SUPERPARAMAGNETIC IRON OXIDE NANOPARTICLES AS VERSATILE DRUG DELIVERY CARRIERS

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Introduction

Superparamagnetic iron oxide nanoparticles (SPIONs) poses numerous advantages as drug delivery carriers and hyperthermia agents in cancer treatment[1]. Good magnetic properties of SPIONs allow for their precise guidance and accumulation directly at the tumour site. However unmodified SPIONs can release significant amount of iron ions. It was proved that those ions can increase proliferation of cancer cells[2]. Thus, it is crucial to modify the surface of SPIONs to reduce potential release of iron ions. Besides its protective function, surface modification of SPIONs can be utilized for attachment of anticancer drugs or other biologically active molecules. The aim of the present study was to modify Fe_3O_4 nanoparticles with different silica layers, to evaluate their physico-chemical properties and cytocompatibility with human lung epithelial cells.

Materials and Methods

Fe_3O_4 nanoparticles (NP) were coated with SiO_2 layer (non-porous: NP@SiO_2, mesoporous: NP@$mSiO_2$ or both of them: NP@SiO_2@$mSiO_2$) using a sol-gel method with TEOS as a precursor and CTAB as a progen. Chemical composition of modified SPIONs was studied by FTIR. Iron release studies were performed for 24 h in ultrahigh purity water and iron concentration was measured with AAS electrothermic method. NP size and morphology were assessed using transmission electron microscopy (TEM) and atomic force microscopy (AFM); surface zeta potential was also measured (Litesizer, Anton Paar). The hysteresis loops of the nanopaticles M(H) were measured at 5K and at room temperature with SQUID Magnetometer MPMS XL (Quantum Design). NP uptake and its influence on cell viability and migration were evaluated in vitro in contact with malignant (A549) and non-malignant (BEAS-2B) human lung epithelial cells (Prussian blue staining, real-time impedance measurement – xCelligence system). Cell migration was studied and analysed based on real-time phase contrast images (IncuCyte ZOOM).

Results and Discussion

Silica layers were successfully deposited on Fe_3O_4 nanoparticles. FTIR spectra of silica coated NP showed bands in the range of 1000-1200 cm^{-1} corresponding to Si-O-Si bonds, which were not present for unmodified NP (FIG. 1A). Surface zeta potential changed from +20.1 mV for unmodified NP to between -12.6 mV to -23.4 mV for silica coated NP. Deposition of silica layer on NP significantly decreased iron release (FIG. 1B). Formation of silica coating also influenced magnetic properties of NP. Magnetic moment of particles covered with silica was 30% smaller than for unmodified NP. This certifies that approximately 30% of modified NP is silica. We have seen the paramagnetic/superparamagnetic contribution for mesoporous and amorphous silica coating. For unmodified NP and NP@SiO_2 we have also observed the Verwey phase transition resulting from the change of Fe_3O_4 crystallographic structure from cubic to monoclinic. On the other hand, the largest coercive field was observed for NP@$mSiO_2$ and NP@SiO_2@$mSiO_2$.

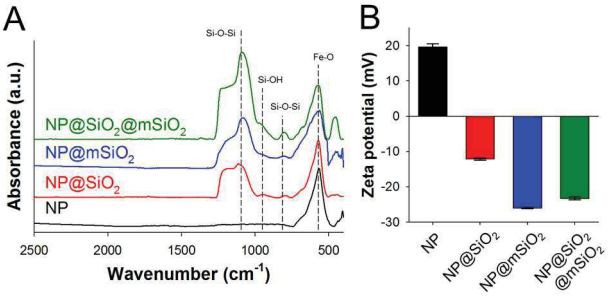

FIG. 1. FTIR spectra (A) and surface zeta potential (B) of unmodified and silica coated NP.

All types of NP were efficiently internalised by lung epithelial cells and they did not show any influence on viability of malignant lung epithelial cells at concentration of 10 µg/ml. In the case of non-malignant lung epithelial cells reduced proliferation was observed, which was correlated with more intensive cell migration and increased cell velocity as shown by real-time phase contrast analysis by IncuCyte (FIG. 2).

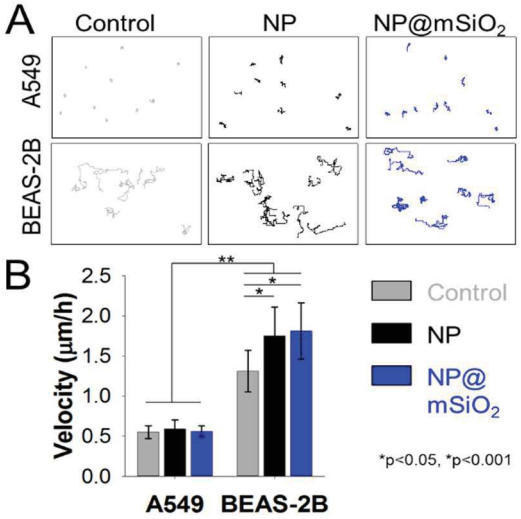

FIG. 2. Paths of single cell migration (A) and average velocity of cells (B) after addition of unmodified NP and NP@$mSiO_2$ (10 µg/ml).

Conclusions

Silica modified SPIONs are promising materials for hyperthermia and drug delivery purposes as they do not release iron ions and do not show significant cytotoxic effects towards lung epithelial cells. Silica coatings can be further modified with different drugs or biologically active molecules to enhance anticancer treatment.

Acknowledgments

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References

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