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Recent advances in the synthesis of Fe_3O_4@AU core/shell nanoparticles

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ABSTRACT

Fe_3O_4@Au core/shell nanoparticles have unique magnetic and optical properties. These nanoparticles are used for biomedical applications, such as magnetic resonance imaging, photothermal therapy, controlled drug delivery, protein separation, biosensors, DNA detection, and immunosensors. In this review, recent methods for the synthesis of core/shell nanoparticles are discussed. We divided all of the synthetic methods in two groups: methods of synthesis of bi-layer structures and methods of synthesis of multilayer composite structures. The latter methods have a layer of “glue” material between the core and the shell.

1. Introduction

Many types of magnetic nanoparticles (MNPs) have been synthesized over the past decade. There are a number of recent reviews that describes the synthesis and biomedical applications of MNPs [1–5]. The most important features of MNPs for biomedical applications are:

(1) Superparamagnetism to prevent aggregation;
(2) Good magnetic responsiveness for separation and delivery, which is controlled by an external magnetic field;
(3) Appropriate particle size for optimized electrical, optical, and magnetic properties of MNPs;
(4) Good dispersion, stability, and biocompatibility to avoid macrophage endocytosis and to extend blood circulation time;
(5) Appropriate surface for functionalization.

Different MNPs have different properties, methods of synthesis and applications. Among these MNPs are Mn_3O_4, Co, Ni, NiO, Nd and others [6–9]. Iron oxides are the most commonly used MNPs because of the toxicity and rapid oxidization of the other MNPs [10]. Surface modifications of MNPs are very important for medical applications, including magnetic resonance imaging, controlled drug delivery, photothermal therapy, protein separation and immunoassays [11–17].

However, there are some disadvantages of uncoated iron oxide nanoparticles for biological applications:

- Their instability under physiological conditions [18]
- Formation of harmful free radicals promoted by them [19]
- Inappropriate surface binding of the ligand, which results in failure in controlled drug delivery [20]

There are many different approaches to the modification or functionalization of the MNPs surfaces with different materials such as polymers, organic monolayers, oxides, and metals. One of the most promising modifications is adding a gold shell. Gold nanoparticles are commonly used in biomedical applications due to their simple synthesis, possibility of bioconjugation and good biocompatibility [21]. Moreover, gold nanoparticles are already used for drug delivery [22]. One of the most important properties

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Abbreviations: MNP, magnetic nanoparticles; TEM, transmission electron microscopy; CTAB, cetyltrimethylammonium bromide; PZS, polyphosphazene; PEI, polyethyleneimine; PB, Prussian Blue; PANI, polyaniline; PDADMAC, poly(diallyldimethylammonium chloride); MRI, magnetic resonance imaging; DLS, dynamic light scattering; PSS, poly-(sodium 4-styrenesulfonate)

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of gold nanoparticles is so called “surface plasmon”, which results in significant optical absorption in the visible and near-infrared region. The optical properties of Fe_3O_4@Au nanoparticles are desired in biological applications, such as imaging and photothermal therapy. However, Fe_3O_4@Au nanoparticles are of low solubility in water [23]. This low solubility leads to the aggregation and precipitation of nanoparticles, which is unsuitable for biomedical applications [24]. For improved solubility in water, the surface of Fe_3O_4@Au nanoparticles may be functionalized with hydrophilic thiols [25,26].

One of the most challenging issues in core/shell MNPs efficacy is the need to overcome biological barriers to reach their target, such as tumours. Major clearance routes for these MNPs, according to their physicochemical properties, are the liver, spleen and kidneys. Particles must be able to evade clearance to be delivered to a tumour. Thus, their physiochemical properties, including size, charge, surface properties and morphology, must be precisely controlled [27].

In our previous work we described the distinct effect of non-heating super-low-frequency magnetic fields as well as radio-frequency magnetic fields on the kinetics of chemical reactions catalysed by the enzymes immobilized on Fe_3O_4@Au MNP aggregates. Exposure to an alternating current magnetic field resulted in a reduction in enzyme activity. This observation suggests the significance of magneto-mechanochemical effects induced by the realignment of MNP magnetic moments in an alternating current magnetic field rather than traditional heating [28].

In this article, we discuss the work on the synthesis and characterization of Fe_3O_4@Au nanoparticles for a biomedical application that has occurred since 2006. We exclude the methods of synthesis of dumbbell, cluster/shell nanoparticles and iron oxide MNPs with Au seeds on the surface; other methods are described in other excellent reviews [29–31].

2. Synthesis of Fe_3O_4@Au core/shell nanoparticles: typical approaches.

During the last few years, many articles have described effective chemical techniques to synthesize stable monodispersed Fe_3O_4@Au nanoparticles with the required size. The surface of the nanoparticles could be further functionalized to produce prospective structures for biomedical applications. The most common synthetic methods for core synthesis are described in other excellent reviews [32–34]. These methods include co-precipitation, thermal decomposition, reversed micelle technique and the solvothermal method. There are two types of Fe_3O_4@Au nanoparticles: bi-layer and multilayer composite structures (Fig. 1). Bi-layer structures, which are the standard structures, consist of two layers: the core and Au shell. Multilayer composite structures consist of more than two layers. Typically, there are three layers: the core, the “glue” material (SiO_2, polymers, etc.) and the Au shell. There are two different approaches to the synthesis of Fe_3O_4@Au nanoparticles. The first approach is used to produce bi- layer structures (Scheme I), and the second approach is used for multilayer composite structures (Scheme II).

3. Synthesis of Fe_3O_4 bi-layer structures (Scheme I)

One of the most common methods of the synthesis of Fe_3O_4@Au core/shell nanoparticles is the formation of a gold shell directly onto the magnetite surface [11,23,35–45]. For example, small Fe_3O_4 (9–20 nm) nanoparticles were first synthesized using the co-precipitation of $FeCl_2$ and $FeCl_3$ in diluted NH_3 solution. Next, a $HAuCl_4$ solution was boiled and Fe_3O_4 nanoparticles were added, followed by the addition of sodium citrate as a reducing agent for Au shell formation. L-Homocysteine was added to the boiling solution to form Fe_3O_4@Au@homocysteine nanoparticles [23,35,45]. These nanoparticles are well dispersed in water, which is essential for biomedical applications. Moreover, the surface functionalization with homocysteine is useful for the further functionalization of the Fe_3O_4@Au nanoparticle surface. Amine and carboxylate groups on the nanoparticle surface may allow subsequent transformations, as was shown for a Au nanoparticle ligand sphere [47] and for carboxylated Fe_3O_4@Au nanoparticles [45]. According to transmission electron microscopy (TEM) data, the nanoparticles are nearly spherical in shape, with small average sizes (12.3 nm [23] and 22 nm [35]). Fe_3O_4 nanoparticles can also be coated with gold using the $NaBH_4$ reduction of $HAuCl_4$ in a sonicator. The sonication procedure leads to improved nanoparticle monodispersity and prevents agglomeration due to ionic interactions. The resulting core/shell nanoparticles are also small, with an average size of 12.5 ± 3 nm, according to transmission electron microscopy (TEM) images [37]. Hydroxylamine hydrochloride can also be used as a reducing agent. The next approach to the coating of Fe_3O_4 with gold is $HAuCl_4$ reduction using sodium citrate and hydroxylamine hydrochloride. This reduction process requires a longer time than other methods [23,35,37] and took up to 5 h. The resulting nanoparticles were spherical in shape, with an average diameter of 20 nm. [38] Subsequently, Fe_3O_4@Au nanoparticles were functionalized with 11-mercaptoundecanoic acid and 11-dodecanethiol (Table 1). $HAuCl_4$ reduction with sodium citrate and hydroxylamine hydrochloride may be performed in two steps. First, sodium citrate was added to Fe_3O_4, and the solution was stirred before $NH_2OH \cdot HCl$ and $HAuCl_4$ were added. This process took up to 30 min. [48] Next, Fe_3O_4@Au were modified with 3′-(alkanethiol) oligonucleotides and used for detection of DNA point mutations. The average diameter of the core/shell nanoparticles was 100 nm [48].

The magnetite surface is often modified to attract Au ions. One of the modifications is a sodium citrate coating of Fe_3O_4. Fe_3O_4@Au nanoparticles with a diameter of 15–40 nm were obtained using

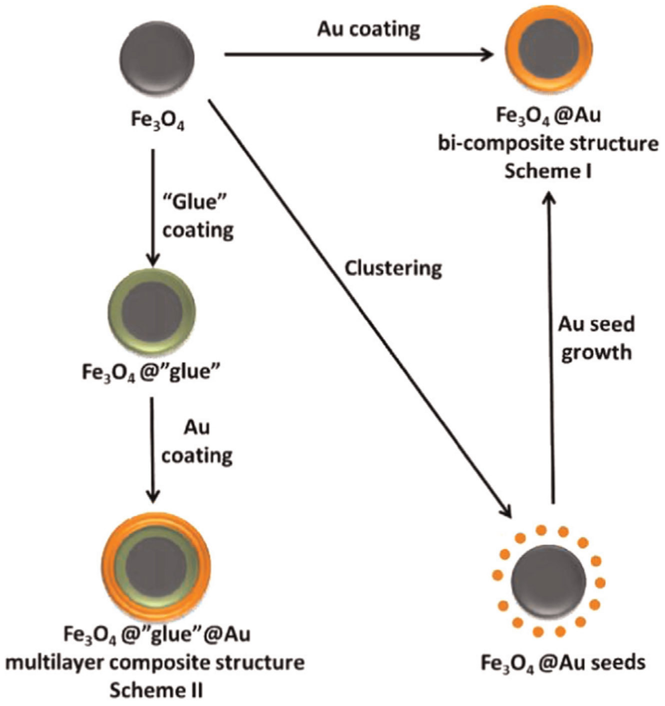

Fig. 1. Schematic representation of three different techniques for the synthesis of Fe_3O_4@Au core/shell nanoparticles.