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Surface modification of metallic Co nanoparticles

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Abstract

Monodisperse Co nanoparticles were synthesized by thermal decomposition in the presence of aluminium alkyls yielding air-stable Co nanoparticles after surface passivation. Several procedures for surface modification of these *pre-stabilized*, metallic Co nanoparticles are presented, including direct anchoring of surface-active functional groups and biocompatible dextran layers as well as silica and polymer coatings. As a result, individually coated nanoparticles as well as microspheres can be obtained.

Keywords: Nanoparticles; Microspheres; Co nanoparticles; Surface modification; Synthesis

Recently, the combination of the interesting optical, magnetic, and electrical properties of nanoparticles together with the high specificity of biomolecular binding [1–3] has shown promising results in various areas of biomedical *in vitro* and *in vivo* application. Magnetic particles (including microspheres and nanoparticles) have been widely studied for various fields of application in biology and medicine, e.g., magnetic drug targeting, magnetic resonance imaging, hypothermia, immunoassays, separation/purification of nucleic acids, proteins, and cells [4,5]. The combination of magnetic particles and biomolecules has been mainly focused on iron oxide nanoparticles; reports on biofunctionalized magnetic metal nanoparticles are rather rare.

Compared to magnetic iron oxide particles, the significance of using magnetic metal nanoparticles, e.g., Co, Fe, FeCo, or FePt is manifold: firstly, they can be prepared with a narrow size distribution whereas the direct synthesis of iron oxides often results in rather broad particles size distributions. For numerous biomedical applications monodisperse particles are required. Secondly, magnetic metal nanoparticles exhibit a high saturation magnetization, e.g., the saturation magnetization M_s of bulk cobalt is 162 A m^2/kg. Moreover, based on the higher magnetization, Co nanoparticles exhibit a higher specific loss power than the iron oxide ones, which makes them interesting as potential candidates for applications in hyperthermia (770 W/g for a Co magnetic fluid in kerosene at 400 kHz, 10 kA/m) [6]. However, stability is an important issue; usually, metal nanoparticles get easily oxidized when exposed to air and, thus, loose their magnetic properties. Co, for example, easily oxidizes in air (free heat of formation CoO −237.9 KJ/mol, Co_3O_4 −891.0 KJ/mol). Co films with a thickness greater than 5 nm were shown to instantaneously oxidize in air forming a 2.5 nm cobalt oxide layer [7]. In addition, the synthesis of magnetic metal nanoparticles is typically performed in organic media and, thus, phase transfer of the as-prepared particles into the aqueous phase is important for biomedical application. Besides, the potential toxicity for *in vivo* applications of Co nanoparticles has to be explored. On the other hand, using magnetic metal nanoparticles, only small amounts of particles would be required due to the excellent magnetic characteristics, minimizing potential side effects. Moreover, appropriate surface engineering of the particles not only allows binding of bioactive molecules to the particle surface but also generates biocompatible particle surfaces.

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We prepare metallic Co nanoparticles by thermolysis of $Co_2(CO)_8$ in the presence of an aluminium alkyl catalyst yielding metallic Co nanoparticles. Details of the synthesis are reported in Ref. [8]. The metal particles were protected against oxidation by careful surface passivation (pre-stabilization), exposing the Co nanoparticles to a controlled, small amount of oxygen. The stabilization of the metallic particles occurs via formation of a CoO layer and via remaining surface carbonyls as well as surface carbonates as shown by XPS and XAS analysis [8]. The mean diameter of the applied *pre-stabilized* Co nanoparticles was 9 nm. The magnetic nanoparticles and their surface modification were characterized by a wide range of techniques including transmission electron microscopy (TEM), energy-filtered TEM (EFTEM), infrared (IR) spectroscopy, atomic emission spectroscopy with inductively coupled plasma (AES–ICP), dynamic light scattering (DLS), and magnetic measurements by an alternating gradient magnetometer (AGM).

