Abstract

Aim of this thesis was to design and prepare polymer-coated monodisperse Fe$_3$O$_4$ nanoparticles as a safe and non-toxic contrast agent for magnetic resonance imaging (MRI) and heat mediator for hyperthermia. Uniform superparamagnetic Fe$_3$O$_4$ nanoparticles were synthesized by thermal decomposition of Fe(III) oleate, mandelate, or glucuronate in high-boiling solvents at temperature $>$285 °C. Size of the particles was controlled in the range of 8-27 nm by changing reaction parameters, i.e., temperature, type of iron precursor, and concentration of stabilizer (oleic acid and/or oleylamine), while preserving uniformity of the nanoparticles. Because particles contained hydrophobic stabilizer on the surface, they were dispersible only in organic solvents. To ensure water dispersibility, oleic acid on the particle surface was replaced by hydrophilic and biocompatible methoxy-poly(ethylene glycol) (PEG) and poly(3-O-methacryloyl-α-D-glucopyranose) by ligand exchange. Polymers were previously terminated with anchoring-end groups (hydroxamic or phosphonic) to provide firm bonding to iron atoms on the particle surface. Fe$_3$O$_4$ nanoparticles were also hydrophilized by encapsulation into a silica shell by reverse microemulsion method. Tetramethyl orthosilicate was used to prepare Fe$_3$O$_4$@SiO$_2$ nanoparticles, which were further functionalized with amino groups using (3-aminopropyl)triethoxysilane. Finally, the amino groups were used to introduce PEG on the particle surface to ensure colloidal stability in physiological medium.

Magnetic Fe$_3$O$_4$ nanoparticles were characterized by a variety of techniques, including dynamic light scattering and transmission electron microscopy to determine hydrodynamic size and morphology, respectively. X-ray powder diffraction and vibrating sample magnetometry were used to investigate particle composition and magnetic properties. The content of iron, iron oxide, and presence of polymer shell were determined by atomic absorption spectroscopy, thermogravimetric analysis, and attenuated total reflectance Fourier-transform infrared spectroscopy (ATR FTIR), respectively. Chemical structure of the modified polymers was confirmed by $^1$H and $^{31}$P NMR, and ATR FTIR spectroscopies.

Toxicity of newly developed polymer-coated nanoparticles was tested in vitro on selected cell lines; non-toxicity of the particles was confirmed. Relaxivity measurements showed good imaging properties of particles compared to commercially available agents. Moreover, calorimetrically measured specific absorption rate of the particles revealed their potential applicability as a heat mediator for hyperthermia treatment.

Keywords: polymer; superparamagnetic; monodisperse; nanoparticle; iron oxide; toxicity.