Synthesis of Magnetic Nanoparticles and its Application in Drug Delivery Systems

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ABSTRACT

Sonochemical and reactions under autogenic pressure reactor techniques were used in the synthesis of magnetic nanoparticles for drug delivery applications. Magnetite (Fe3O4) was synthesized using ultrasonic irradiation of a solution of iron (II) acetate and PEG (polyethylene glycol) under an Ar atmosphere for 3hrs. Iron carbide (Fe3C) was synthesized using autogenic pressure reactions whereby a mixture of iron pentacarbonyl (Fe(CO)5) and hexane was heated at a rate of 10°/min from room temperature to 900°C and held for 1 hr. The structure of the samples was determined from XRD (X-ray Diffraction) analysis, and morphological properties were studied using TEM (Transmission Electron Microscopy). These results clearly shown that the Fe3O4 nanoparticles are highly crystalline and spherical in shape. The sizes measured were about 5-10nm. The Fe3C nanoparticles were also spherical in shape and the sizes measured were about 100-200nm.

Keywords: Magnetic nanoparticles, Drug delivery systems, Nanobiomagnets.

1 INTRODUCTION

The need to improved drug efficiency for both patient convenience and effective therapeutic uses has led to novel areas of research being explored and developed. For example, drug targeting to tumors or cancerous regions are especially needed due to the nonspecific toxicities exhibited by anti-cancer drugs that limits their use [1]. Magnetic nanoparticles used in bio-related applications are the result of a new class of magnetic materials called nanobiomagnets. This area of nanobiomagnetism combines nanomagnetism with medicine for uses in biological systems and processes. Nanomagnets have a promising future in biomedical applications due to their size compatibility with cells, viruses, and genes [2].

Magnetic materials exert attractive or repulsive forces on other materials and can be found in applications that range from refrigerator magnets to uses in biomedical applications. The unique potential and properties of magnetic materials can be realized alone, in the presence of external magnetic fields as well as with coatings for sustainability in destructive environments. The type of magnetic material used is dependent on the potential application and the environment in which the materials will be used. Currently, bio-applications are being used both in vivo and in vitro. In vivo, applications include drug delivery in which the magnetic particles are typically coated with a polymer and used with an external magnet to guide the drugs to a specific location. The directed movement of the system is to reduce the number of non-specific toxicities that exist with some drugs and to increase the amount of drug being released in an exact location. Hyperthermia, another application of magnetic particles, involves increasing the local levels of the body temperature above the normal temperature to kill the infected cells. NMR imagining uses magnetic particles to enhance the contrast between healthy and unhealthy tissue and to indicate the status of blood flow by the accumulation of the magnetic particles in certain tissue compositions and the endocytotic uptake of the particles. In vitro applications include separation and removal which involves functionalizing an object with a magnetic material and then introducing a magnet to separate the tagged material from the untagged [3]. There are many potential applications of magnetic materials, however whether the material should be used in its natural state, in the presence of an external magnetic field, or with a polymer coating depends on its application. Magnetic nanoparticles can be synthesized through various methods including solution precipitation, decomposition, sonochemical, and microwave heating [3-5]. For applications such as this project in which the particles will interact with an external magnetic field, the material must maintain a minimum magnetization even after it is inside the body, regardless of the synthesis method chosen. For magnetic drug carrier systems, the magnetization must be strong enough to respond to the magnetic field, and it must not retain its magnetization while out of the presence of the field. There are also size restrictions of the material; the material must be large enough (> 10 nm) to avoid rapid removal by the MPS (Mononuclear Phagocyte System), and small enough (< 5 μm) to not cause capillary blockage [6]. The materials reported in this paper were synthesized through thermal decomposition (autogenic pressure reactions) and sonochemical techniques. Thermal decomposition simply involves heating a organometallic precursor to temperatures high enough to break the bonds, decomposing the material and leaving the metallic material. This procedure has been reported in literature and is a relatively simple procedure [7]. Sonochemistry arises from acoustic cavitation phenomenon. During sonication, ultrasound waves create cavitations that form, grow and
burst, producing high temperature and pressure points that provide the ideal environment for a chemical reaction. Only nanosized materials are produced from this method due to the rapid cooling after the bursting of the bubble. Using these extreme conditions, Suslick and co-workers have prepared amorphous iron by the sonochemical decomposition of metal carbonyls in an alkane solvent [5]. We have also synthesized various magnetic nanomaterials from metal acetates and metal carbonyls [8-10].

Any material, including magnetic materials that have a potential in bio-related applications must be evaluated for biocompatibility and must meet the minimum requirements. Foreign materials that enter the body can induce an immediate response from the immune system to remove it from the body. Additional steps are required to reduce premature metabolism, immunological reactions, rapid excretion and specific and non specific toxicities of the material. One method to increase the biocompatibility is to coat the particles with a biocompatible material.