Surface engineering as well as the conjugation method are crucial because they may affect not only the particle stability and biocompatibility but also the biological functionality of the prepared materials. There are several ways to modify the particle surface and connect biofunctional molecules to the surface of a nanoparticle. First, the molecule contains a surface-active group, e.g., a thiol and is chemisorbed directly on the nanoparticle surface. A monolayer of molecules that bear a functional thiol group can be attached to the surface of the *pre-stabilized* Co particles, allowing further functionalization with bioactive molecules in a second step. We have peptized *pre-stabilized* Co nanoparticles by L-cysteine ethyl ester after extensive washing with ethanol and water, forming stable colloidal solutions in water or ethanol. As shown by IR spectra and X-ray absorption spectroscopy, the binding of L-cysteine ethyl ester occurred via the thiol group, with the amino group remaining free for further functionalization (see Fig. 1) [9]. Other groups have reported nitrilotriacetic acid-modified FePt nanoparticles obtained via a functional thiol group which acted as anchoring group to the particle surface [10]. The L-cysteine ethyl ester-modified Co nanoparticles provide a basis for further surface modification and functionalization with biocompatible layers or bioactive molecules. Dextran coating of iron oxide nanoparticles, for example, has been widely studied due to its biocompatibility and its surface properties such as its hydrophilic character. When colloidal solutions of L-cysteine ethyl ester-modified Co nanoparticles in ethanol were reacted with dextran (molecular weight 10,000) or carbomethoxydextran nanoparticle aggregates covered by the polysaccharide were formed [11]. The TEM images display the formation of aggregates of 9-nm-sized Co particles (Fig. 2). The corresponding EFTEM images show the Co core of the particles covered by an oxygen-rich

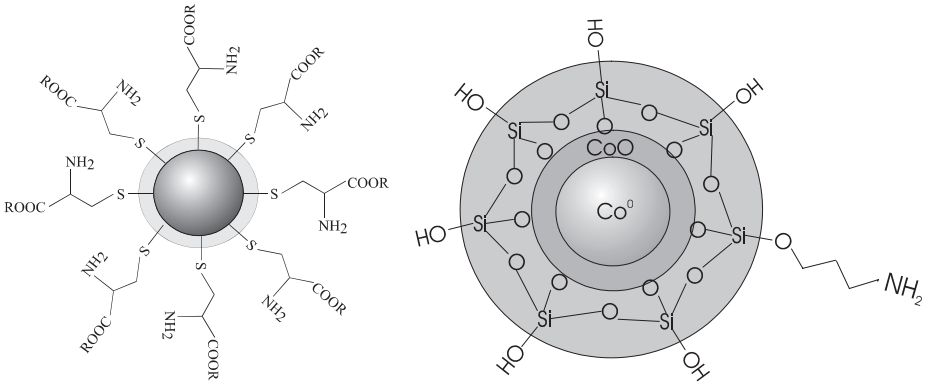

Fig. 1. Surface-modified Co nanoparticles: surface modification via a surface-active thiol group using L-cysteine ethyl ester and via a silica network exhibiting functional silanol groups.

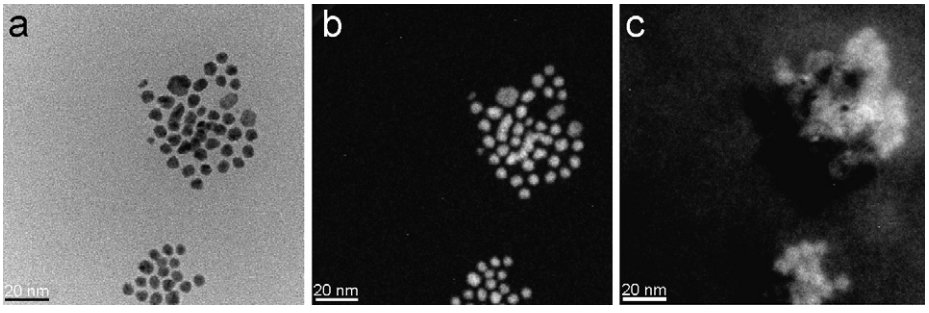

Fig. 2. Co nanoparticles coated by carbomethoxydextran and corresponding EFTEM images (Co map (Co $L_{2,3}$ edge) (b), and O map (O K edge) (c)) (scale bar 20 nm).

carbomethoxydextran layer. Dextran coating could be also performed on unmodified Co nanoparticles in alkaline solution.

