DETERMINATION INVIVO CONCENTRATION OF NANOSIZED DRUGS TO REDUCE THE VALUE OF THEIR EFFECTIVE DOSE

Rakhimova M.V., Bondarenko I.S., Avrunin O.G., Perekhoda L.A.
National University of Pharmacy, Kharkiv, Ukraine,
RakhimovaMV@gmail.com

Among magnetic nanoparticles suitable for use in medicine, particles of iron oxide Fe_3O_4 can be distinguished due to their biological compatibility with biological objects. These particles possess supermagnetic properties and functionalized by biomolecules (antibodies, enzymes, nucleotides, etc.) for targeting or recognition of biological systems can be used as materials for targeted drug delivery.–

Particles can be delivered to tumors in three ways: directly injected by a syringe, either using antibodies against specific tumor antigens, or sent to a tumor using an external or internal magnet

The essence of targeted delivery is that the drug itself, and more often the delivery method (vector, container), is modified by molecules that recognize receptors on target cells. Antibodies can be universal molecules that recognize the surface of a target cell. The presence of recognition molecules on the surface of a vector allows it to be concentrated in a given area (tumor, inflammation area, near the ischemic zone, etc.) and deliver the drug substance there

In contrast to the usual administration of a drug substance and its distribution throughout the body, targeted delivery using passive targeting, active targeting with the recognition part (for example, an antibody) or active targeting with a magnetic field can reduce the dose of the drug administered and minimize its effect on other cells (side effect). With aggressive therapy of tumors, the aspect of targeted delivery of highly toxic oncological drugs acquires special significance and allows to reduce the effective dose to 20% [1]. Additionally, it becomes possible to control the release of the drug.

The drug administration by magnetic targeting is associated with the need for prompt (in a short period of time) in vivo determination of the amount of the drug by determining the concentration of magnetic drug nanocarriers.

Currently, MRI method is an effective method for recording magnetic nanoobjects. Its features are the high cost and the associated insufficient accessibility and efficiency of the procedures, as well as a large permanent magnetic field, unsafe for the patient, in the long term up to 8 or more Tesla. In addition, the recorded spectra give only a qualitative assessment of the concentration, limiting the accuracy of MRI and have distortions under certain endogenous conditions, such as calcification, the presence of fat, hemorrhage, the presence of blood clots, air.

Another technique for fixing magnetic particles by the acoustomagnetic method is simpler and more affordable, has a safe level of the magnetic field (less than 1T). The results of an experimental verification of this method [2] under conditions simulating invivo measurements using a suspension of Fe_3O_4-based nanoparticles with a size of 50-150 nm in a mixture of oleic acid and kerosene confirmed the sensitivity of the procedure when their allowable amount is 0.015 mg / kg, which does not exceed the therapeutic dose. Oleic acid prevented nanoparticles

from sticking together in a liquid, and kerosene provides a viscosity close to blood viscosity.

The essence of the method is to record the effects of ultrasound and a constant magnetic field on a colloidal liquid with magnetic nanoparticles and to measure the secondary magnetic field caused by vibrations of the magnetic nanoparticles.

According to the results of model experiments, the concentration (k) of nanoparticles can be determined on the basis of the variable (at ultrasound frequency f) magnetic flux Φ generated by oscillating nanoparticles and measured by a magnetometer located at a distance R from the volume under study with them:

$$\Phi \approx [\mu_0 J_0 c^{1,5} / (32 \pi^2 \rho^{0,5})] [I^{0,5} d^2 / (R^3 f^3)] \kappa , (1)$$

where $\mu_0 = 4\pi\ 10^{-7}$ Gn/m ; J_0, c, ρ, I, d - respectively, the magnetization of one nanoparticle, the speed of sound in a colloidal solution, the density of the solution, ultrasound intensity, diameter of a model cylindrical volume with a solution.

The determination of the concentration of nanoparticles by the acoustomagnetic method promises to be more accurate, simple and less harmful in terms of the influence of a constant magnetic field on a biological object. In addition, the acoustomagnetic method is direct rather than indirect, unlike MRI method.

The proposed method for determining the concentration by the acoustomagnetic method can be further used to initiate the release of a drug delivered by magnetic nanoparticles in a constant magnetic field under the action of ultrasound as a result of the manifestation of a nanomechanical mechanism for the drug release, and this can occur simultaneously with the determination of the concentration.

1. Jurgens R. Drug loaded magnetic nanoparticles for cancer therapy. / Seliger C.. Hilpert A., L Trahms L., Odenbach S., Alexiou1 C./ J. Phys. Condens. Matter. - 2006.- Vol. 18.- P.2893-2902. doi:10.1088/0953-8984/18/38/S24
2. Avrunin O.G. Possibilities of joint application of acoustic radiation and direct magnetic field for biomedical research. / / BondarenkoI.S, Rakhimova M.V.//International journal of bioelectromagnetism. - 2018. – Vol. 20 -№1.- P. 66-67. http://openarchive.nure.ua/bitstream/document/8253/1/Proceedings_ICBEM_2018_bondarenko.pdf