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Full Length Article

Development of new magnetic nanoparticles: Oligochitosan obtained by γ-rays and –coated Fe_3O_4 nanoparticles

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ABSTRACT

Oligochitosan (OCS) have been utilized as a potential bioactive material for improving food quality and human health. In this study, superparamagnetic iron oxide (Fe_3O_4) nanoparticles were originally coated with OCS irradiated by gamma rays for their possible biomedical applications. The formation of Fe_3O_4@OCS was characterized by Fourier transform infrared (FT-IR), X-ray diffraction patterns (XRD), energy dispersive X-ray spectroscopy (EDS) and thermogravimetric analysis (TGA). In addition, the superparamagnetic properties and sizes and morphologies of Fe_3O_4 and Fe_3O_4@OCS nanoparticles were demonstrated by vibrating sample magnetometer (VSM) and transmission electron microscopy (TEM), respectively. These results indicated that Fe_3O_4@OCS nanoparticles still maintained their superparamagnetic properties after polymeric coating, and were nearly spherical in shape with average diameter of 14.4 ± 0.31 nm, compared with 11.8 ± 0.52 nm of bare Fe_3O_4 nanoparticles, respectively. As a result, Fe_3O_4@OCS nanoparticles may serve as a promising platform for the development of new magnetic materials, which could be useful for biomedical applications.

1. Introduction

Iron oxide nanoparticles (NPs), Fe_3O_4 and γ- Fe_3O_4, is one of the most prominent features of magnetic nanoparticles (MNPs), has been widely used in biomedical applications such as *in vivo* magnetic resonance imagining, magnetic-mediated hyperthermia for cancer treatment and tissue-specific delivery of therapeutic agents [1–4]. In addition, if the size of magnetic structure is small enough MNPs may have superparamagnetic properties, becoming magnetized in the presence of a magnetic field and showing no magnetization without the presence of magnetic field [5,6]. However, MNPs tend to aggregate and form a larger clusters because of magnetic dipole–dipole attractions between NPs, which may limit their potential biomedical uses [7]. To overcome this drawback, the surface of MNPs were often modified with many materials such as silica, carbon, and biopolymers. These modifications are not only increase the chemical stability but also improve the biocompatibility of MNPs [8].

Chitosan (CTS), a biopolymer with several advantages including biocompatibility and biodegradability, can be used to covalently attach to biomolecules due to its amino/hydroxyl groups [9–13]. There is some research using CTS-coated MNPs for delivery of chemo- and bio-therapeutic agents [7,14,15]. Qu et al. developed poly(ethylene glycol) (PEG)-CTS-coated iron oxide NPs for 10-hydroxycamptothecin delivery. In detail, Fe_3O_4 NPs were used as cores, CTS was prepared as a polymeric shell and PEG chains were conjugated to CTS-Fe_3O_4 NPs for improving the biocompatibility for entire system (PEG-CTS- Fe_3O_4 NPs). This study demonstrated the potential of PEG-CTS-Fe_3O_4 NPs as stable magnetic nanocarriers for the treatment of cancer [7]. Additionally, Arami et al. designed and developed novel MNPs for siRNA delivery into human breast cancer MCF-7 and leukemia K562 (K562) cells. The obtained MNPs containing three different layers, PEG-lactase polymer (PEG-LAC), CTS, and polyethyleneimine (PEI) were successfully synthesized and should be actively considered as potential MNPs for siRNA

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delivery into the cells [16]. Despite the proven effectiveness of the surface CTS-coated MNPs, such NPs are likely to be adsorbed or scattered on normal tissue during blood circulation owing to the good muco- and bio-adhensive properties of CTS [7]. Moreover, different characteristic of CTS, poor aqueous solubility limits its applications in food and biomedicine [15,17]. To solve these challenges, the synthetic process of these CTS-coated MNPs requires many steps to produce a desired product.

Unlike CTS, its derivatives like oligochitosan (OCS) is highly water-soluble caused by its shorter chain lengths and free amino groups in D-glucosamine units. It is well known as a promising materials for improved human health such as to lower blood cholesterol, to lower high blood pressure, to protect against infections, and to enhance antitumor properties [18]. For instance, Bae et al. introduced CTS oligosaccharide-stabilized ferromagnetic iron oxide nanocubes (Chito-FIONs) as an effective heat nanomediator for cancer hyperthermia. These Chito-FIONs showed outstanding antitumor efficacy on an animal tumor model without any significant toxicity [19]. Shukla et al. synthesized CTS oligosaccharide coated iron oxide NPs (CSO-INPs) to evaluate the effect of surface coating on the stability and toxicity of NPs. Synthesized NPs were spherical, well-dispersed and stable at different pH values, indicating their suitability for biomedical and environmental applications [20]. Furthermore, Zhu et al. prepared and evaluated NPs composed galatosylated CTS oligosaccharide (Gal-CSO) and adenosine triphosphate (ATP) (Gal-CSO/ATP) for hepatocellular carcinoma cell-specific uptake. The obtained results demonstrated that the Gal-SCO/ATP could be a promising candidate for intracellular drug delivery nanocarrier in hepatocellular carcinoma cell targeting [21]. Several different approaches such as chemical, enzymatic and gamma-ray methods have been used to prepare OCS [22–24]. Amongst these methods, chemical hydrolysis is more frequently used, low cost and effective method, but concentrated acidic waste generated by this method will disperse in the environment. Besides, enzymatic method requires multi-steps, especially preparation of enzymes and purification of products. Therefore, this method is unsuitable for the large-scale production of OCS [25]. In comparison with gamma radiation, one of the most powerful techniques for producing OCS, this method has numerous advantages, including no chemical used, free from chemicals leftover and products used without further purification [22,23].