By covalent attachment of functional biomolecules to nanoparticle surfaces, problems of ligand exchange reactions in solution may be overcome. Therefore, the nanoparticles must be derivatized with a cross-linked surface shell, which exhibit potential binding sites for bioactive molecules. This cross-linked surface shell could consist of polymer or inorganic networks. Such biomolecule-particle conjugates are stable, as long as covalent bonds have to be broken to disintegrate them.

Coating with silica enables covalent functionalization via its numerous surface silanol groups, easily reacting with silane coupling agents, e.g., 3-aminoproyl silane as covalent anchorage for bioactive molecules (Fig. 1). As mentioned above, Co is easily oxidized, and thus stability is an important issue during the procedure of silica coating, even when *pre-stabilized* Co nanoparticles were applied. Co nanoparticles were coated by hydrolysis of tetraethoxysilane (TEOS), a method related to the Stöber process [12]. In brief, Co particles peptized with oleic acid in toluene were coated with silica via the base-catalyzed hydrolysis of TEOS under argon atmosphere [11]. The surface of the Co particles exhibited an affinity toward silica, and, in contrast to Au and Ag particles, no primer was applied to promote the deposition and adhesion of silica on the Co particles. TEM images show that an amorphous silica layer of about 3.5 nm was formed homogeneously around each individual Co particle (Fig. 3, magnetization curve see Fig. 6b). Besides a broad band at 1052 cm^{-1}, which is characteristic for Si–O–Si bonding, IR spectra display the bands of alkyl chains at 2854–2966 cm^{-1} suggesting unhydrolyzed ethoxy groups at the particle surface. After separation and extensive washing with ethanol, the silica coated particles form colloidal solutions in ethanol. As determined by DLS experiments, the particles were dispersed as individual particles exhibiting a hydrodynamic radius of around 10 nm and only few aggregates were observed (Fig. 3). Aside from using peptized nanoparticles together with the base-catalyzed hydrolysis of TEOS, the Co particles could be directly covered by TEOS with a very thin SiO_2 layer even without peptizing oleic acid and in the absence of the ammonium hydroxide catalyst, avoiding complexation and oxidation reactions with the Co core which might destroy the protective, *pre-stabilizing* cobalt oxide shell. TEM and energy-filtered TEM images show the metallic Co core with its stabilizing cobalt oxide layer covered by a thin silica layer (Fig. 4). The saturation magnetization of the sample was 80 $A\,m^2/kg$ (Fig. 6c), which is comparable to the saturation magnetization of the *pre-stabilized* Co particles (Fig. 6a) representing about 50% of the Co bulk value. It has to be stressed that these are raw data, including the diamagnetic silica shell and the passivating, antiferromagnetic CoO layer (Co content of the sample as determined by AES–ICP was 70 wt%). These particles were stable in water, although they did not form a colloidal solution. Preliminary experiments with 3-aminopropylsilane reveal anchored amino groups (1.3% N as determined by elemental analysis).

Depending on the area of application, magnetic microspheres, e.g., for cell separation or individually coated

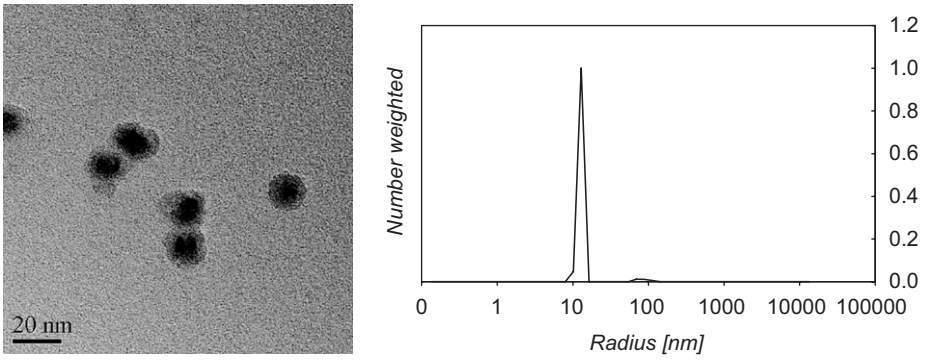

Fig. 3. TEM image of SiO_2 coated Co particles (scale bar 20 nm) and dynamic light scattering (DLS).

