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STABILIZATION OF AQUA SUSPENSIONS OF IRON OXIDE MAGNETIC NANOPARTICLES USING NATURAL HUMIC POLYELECTROLITES

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Capsules containing magnetic nanoparticles are the most attractive objects in number of medical and biological fields including target drug delivery, hyperthermia, magnetic separation of biopolymers, MRI etc.

The most important parameters of the nanoparticles are chemical composition, size, anisotropic properties, morphological features (pore structure etc.), magnetic properties and non-toxicity. Many different techniques are used for achievement of required properties. One of multitude techniques is aerosol spray pyrolysis method which permits to obtain highly disperse particles and also to control their micromorphology. On the other hand there is an evident idea to prevent aggregation of nanoparticles and it demands new solutions because of a very high practical importance of such an approach. One of the solutions is the development of techniques yielding composites liberating nanoparticles after long-term storage upon a contact with water or medical liquids like Body-Simulated-Fluid. Unfortunately, behavior of magnetic nanoparticles entrapped in water soluble inorganic matrix are not yet investigated in details. Thus the actual aim of this work was systematical development and optimization of complicate approaches of required magnetic nanoparticles.

A significant problem is preparation of colloidal solutions of magnetic nanoparticles using suitable biocompatible surfactants connectable with bioactive molecules, drugs etc. One of the promising objects to use as biocompatible surfactants are the different humic substances (HS). Contrary to artificial dendrimers with a regular structure already considered as perspective objects for nanomedicine HS possess highly developed branches with irregularly located organic functional groups originating from biochemical and microbiological transformation processes occurring with various organic materials under environmental conditions. It provides a readily available source of a whole spectrum of naturally produced highly branched dendrite-like surfactants potentially suitable to serve as protective/stabilizing shells for nanoparticles.

In the present work we have developed a scalable and continuous production technique of magnetic iron nanoparticles isolated in water-soluble microspheres. This composite can liberate nanoparticles after long-term storage upon a contact with different water solutions.

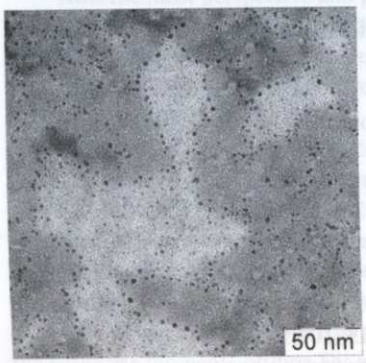

Fig. 1. The micromorphology of the dried colloidal particles

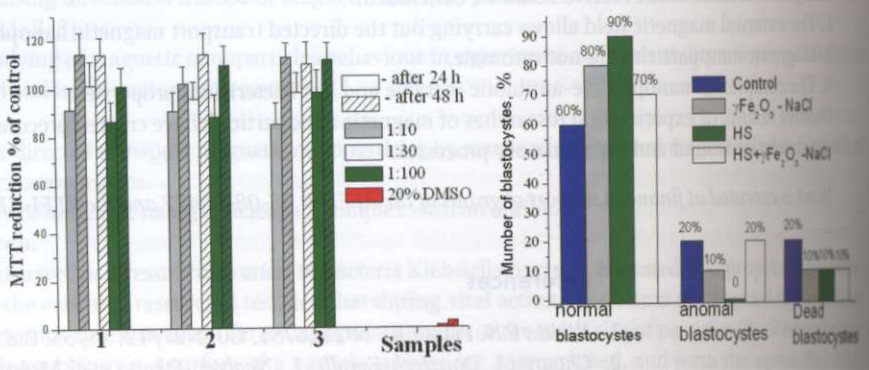

Fig. 2. *a* — MTT-test on DMEM + γ-Fe_2O_3-NaCl (1), DMEM + HS (2), DMEM + HS + γ-Fe_2O_3-NaCl (3); *b* — Embriotoxicity test

The starting solutions of NaCl and iron(III) nitrate were atomized using an ultrasonic nebulizer with a resonant frequency o MHz. The aerosol stream was introduced into a horizontal quartz reactor preheated at 650°C. The obtained dust consisted o ow microspheres 0.1–2 μm in diameter containing 5 nm nanoparticles of γ- Fe_2O_3. To prevent aggregation after liberatin particles from salt matrix, the composite samples were dispersed into HS solution. Thus was obtained suspension stable for th time.