In this study, superparamagnetic iron oxide (Fe_3O_4) NPs were first coated with OCS produced by gamma rays for their potential biomedical applications. At first we prepared Fe_3O_4 NPs by coprecipitation method and then coated them with OCS (Fe_3O_4@OCS NPs). Next, we evaluated the characteristics of Fe_3O_4@OCS NPs by several methods, Fourier transform infrared (FT-IR), X-ray diffraction patterns (XRD), energy dispersive X-ray spectroscopy (EDS), thermogravimetric analysis (TGA), vibrating sample magnetometer (VSM) and transmission electron microscopy (TEM). This study is expected to provide insights into the biomedical use of Fe_3O_4@OCS NPs.

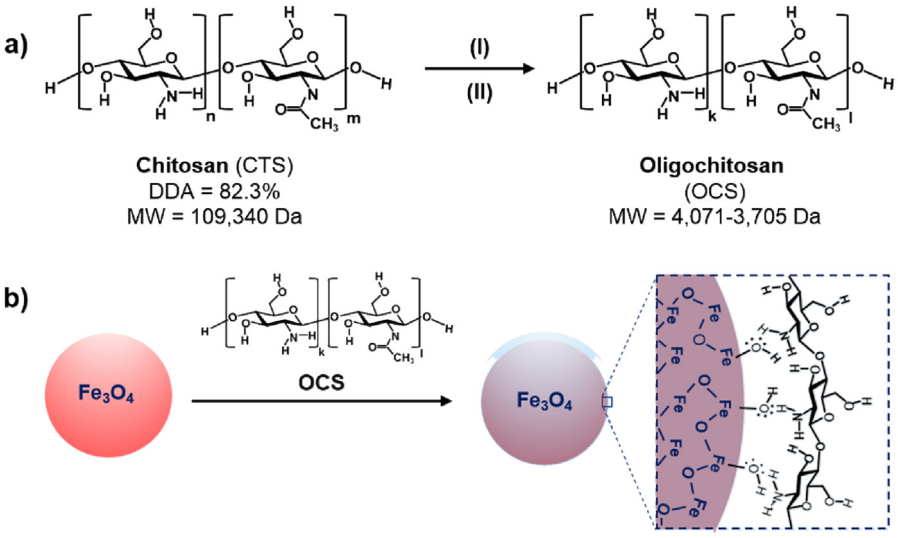
2. Materials and methods

2.1. Materials

CTS made from crab shell chitin with degree of deacetylation of 82.3% and Mw of 109,340 was supplied by Research and Development Center for Radiation Technology (VINAGAMA, 202A Street 11, Linh Xuan Ward, Thu Duc, Ho Chi Minh City). H_2O_2 30% (d: 1.11 g/mL), Iron (III) chloride hexahydrate ($FeCl_3{\cdot}6H_2O$, 97%), iron (II) chloride tetrahydrate ($FeCl_2{\cdot}4H_2O$, 99%) and tetrahydrofuran (THF) were purchased from Merck (Germany). Amonium Hydroxide (28–30%) was obtained from Tianjin Bodi Chemical Co., Ltd. (China). All chemicals and solvents were of highest analytical grade and used without further purification.

2.2. Preparation of OCS

OCS was prepared using two main steps, including heterogeneous degradation of CTS by oxidation of H_2O_2 and homogeneous degradation of CTS by radiation γ/H_2O_2 (Scheme 1a). In detail, CTS in flake form was soaked in 2% (w/v) H_2O_2 solution for 24 h and the mixture was then poured through a cloth filter and washed with deH_2O several times. Thereafter, the sample was dissolved in 1% (w/v) lactic acid, which was filtered through a stainless steel mesh, neutralized with 5% (v/v) NH_4OH solution, and later ethyl alcohol was slowly added into the mixture under stirring. The precipitated CTS was obtained by filtering, washing with alcohol several times and drying in an oven at 60 °C [24]. The obtained CTS was continually degraded by radiation γ/H_2O_2. First, 2% (w/v) lactic acid was added into the obtained CTS solution which was soaked in



Scheme 1. Schematic illustration of (a) the OCS formation via two steps: (I) heterogeneous degradation of CTS by oxidation of H_2O_2 and (II) homogeneous degradation of CTS by radiation γ/H_2O_2, and (b) the formation of Fe_3O_4@OCS.