The goal of this research is to produce magnetic nanoparticles that can be used in drug carrier systems and in conjunction with an external magnetic field that directs the drugs to a specified location while in vivo. The requirements of such a system include size restrictions, minimum magnetization properties and biocompatibility. In this manuscript we are reporting the synthesis and characterization of iron carbide and iron oxide nanoparticles from sonochemical and thermal decomposition techniques.

2 EXPERIMENTAL SECTION

2.1 Synthesis of Fe3C

Fe3C was synthesized through thermal decomposition of a solution of 1.5 mL of iron pentacarbonyl (Fe(CO)5) and 2.0 mL of hexane; both the chemicals were purchased from Sigma Aldrich. The reaction mixture was added to a Swagelok 1”, 316 SS VCR connector body with matching 1” 316 SS VCR face seal fitting cap. The Swagelok vessel was tightened and placed in a glass tube in the center of a Barnstead/Thermolyne 21100 tube furnace. The heating was raised at a rate of 10ºC/min from room temperature to 900ºC, and held for 1 hr. Upon cooling, the vessel was cautiously open and the black powder obtained was characterized using XRD and TEM.

2.2 Synthesis of Fe3O4

Fe3O4 nanoparticles were synthesized using an ultrasonic irradiation of a mixture of 1.0 g of iron acetate (Fe(II)(CH3CO2)2) and 60 mL of PEG (Sigma Aldrich) using a high intensity ultrasonic horn (Ti-horn, 20kHz, 100W/cm2). The mixture was added to a stainless steel reaction vessel, connected to the horn and sonicated under an Ar atmosphere for 3 hrs at 50% power. Upon cooling to room temperature, the black solution was diluted in ethanol and centrifuged (Allegra 64R centrifuge) at 15,000 rpm at 5ºC. The precipitate was washed several times and dried overnight in a vacuum. The as-prepared sample was characterized using XRD and TEM.

2.3 Characterization

X-ray diffraction studies were carried out to determine the crystal structure and crystalline nature of the as-prepared nanoparticles. The diffraction patterns were collected from 10 to 80 degrees of 2θ at a scan speed of 2º/min. Morphological analysis was carried out using a JEOL-2010 microscope. The as-prepared powdered sample was dispersed in ethanol by sonication and dropped on a conventional carbon-coated grid and air dried.

3 RESULTS AND DISCUSSION

The X-ray diffraction patterns of the as prepared materials are shown in Figure 1. The powder X-ray pattern of Figure 1(a) clearly shows that the material is highly crystalline and all the peaks are assigned to the magnetite JCPDS file number 19-0629. No impurities were observed in this sample. Figure 1(b) also shows a highly crystalline material with an amorphous background. All the diffraction peaks matches very well with the Cohenite (Fe3C) JCPDS file number 35-0772.

TEM analysis was conducted to understand the morphology, surface coatings, and amorphous or crystalline nature of the particles. This information is crucial for drug delivery applications, it is necessary that they meet a minimum standard. TEM analysis of both the Fe3O4 and Fe3C samples shows the particles are crystalline and spherical in shape. Figure 2a represents the TEM picture of Fe3O4 particles. The micrograph clearly shows that the particles are relatively mono-dispersed with minimum agglomeration and the sizes measured are ~5-10nm. Figure 2(b) depicts the TEM micrograph of as-prepared iron carbide/carbon nanoparticles. These micrographs clearly show that the iron carbide nanoparticles are uniformly coated with an amorphous carbon layer. The particle sizes measured from the micrographs are ~100-200nm. We also found free amorphous carbon particles. These results are consistent with the X-ray results. The most important information is that the particle sizes observed fell within the critical limits for drug delivery applications. The particles sizes range between 100 – 200 nm. Also, a carbon coating appears to surround the entire surface of the iron core, thereby protecting it from potential oxidation encountered once in vivo, thereby yielding a more biocompatible material. It is predicted that the magnetization properties will be sufficient for the proposed application. While the ultimate goal is unrestricted iron carbide nanoparticles, it has not been determined whether the amorphous carbon will have an effect on the biocompatibility of the material.
4 CONCLUSIONS

- Sonochemical method has been confirmed as a method to synthesize Fe₃O₄ nanoparticles using iron (II) acetate and PEG.
- PEG proved to be a suitable reducing agent during ultrasound.
- Autogenic pressure reactions can be used to synthesize Fe₃C nanoparticles from Fe(CO)₅ and hexane.

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REFERENCES