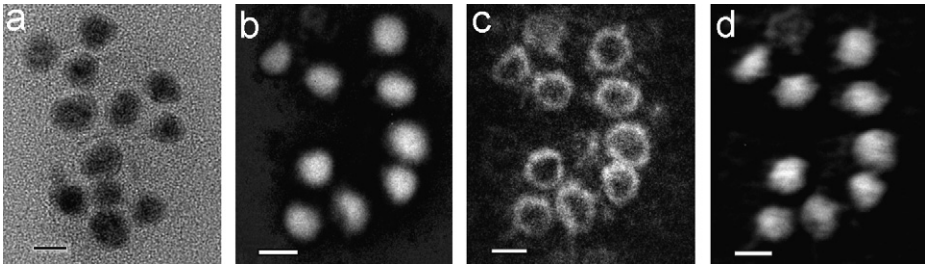

Fig. 4. TEM image of SiO_2 coated Co particles (a) and EFTEM images (Co map (Co $L_{2,3}$ edge) (b), O map (O K edge) (c), and Si map (Si $L_{2,3}$ edge) (d)) (scale bar 10 nm).

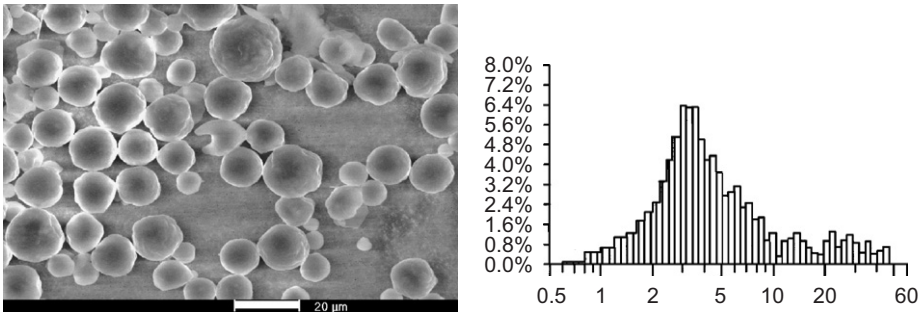

Fig. 5. SEM image of Co nanoparticles embedded in poly(MMA–DVB) microspheres (size around 15 µm) and size distribution of poly(VA–DVB) microspheres (size around 3 µm).

nanoparticles, which are able to penetrate small capillaries within the body tissue or cell membranes, are preferable. Due to the high saturation magnetization and the high magnetophoretic mobility, microspheres equipped with magnetic metal nanoparticles can be made much smaller than commonly used ones containing iron oxide.

Silica microspheres containing Co particles could be prepared by applying a two-step procedure [11]: firstly, the pre-stabilized Co particles were treated with 3-aminopropyl silane and active silica, followed by the ammonia-catalysed hydrolysis of TEOS in a second step. The resulting uniform silica spheres were about 520 nm in size exhibiting a saturation magnetization of 21 A m^2/kg (Fig. 6d; Co content as determined by AES–ICP was 24 wt%). The diameter of the microspheres was dependent on the reaction time. Further increase of the SiO_2 microsphere diameter could be achieved by applying a third step of ammonia-catalysed hydrolysis of TEOS after washing the above microspheres.

