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Recent advances in synthesis and surface modification of superparamagnetic iron oxide nanoparticles with silica

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Research on synthesis of superparamagnetic iron oxide nanoparticles (SPION) and its surface modification for biomedical applications is of intense interest. Due to superparamagnetic property of SPION, the nanoparticles have large magnetic susceptibility, single magnetic domain and controllable magnetic behaviour. However, owing to easy agglomeration of SPION, surface modification of the magnetic particles with biocompatible materials such as silica nanoparticle has gained much attention in the last decade. In this review, we present recent advances in synthesis of SPION and various routes of producing silica coated SPION.

1. Introduction

Superparamagnetic iron oxide nanoparticles (SPION) are inorganic nanomaterials of ferromagnetic substances with sizes between 1–100 nm. Owing to the nano sizes, SPION is superparamagnetic (ability to have zero magnetism in the absence of external magnetic field). This enables the particles to have large magnetic susceptibility and single magnetic domain. Superparamagnetism occurs when size of a ferromagnetic material is so small that the ambient thermal energy is sufficient to induce free rotation of the entire crystallite [1]. SPION can be classified into two: SPION with hydrodynamics sizes greater than 50 nm (coating included) and those with sizes less than 50 nm which are called ultrasmall superparamagnetic iron oxide nanoparticles (USPION). The two common forms of SPION are Magnetite (Fe_3O_4) and Maghemite (γ-Fe_2O_3). SPION has got widespread applications in several areas including magnetic fluids, catalysis, environmental remediation, data storage, and biomedical research and development [2,3]. This is due to easy synthesis and magnetically controllable property of the nanoparticles. In addition, SPION offers several properties that allow its biomedical applications. First, it has controllable sizes ~1–100 nm, which places it at dimensions smaller than or comparable to some of the biomedical system such as cell (10–100 μm), virus (20–450 nm), protein (5–50 nm) and gene (2 nm wide and 10–100 nm long) [4]. Second, due to the superparamagnetic features of SPION, it can be manipulated and driven by an external magnetic field gradient to a particular body area and target biological entities [5]. This allows SPION to be applied in labelling, sensing, separation of biomolecules, drug and gene delivery [6]. Third, due to single-domain property of SPION, it has magnetic moment which can undergo orientational thermal fluctuations from either Brownian or Ne´el fluctuations in the presence of an external AC magnetic field to generate localized temperature up to 45–47 °C [7,8]. This heat is employed in hyperthermia therapy to kill cancer cells [9]. Finally, SPION's superparamagnetic behaviour plus its large magnetic susceptibility cause microscopic field inhomogeneity and activate dephasing of protons in the presence of external magnetic field. Therefore, SPION can be used as MRI probe (contrast agent) to shorten T2 and $T2^*$ relaxation times of the neighbouring regions, and produce a decreased signal intensity in T2- and $T2^*$-weighted MR images [10].

The successful biomedical applications of SPION depend mainly on its stability under biological environments. The major drawbacks of SPION are agglomeration and lack of affinity for biomolecules. The causes of agglomeration in SPION can be related to high surface area, Van der Waals forces of attraction and dipole to dipole interactions between the particles [11]. Surface modification of SPION with biocompatible materials is one the strategies

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used to achieve biomedical applications of SPION. A number of materials such as chitosan, glucose, carboxylic and amine group, surfactant, polymer and inorganic materials (silica or gold) can be used to modify the surface of SPION [12–16]. These materials prevent agglomeration of SPION through either electrostatic repulsion or steric stabilization. Although, application of SPION's synthesis determine type of coating material, silica nanoparticle is one of the preferred inert inorganic materials used for surface modification [17,18]. Advantages of silica as a surface modifying material include chemical stability, optical transparency, porous structure, size-selective permeability and biocompatibility [19]. Silica coating can prevent agglomeration and provide binding site on the SPION [20]. Due to its dielectric property, silica can screen the dipole-dipole interactions, and prevent agglomeration of the core SPION. Silica is hydrophilic material that can improve stability of SPION in aqueous solution. In addition, it has silanol (Si–OH) functional group which allows the composite nanoparticles to disperse in water or polar solvents. More so, the Si–OH can be modified with other functional groups or provide binding site for bio-conjugation. A number of reports have reviewed the synthesis, functionalization, drug and gene delivery, and biomedical applications of SPION [21–27].

On the other hand, recently several progresses have been made on the various methods of synthesizing SPION. In this review, we present current advances on the various strategies developed to synthesis SPION. In addition, special attention is focused on the surface modification of SPION with silica nanoparticles (Fig. 1). This work is divided into five Sections. Magnetic property of SPION is discussed in Section 2. Recent advances on the synthesis of SPION are presented in Section 3. Highlight and discussion on the various routes of producing silica coated SPION is presented in Section 4. Summary of SPION's synthesis and future perspectives of silica coated SPION is presented in Section 5.

