respectively, the volume of one nanoparticle, its specific weight and the total mass of the solution.

The experimental results confirmed the sufficient sensitivity of the method to determine the concentration of nanoparticles in vivo that is promising for further development of the acoustomagnetic tomograph for medical researches, that in contrast to the well-known expensive and complex magnetic resonance imaging method, promises to be more accurate, simple and less harmful from the point of view of the influence of a direct magnetic field on a biological object, which in these experiments was of 0.1 T, at MRI method the object is exposed to a magnetic field of three or more Tesla, while in a number of works concerning the drug delivery to the site of the disease by magnetic nanoparticles it was enough to have a direct gradient magnetic field equal to 1.7 T [1].

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