

## NEW HYBRID MATERIALS ON THE BASIS OF MAGNETITE AND MAGNETITE-GOLD NANOPARTICLES FOR BIOMEDICAL APPLICATION

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During last decades magnetite nanoparticles (NPs) attract a deep interest of scientists due to their potential application in therapy and diagnostics. However, magnetite nanoparticles are toxic and non-stable in physiological conditions. To solve these problems, we decided to create two types of hybrid systems based on magnetite and gold which is inert and biocompatible: gold as a shell material (first type) and gold as separate NPs interfacially bond to magnetite NPs (second type). An additional advantage of gold is the possibility of its functionalization with a variety of sulphur-containing ligands; that is very important for drug delivery and creating of tissue-specific MRI contrast agents.

The synthesis of the first type hybrid nanoparticles was carried out as follows: magnetite nanoparticles with an average diameter of  $9\pm 2$  nm were obtained by co-precipitation of iron (II, III) chlorides then they were covered with gold shell by iterative reduction of hydrogen tetrachloroaurate with hydroxylamine hydrochloride. According to the TEM, ICP MS and EDX data, final nanoparticles had an average diameter of  $31\pm 4$  nm and contained iron even after hydrochloric acid treatment. However, iron signals (K-line, 7,1 keV) were not localized so we can't speak about one single magnetic core. Described nanoparticles covered with mercapto-PEG acid were non-toxic for human prostate cancer PC-3/ LNCaP cell lines (more than 90% survived cells as compared to control) and had high R2-relaxivity rates ( $>190$  mM $^{-1}$ s $^{-1}$ ) that exceed the transverse relaxation rate of commercial MRI-contrasting agents. These nanoparticles were also used for chymotrypsin enzyme immobilization. The effect of alternating magnetic field on catalytic properties of chymotrypsin immobilized on magnetite nanoparticles, notably the slowdown of catalyzed reaction at the level of 35-40 % was found. The most probable reason for the observed effect is the change of active centers topology on the enzyme surface as a result of its deformation under applied forces.

The synthesis of the second type hybrid nanoparticles also involved two steps. Firstly, spherical gold nanoparticles with an average diameter of  $9\pm 2$  nm were synthesized by the reduction of hydrogen tetrachloroaurate with oleylamine; secondly, they were used as seeds during magnetite synthesis by thermal decomposition of iron pentacarbonyl in octadecene. As a result, so-called dumbbell-like structures were obtained where magnetite (cubes with  $25\pm 6$  nm diagonal) and gold nanoparticles were connected together pairwise. By HRTEM method (first time for this type of structure) an epitaxial growth of magnetite nanoparticles on gold surface with co-orientation of (111) planes was discovered. These nanoparticles were transferred into water by means of block-copolymer Pluronic F127 then loaded with anti-cancer drug doxorubicin and also PSMA-vector specific for LNCaP cell line. Obtained nanoparticles were found to have moderate toxicity for human prostate cancer cells and got into the intracellular space after 45 minutes of incubation (according to fluorescence microscopy data). These materials are also perspective from MRI point of view (R2-relaxivity rates  $>70$  mM $^{-1}$ s $^{-1}$ ).

Thereby, in this work magnetite-gold hybrid nanoparticles, which have a strong potential for biomedical application, particularly in targeted drug delivery and magnetic resonance imaging, were synthesized and characterized. That paves the way to the development of new medicine types – theranostics.

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