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Review

Synthesis and surface engineering of iron oxide nanoparticles for biomedical applications

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Abstract

Superparamagnetic iron oxide nanoparticles (SPION) with appropriate surface chemistry have been widely used experimentally for numerous in vivo applications such as magnetic resonance imaging contrast enhancement, tissue repair, immunoassay, detoxification of biological fluids, hyperthermia, drug delivery and in cell separation, etc. All these biomedical and bioengineering applications require that these nanoparticles have high magnetization values and size smaller than 100 nm with overall narrow particle size distribution, so that the particles have uniform physical and chemical properties. In addition, these applications need special surface coating of the magnetic particles, which has to be not only non-toxic and biocompatible but also allow a targetable delivery with particle localization in a specific area. To this end, most work in this field has been done in improving the biocompatibility of the materials, but only a few scientific investigations and developments have been carried out in improving the quality of magnetic particles, their size distribution, their shape and surface in addition to characterizing them to get a protocol for the quality control of these particles. Nature of surface coatings and their subsequent geometric arrangement on the nanoparticles determine not only the overall size of the colloid but also play a significant role in biokinetics and biodistribution of nanoparticles in the body. The types of specific coating, or derivatization, for these nanoparticles depend on the end application and should be chosen by keeping a particular application in mind, whether it be aimed at inflammation response or anti-cancer agents. Magnetic nanoparticles can bind to drugs, proteins, enzymes, antibodies, or nucleotides and can be directed to an organ, tissue, or tumour using an external magnetic field or can be heated in alternating magnetic fields for use in hyperthermia. This review discusses the synthetic chemistry, fluid stabilization and surface modification of superparamagnetic iron oxide nanoparticles, as well as their use for above biomedical applications.

Keywords: Magnetic nanoparticles; MRI; Drug delivery; Surface modification; Hyperthermia; Cell labelling; Iron oxide

Contents

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1. Introduction

In the last decade, nanotechnology has developed to such an extent that it has become possible to fabricate, characterize and specially tailor the functional properties of nanoparticles for biomedical applications and diagnostics [1–4]. As intermediates between the molecular and the solid states, inorganic nanoparticles combine chemical accessibility in solution with physical properties of the bulk phase [5]. They are thus ideal elements for the construction of nanostructured materials and devises with adjustable physical and chemical properties [1,6]. The application of small iron oxide particles in in vitro diagnostics has been practised for nearly 40 years [7]. In the last decade, increased investigations with several types of iron oxides have been carried out in the field of nanosized magnetic particles (mostly maghemite, γ-Fe_2O_3, or magnetite, Fe_3O_4, single domains of about 5–20 nm in diameter), among which magnetite is a very promising candidate since its biocompatibility has already proven [8]. Magnetite, Fe_3O_4, is a common magnetic iron oxide that has a cubic inverse spinel structure with oxygen forming an fcc closed packing and Fe cations occupying interstitial tetrahedral sites and octahedral sites [9]. The electrons can hop between Fe^{2+} and Fe^{3+} ions in the octahedral sites at room temperature, rendering magnetite an important class of half-metallic materials [10]. With proper surface coating, these magnetic nanoparticles can be dispersed into suitable solvents, forming homogeneous suspensions, called ferrofluids [11,12]. Such a suspension can interact with an external magnetic field and be positioned to a specific area, facilitating magnetic resonance imaging for medical diagnosis and AC magnetic field-assisted cancer therapy [13].

Nanosized particles have physical and chemical properties that are characteristic of neither the atom nor the bulk counterparts [14]. Quantum size effects and the large surface area of magnetic nanoparticles dramatically change some of the magnetic properties and exhibit superparamagnetic phenomena and quantum tunnelling of magnetization, because each particle can be considered as a single magnetic domain [15]. Based on their unique mesoscopic physical, chemical, thermal, and mechanical properties, superparamagnetic nanoparticles offer a high potential for several biomedical applications, such as [16–19]:

(a) cellular therapy such as cell labelling, targeting and as a tool for cell-biology research to separate and purify cell populations;
(b) tissue repair;
(c) drug delivery;
(d) magnetic resonance imaging (MRI);
(e) hyperthermia;
(f) magnetofection; etc.

For these applications, the particles must have combined properties of high magnetic saturation, biocompatibility and interactive functions at the surface. The surfaces of these particles could be modified through the creation of few atomic layers of organic polymer or inorganic metallic (e.g. gold) or oxide surfaces (e.g. silica or alumina), suitable for further functionalization by the attachment of various bioactive molecules [20]. They are either dispersed through a large volume of a polymeric bead or occur as core in colloidal reagent with a biodegradable shell. As the magnetic particles accumulate, e.g., in tumour tissue, they can play an important role in detection through MRI or electron microscopic imaging to locate and measure binding or as drug carrier for certain anti-cancer drugs. The magnetic nanoparticles having suitable surface characteristics have a high potential for the use in a lot of in vitro and in vivo applications. In all cases, superparamagnetic particles are of interest because they do not retain any magnetism after removal of magnetic