Journal of Physics and Chemistry of Solids 148 (2021) 109749

Contents lists available at ScienceDirect

Journal of Physics and Chemistry of Solids

journal homepage: http://www.elsevier.com/locate/jpcs

Chitosan coated magnetic nanoparticles as carriers of anticancer drug Telmisartan: pH-responsive controlled drug release and cytotoxicity studies

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ARTICLE INFO

Keywords:
Magnetic nanoparticle
Chitosan
Controlled drug release
Targeted drug delivery
Telmisartan

ABSTRACT

Chitosan, a natural, hydrophilic and biodegradable polymer was grafted on Fe_3O_4 magnetic nanoparticles (MNPs) and used as a carrier of poorly water-soluble anticancer drug Telmisartan (TEL). The characteristics of MNPs and chitosan coated MNPs (MNP-CS) were determined by using X-ray diffraction, field emission scanning electron microscope, transmission electron microscope, vibrating sample magnetometer, and BET surface area analyzer. The chitosan coating of MNPs was validated by Fourier transform infrared spectroscopy (FTIR) and thermal gravimetric analysis. The drug was loaded on MNP-CS through an amide bond between amino groups of chitosan and carboxylic groups of TEL. The drug loading capacity of ~50% was obtained due to the large BET surface area (134 m^2/g) of mesoporous MNP-CS. Drug loaded MNP-CS (MNP–CS–TEL) showed pH-responsive controlled release characteristics. The MNP–CS–TEL showed dose dependent cytotoxicity towards PC-3 human prostate cancer cells. The results demonstrated the significant antitumor activity of designed nanoformulation.

1. Introduction

In conventional cancer therapy, along with rapidly dividing cancerous cells, anticancer drugs also attack healthy cells [1]. