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Sensors and biosensors based on magnetic nanoparticles

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ABSTRACT

Magnetic nanoparticles (MNPs) have attracted a growing interest in the development and fabrication of sensors and biosensors for several applications. MNPs can be integrated into the transducer materials and/or be dispersed in the sample followed by their attraction by an external magnetic field onto the active detection surface of the (bio)sensor. This review describes and discusses the recent applications of MNPs in sensors and biosensors, taking into consideration their analytical figures of merit. This work also addresses the future trends and perspectives of sensors and biosensors based on MNPs.

Contents

1. Introduction

Nanotechnology has been one of the most important research trends in material sciences. Nanomaterials (nanoparticle (NP) size range 1–100 nm) compared with non-NP materials show remarkable differences in physical and chemical properties, such as unique optical, electrical, catalytic, thermal and magnetic characteristics, due to their small size [1]. In recent years, considerable efforts were therefore made to develop magnetic NPs (MNPs), due to their own advantages, such as their size, physicochemical properties and low cost of production [2,3]. MNPs exhibit their best performance at sizes of 10–20 nm due to supermagnetism, which makes them especially suitable when looking for a fast response due to applied magnetic fields [4]. MNPs also have large surface area and high mass transference. Since the properties of MNPs depend strongly on their dimensions, their synthesis and their preparation have to be designed in order to obtain particles with adequate size-dependent physicochemical properties. MNPs possessing adequate physicochemistry and tailored surface properties have been synthesized under precise conditions for a plethora of applications, such as sample preparation [5–7], wastewater treatment [8], water purification [9], disease therapy [3,10], disease diagnosis (magnetic resonance imaging) [3,11,12], cell labelling and imaging [3,11], tissue engineering [3], and sensors, biosensors and other detection systems [13–17]. Furthermore, MNPs have been used to enhance the sensitivity and the stability of sensors and biosensors for the detection of several analytes in clinical, food and environmental applications. Taking into consideration the broad application of MNPs in sensing and biosensing systems, this review describes and discusses the current state of recent applications of MNPs in sensors and biosensors.

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2. Synthesis, properties and characterization of magnetic nanoparticles

In the past few years, many types of MNP were synthesized, including: iron oxides (Fe_2O_3 and Fe_3O_4); ferrites of manganese, cobalt, nickel, and magnesium; FePt, cobalt, iron, nickel, CoPt and FeCo particles; and, multifunctional composite MNPs, such as Fe_3O_4-Ag, Fe_3O_4-Au, FePt-Ag, and CdS-FePt heterodimers of NPs. MNPs can be synthetized by physical methods (e.g., gas-phase deposition and electron-beam lithography), wet chemical methods (e.g., coprecipitation, high-temperature thermal decomposition and/or reduction, sol-gel synthesis, flow-injection synthesis, oxidation method, electrochemical method, aerosol/vapor-phase method, supercritical fluid method, and synthesis using nanoreactors) and microbial methods [2,3,14].

According to Reddy et al. [3], the physical methods are limited by their inability to control particle size down to the nanometer scale while the microbial approach ensures high yield, good reproducibility and stability associated with low cost. A detailed discussion of MNP synthesis, beyond the scope of this review, can be found elsewhere [3,11,18,19].

MNPs need to be stabilized in order to prevent irreversible agglomeration and to enable dissociation. Such stabilization can be performed by surface coating using appropriate polymers/surfactants [e.g., dextran, and poly(ethylene glycol)], generating polymeric shells that avoid cluster growth after nucleation and hold the particle domains against attractive forces (e.g., nanosphere and nanocapsule), and formation of lipid-like coatings around the magnetic core (e.g., liposomes) [3].

Materials are classified by their response to a magnetic field applied externally and there are the five basic types of magnetism (i.e., diamagnetism, paramagnetism, ferromagnetism, antiferromagnetism and ferrimagnetism) [2]. Materials whose atomic magnetic moments are uncoupled display paramagnetism [2]. Due to their small volume, MNPs are generally superparamagnetic, which means that they have no net magnetic dipole. Thus, thermal fluctuations cause random orientation of the spins (i.e., thermal energy may be enough to cause the spontaneous change in the magnetization of each MNP). Therefore, in the absence of an electromagnetic field, the net magnetic moment of an MNP will be zero at high enough temperatures, but, when a magnetic field is applied to the NP, a magnetic dipole is induced and there will be a net alignment of magnetic moments. After the external magnetic field is removed, the MNPs randomly orient and return to their native non-magnetic state. The shape and the size of NPs will also contribute to determine their magnetic behavior. The superparamagnetism in NPs is determined by the crystallinity of the structures, the type of material, and the number of spins, and there is no general rule that predicts the magnetic properties of an MNP. Magnetism is usually evaluated using a magnetometer that monitors magnetization as a function of applied magnetic field [5].

The common analytical techniques used to measure the concentration and the composition of metallic NPs were recently described by Silva et al. [20], including:

- scanning electron microscopy (SEM), near field scanning optical microscopy (NSOM), transmission electron microscopy (TEM), scanning transmission electron microscopy (STEM), atomic force microscopy (AFM) and environmental scanning electron microscopy (ESEM) to assess the size and the shape of NPs; and,
- energy-dispersive X-ray transmission - electron microscopy (EDX-EM), electron-energy-loss spectrometry (EELS), X-ray diffractometry (XRD) and X-ray fluorescence (XRF) to measure the elemental compositions of single NPs.

Those methods were also the most commonly used for characterization of MNPs applied in sensing and biosensing systems [5,7,21,22], so detailed discussion on such methods is beyond the scope of this review.

3. Sensors and biosensors based on magnetic nanoparticles

Sensing strategies based on MNPs offer advantages in terms of analytical figures of merit, such as enhanced sensitivity, low limit of detection (LOD), high signal-to-noise ratio, and shorter time of analysis than non-MNP-based strategies [23,24]. In sensing applications, MNPs are used through direct application of tagged supports to the sensor, being integrated into the transducer materials, and/or dispersion of the MNPs in the sample followed by their attraction by an external magnetic field onto the active detection surface of the (bio)sensor.

Table 1 shows examples of MNP-based sensors and biosensors for the detection of several analytes in different samples [22,25–59], taking into consideration their analytical figures of merit, such as LOD and linear range. Table 1 shows that these sensors and biosensors are based on different transduction principles (electrochemical, optical, piezoelectric and magnetic field), which we present and discuss in the following sub-sections according to their classification.

3.1. Electrochemical

Electrochemical (EC) devices measure EC signals (current, voltage, and impedance) induced by the interaction of analytes and electrodes that can be coated with chemicals, biochemical materials or biological elements to improve their surface activity [60,61]. EC devices possess advantages of rapidity, high sensitivity, low cost and easy miniaturization and operation, so being attractive in applications, such as clinical, environmental, biological and pharmaceutical [13,60]. EC devices can be classified as amperometric, potentiometric, voltammetric, chemiresistive, and capacitive, according to their working principles [60]. The EC immunosensors, and enzyme, tissue and DNA biosensors are designed through immobilizing biological-recognition elements of antibodies, enzyme, tissue and DNA, respectively, on the working electrode surface. To improve the sensitivity of EC devices, signal amplification has been attempted using MNPs. MNPs can be used in EC devices through their contact with the electrode surface, transport of a redox-active species to the electrode surface, and formation of a thin film on the electrode surface. For MNP-based EC biosensors [22,25–27,32–39], Table 1 shows different detection modes, such as voltammetry [25–31], amperometry [32,33], potentiometry [34,35], electrochemiluminescence (ECL) [36,37] and EC impedance [38,39], which were used for analyte detection and quantification. Among the sensors, the detection mode most used was voltammetry [28–31].

Due to its superparamagnetic property, biocompatibility with antibodies and enzymes and ease of preparation, Fe_3O_4 is most commonly used in developing biosensors. However, Fe_3O_4 magnetic dipolar attraction and its large ratio of surface area to volume may lead to aggregation in clusters when exposed to biological solutions. Functionalization can overcome this problem and also enhance biocompatibility.

A broad variety of functionalized MNPs have been used, such as core-shell Au-Fe_3O_4 [25], core-shell Au-Fe_3O_4@SiO_2 [32], core-shell Fe_3O_4@SiO_2 [28], Au-Fe_3O_4 composite NPs [22], Fe_3O_4@SiO_2/MWCNTs [33], Fe_3O_4 anchored on reduced graphene oxide [29] and Fe_3O_4@Au-MWCNT-chitosan [30].

Core-shell Fe_3O_4@SiO_2 is one of the most used in biosensors, since it contributes to stabilization of MNPs in solution and enhances the binding of ligands at the surface of MNPs. Core-shell Fe_3O_4@SiO_2 is also much used in modifying electrode surfaces, since its characteristics, such as good electrical conductivity, large surface area and