Besides silica beads, magnetic polymer microspheres are very interesting for various applications in biology and medicine. The surface of such polymer spheres can be further functionalized with bioactive groups. *Pre-stabilized* Co nanoparticles were encapsulated into polymer microspheres by applying a suspension polymerization process [11]. In brief, a magnetic fluid of *pre-stabilized* Co nanoparticles was prepared with KorantinSH (*N*-oleyl sarcosine) in dichloromethane/hexane (1:1) and mixed with the monomers (methylmetacrylate, MMA, or vinylacetate, VA, and divinylbenzene, DVB) and the initiator (benzoyl peroxide, BPO). Polyvinylalcohol as stabilizer and sodium chloride were dissolved in the aqueous phase at 60 °C and a few microlitre methylene blue were added. The two phases were vigorously mixed under stirring and the formed emulsion was heated for 4 h. Depending on the polymerization conditions such as speed of mixing, concentration of magnetic fluid, and the kind of monomer, different microspheres were obtained, e.g., the use of MMA instead of VA yielded 15 µm-sized polymer spheres instead of 3 µm-sized spheres. Fig. 5 displays the products after size fractioning by sedimentation. The SEM image in Fig. 5 shows poly(MMA–DVB) microspheres containing Co nanoparticles in the range of 15 µm and the size distribution of poly(VA–DVB) microspheres in the range of 3 µm. The saturation magnetization of poly(MMA–DVB) microspheres was 33 A m^2/kg (Fig. 6e) which is higher than those reported for Fe_3O_4 (Co content as determined by AES–ICP was 35 wt%) [13].

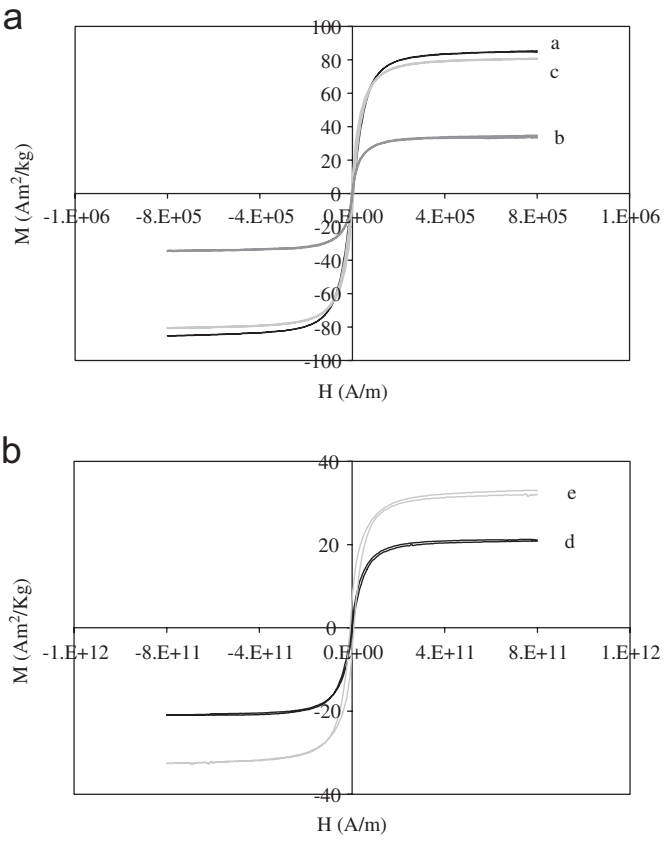

Fig. 6. Magnetization curves of *pre-stabilized* Co nanoparticles (a), individually SiO_2 coated Co nanoparticles (SiO_2 coating of Co nanoparticles stabilized by oleic acid, 50 wt% Co (b), and SiO_2 coating of Co nanoparticles in the absence of NH_4OH, 73 wt% Co (c)) and Co nanoparticles embedded in SiO_2 microspheres (24 wt% Co (d)) and poly(MMA–DVB) microspheres (35 wt% Co (e)).

In summary, we report the synthesis of air-stable Co nanoparticles and several procedures for their surface modification. These methods for surface engineering will allow future biofunctionalization of the particles with

proteins, nucleic acid or other biomolecules, opening up possibilities for biomedical applications. The toxicity of such Co nanoparticles will be the issue of further studies.

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