The obtained samples were characterized by several analytical methods such as Moessbauer spectroscopy, magnetic measurement TEM (fig. 1.). In addition the samples were investigated for their cytotoxic and embriotoxic effects (fig. 2, *a*, *b*). Cytotoxic effe investigated with MTT test. The suspension of magnetic nanoparticles was diluted with DMEM/F12 medium (1:10, 1:30, 1:10 added to fibroblasts culture. Embriotoxic activity was analyzed on cells of mouse blastocystes.

FORMULATION OF NANOSYSTEM OF BETULIN FOR INHALATION

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Introduction. In last decade interest to nanosystem of drugs has sharply increased. Nanosystem can be used as drug delivery sy at various ways of introduction, including inhalation.

The basic limitation of drugs for inhalation is low bioavailability. Low bioavailability is caused by deposition of particles of drug oral cavity. Use nanosystem will allow to increase bioavailability of drugs, to expand assortment of inhalation drugs, and also ef cy of drug delivery in various departments of respiratory system.

Betulin, has a wide spectrum of biological activity, showing, anti-inflammatory, antiviral, antimicrobial and antitubercular effe 2]. Betulin can will be applied at various pulmonary diseases [3], for which inhalation therapy is an optimum way of delivery parations directly in the respiratory ways.

The purpose of the present work was development of a powder of betulin for inhalation.

Materials and methods. Substance of betulin (98%) was received from the company SNS-Pharma.

Particle size distributions of the dry powders of betulin were determined by photon correlation spectroscopy using a Malvern Ze r 3000HSA (Malvern instruments, Worcestershire, UK).

The thermal behavioral of betulin, lactose and each of the powders was analysed using a differential scanning calorimeter Mett edo DSC 823 (Switzerland).

Particle density of the dry powders of betulin was determined by means of the apparatus for vibrating condensation of powders 5 AK-3 (Mariupol).

Theoretical aerodynamic diameter (daero) was calculated using the following equation:

$$daero = \frac{dg}{\gamma} \cdot \sqrt{\rho / \rho ref} \ ,$$

ere dg is the particle geometric diameter, ρ is the particle density, ρ_{ref} = 1 g/cc, γ is a shape factor (for a spherical particle, γ = 1).

Results and discussions. One of the main parameters of efficiency of inhalation is deposition of drugs in respiratory tract. A ma tor definin g of deposition of particles in respiratory tract, is the particle size of drug (the aerodynamic diameter of particles). Parti ger than 25 μm usually deposit in the oral cavity. Drug particles of 25–5 μm are delivered to trachea and bronchi, drug particle 5 μm are delivered to bronchiole and alveole, drug particles the 0,5–2 μm are delivered to the lungs. Particles under 0.5 μm are ed.

The substance of betulin has the sizes 50 μm. Thus, the substance was not thought to have an optimal particle size for inhala was subsequently micronised.

Nanoparticles tend to agglomerate when they are not formulated with a carrier and will not, therefore, reach the lungs. As a ca dry powder of betulin lactose was chosen. Two powders with the various content of betulin (20 and 30%) were prepared.

Betulin, lactose and nanosystem was analysed using a differential scanning calorimeter (DSC).

The DSC thermograms of betulin showed endothermic peak at 262°C. The DSC thermogr ams of lactose showed endothe aks at 150 and 220°C. The DSC thermograms of dry powder of betulin showed endothermic peaks at 138 and 145°C respectively, 238°C, 220°C (peaks characteristic for lactose). Thus, data of the thermal analysis testify to formation of molecular complexe ulin with lactose.

Physical-chemical parameters of nanosystems of betulin were investigated (table 1).