2. Magnetic property of SPION

Magnetism is an intrinsic property of matter. However, some materials are more magnetic than the other. Magnetic moments of materials originated from the orbital and the spin motion of electron, and the electron interactions with one another. Atom with completely filled electron shell will experience total cancellation of both orbital and spin moments. Therefore, materials like noble gases (He, Ne, Ar, etc.) are not capable of being permanently magnetized. Based on the response to external magnetic field, materials can be classified into three major groups: diamagnetism, paramagnetism and ferromagnetism. Antiferromagnetism and ferrimagnetism are subclasses of ferromagnetism. However, nanoparticles of ferromagnetic and ferrimagnetic materials display superparamagnetic behaviour. Superparamagnetism occurs in nanoparticles with *Single Domain* (region whereby the magnetic fields of atoms are grouped together and aligned). More importantly, SPION displayed *Magnetic Anisotropy* (show preference to the direction along which their magnetization aligned). Therefore, SPION can randomly flip to the direction of their magnetization. In the presence of external magnetic field the total magnetic moment of the particles aligned parallel to the field like a single giant magnetic moment [28]. More so, SPION has zero magnetization in the absence of an external field. The explanation for why SPION show much variation in their magnetic properties compare to their bulk materials can be attributed to two reasons: (1) surface effect, the fraction of atoms at the surface have fewer neighbour compare to their bulk materials and (2) quantum effects, the nanoparticles show discontinuous behaviour due to completion of shells in systems with delocalized electron [29]. The various forms of magnetism can be summarized with plot of M against H in Fig. 2. Comprehensive review on magnetism and magnetic Nanoparticles can be found elsewhere [28,30].

3. Synthesis of SPION

Extensive research works focused on preparation and understanding the magnetic behaviour of SPION have been reported. However, the various reported routes of synthesizing SPION are faced with the challenges of producing suitable sized, shaped, structured and monodispersed SPION with high magnetic moment. Although several review papers have presented in-depth discussion and comparison on the synthesis of SPION, most of which aimed at the chemical method. In this section, we present recent advances made in the last decade on the various methods of producing SPION. The synthetic routes can be classified into three: physical, chemical and biological methods. The chemical method is the most cited method of producing SPION.

3.1. Physical methods of SPION synthesis

Physical method of producing SPION is a top-down approach

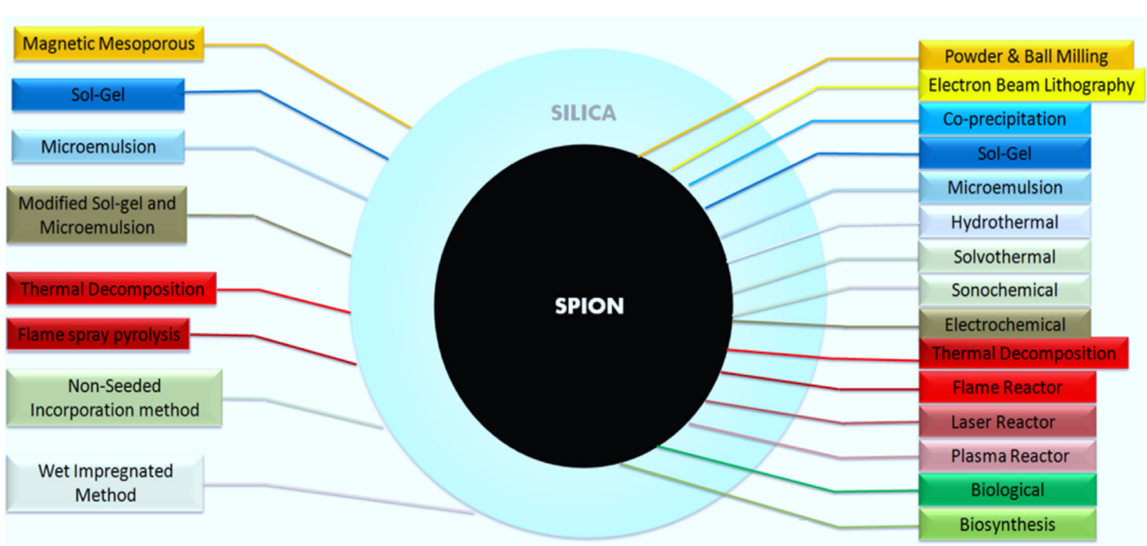

Fig. 1. Showing the various methods of producing SPION and its surface modification with silica nanoparticles.