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# INTRODACTION

The use of nanoparticles in the last few decades has been one of the priority areas in biomedicine, in particular in the treatment of various cancers. The greatest interest for cancer medicine represent nanostructures with high colloidal and photothermal stability while exhibiting a low percentage of non-specific binding to the biological sample and having a low toxicity for the organism [[,,]](#Veiser). These include various inorganic gold and magnetic nanoparticles, polymer nanoparticles, as micelles, dendrimers polipleksnyh structures, etc. [,,]. But, particular attention attracted the nanoparticles possessing magnetic properties due to which are possible MNPs and conjugates control based on them at a distance by applying an external magnetic field [,].

MNPs is functionalized often with different coatings or embedded in a polymer or organic matrix in order to improve biocompatibility, colloidal stability, increasing of circulation time in biological media, modified with target agents specific for the tumor cells, or loaded with drug [,,]. Functionalized MNPs are used in modern diagnostic methods, including MRI, PET, SPECT, based on the use of magnetic nanoparticles as contrast agents. Also, there are a large number of therapies which use magnetic particles. The best known is the method of localized heating of the tumor – hyperthermia [,].

Recently, methods of gene transfection are developing with the use of magnetic nanoparticles - magnitofection [,]. One of the most studied areas of medicine is the targeted drug delivery to the tumor target []. Often targeted drug delivery is used in conjunction with hyperthermia []. But, perhaps, the main interest in magnetic particles is due to the possibility of combining methods for diagnosis and therapy [,]. Thus, this article will be considered magnetic particles as diagnostic, therapeutic and targets agents in modern biomedical cancer.

# CHAPTER 1. LITERATURE REVIEW

## 1.1.1 Characterization of Magnetic nanoparticles

Magnetic nanoparticles are nanostructures with a highly active surface and size-dependent physical properties such as magnetic characteristics. Typical magnetic properties: ferromagnetic and superparamagnetic occur in the transition of substances to nanostate. The magnetic properties of nanoparticles influence the chemical composition, the type of crystal lattice, the shape of the particles, their interactions with neighboring particles [, ,].

Nanoparticle form can vary significant. At present, most attention is focused on the study of the properties and capacity of synthesis and use of magnetic particles having an anisotropic shape. Furthermore, due to their nano-sized (less than 100 nm), comparable to cell size (10-100 micrometers), viruses (20-100 nm), proteins (5-50 nm) DNA (width 1 nm, 10-100 nm), nanoparticles may approach the biological objects to interact and communicate with them as Figure 1 []. An important addition to the size is surface charge MNPs, which must be neutral, for greater specificity, since positively charged particles tend to non-specifically adjacent to the cells, and the maximum circulation time in the bloodstream, which is important for their use in biomedicine as therapeutic agents and, agent targeted drug delivery, etc. [,,].

Figure 1 – Size scale of MNS as compared to biomolecules [].

By now there are a variety of magnetic nanoparticles actively used in biomedicine: iron-based oxides, metals Co, Fe, Ni, ferrites MgFe2O4, SoFe2O4, MnFe2O4, as well as Multifunctional MNPs with two or more different functional units, such as Au-Fe3O4, FePt – CdS, and Fe2O3-carbon nanotube can be synthesized through seed mediated growth. In such a heterogeneous nanostructure, each unit exhibits its unique magnetic, optical, or electronic properties []. However, it should be noted that the oxide particles have weaker magnetic properties than the metal-based nanoparticles, but they are more resistant to oxidation. Currently, the widest application in biomedicine received nanoscale particles of iron oxide, which is due to their low toxicity and stability of the magnetic characteristics [,]

Therefore, to create a particular size MNPs, functionality, stability, on which depend magnetic properties of the nanoparticles, there are several strategies for the synthesis of particles:

1. Physical methods include gas-phase deposition and electron beam lithography. These methods suffer from their inability to control the particle size to the nanometer scale []. In the article [] is described a lithography and magnetron sputtering technique, allowing the obtaining of a particle diameter of 1 to 2.5 m, consisting of three layers: a layer of permalloy is located between two layers of gold.
2. Wet chemical preparation methods, such as sol−gel synthesis, oxidation method, chemical coprecipitation, hydrothermal reactions, flow injection synthesis, electrochemical method, aerosol/vaporphase method, sonochemical decomposition reactions, supercritical fluid method, and synthesis using nanoreactors []. Chemical routes are preferred because they can synthesize MNPs with uniform composition and size []. The most common synthetic strategy involves aqueous precipitation of iron salts with in situ or post-synthesis addition of surfactant. The micelles are used as nanoreactors: they are able to impose certain kinetic and thermodynamic limitations on forming nanoparticles []. Also relevant the method of thermal decomposition / reduction method have gained considerable attention since this technique offers fine control over the final particle size, shape, and crystal structure compared to other methods and is scalable [].
3. Biological methods or other microbiological methods are generally simple, versatile, and efficient with appreciable control over the composition and the particle geometry of the resulting material []. The used microorganisms are bacteria, actinomycetes, fungi and algae. Synthesis of nanoparticles can be intracellular or extracellular location in accordance with the nanoparticles. In biomedicine method is used in which magnetic nanoparticles can be isolated from cells magnetotactic bacteria [].

## 1.2 Application in the diagnostics

### 1.2.1 Magnetic resonance imaging

## 1.3 Application in Therapy

### 1.3.1 Chemotherapy or drug delivery

### 1.3.2 Hyperthermia

Due to the fact that tumor cells are more sensitive to heat than normal tissue, a method is developing for selective thermal destruction of tumor cells by means of transformation of AMF energy into thermal energy by functionalized magnetic nanoparticles, which is defined as heating the tissue in the range of 41- 47° C. []. Energy conversion nanoparticles are effective due to the fact that the rate of adsorption is correlated with a heating rate of particles placed in the alternating magnetic field. In the work [] investigations into the dependence the adsorption rate on the size of the nanoparticles, it was shown that the optimum the rate of adsorption for hyperthermia was observed in particles whose size was 18 nm. Hyperthermia or rather magnetic mediated hyperthermia has an advantage because the heating is localized only in the center of the tumor tissue by the selectively bind of functionalized magnetic nanoparticles with tumor cells and the use of AMF. In many articles, magnetic mediated hyperthermia is described as an effective method of treatment. [,, ].

In addition, different variants of the local magnetic hyperthermia are currently being actively developed, in which a magnetic material is injected into the affected area and heated from the outside by means of electromagnetic radiation range of 100-800 kHz, with little absorbtion by the body tissues, but strongly interacts with ferro magnets and super paramagnets [].

Susanne Kossatz et al, in an article, reported the use of modified superparamagnetic iron oxide nanoparticles (MF66), Nucant 6L (MF66-N6L), doxorubicin (MF66-DOX) or both (MF66-N6LDOX) together with the magnetic hyperthermia for the treatment of breast cancer. The results showed that the MF66-DOX and MF66-N6LDOX combined with hyperthermia were more toxic to breast cancer cells than the corresponding with ligands. There was a significant inhibition of tumor growth and, in many cases a complete disruption [].

A similar approach has been reviewed in an article Christopher A. Quinto et al., which was synthesized SPIOs with a phospholipid-polyethylene glycol (PEG) coating, and loaded doxorubicin for joint hyperthermia and chemotherapy of tumor diseases []. The particles are presented in Figure 2.

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Figure 2 – Phospholipid PEG – coated iron oxide nanoparticle loaded with doxorubicin [].

Faruq Mohammad, Nor Azah Yusof obtained and investigated the probe doxorubicin (Dox) loaded gold-coated superparamagnetic iron oxide nanoparticles (SPIONs / Au) for a combination therapy of cancer by means of both hyperthermia and drug delivery. In one way, the probe generates local hyperthermia in accordance with the external magnetic field while in the second way, and the outer controlled delivery of conjugated drug can be achieved from the oscillation of particles with the help of same field, effectively induced tumor cell death [].

Jelena Kolosnjaj-Tabi et al. In their study, created PEG-coated iron oxide nanocubes to mediate mild tumor magnetic hyperthermia treatment. Heat-generating PEG-coated iron oxide nanocubes showed interference with the tumor extracellular matrix and the potential to destroy the matrix under magnetic influence, which leads to a decrease in tumor growth [].

Other authors have reported the use of a multifunctional platform for drug delivery and magnetic hyperthermia of malignant tumors, where the foundations were Carbon-encapsulated magnetic colloidal nanoparticles with silica coating (MCN / C / mSiO2), and the rattle-type structured MMS nanoparticles (MCN / mSiO2 ). The MCN / C / mSiO2 nanoparticles exhibited higher magnetic hyperthermia ability compared to the MCN / mSiO2 nanoparticles, but the MCN / mSiO2 nanoparticles had higher drug loading capacity. Research has shown that drug release from two types of complexes were temperature-dependent [].

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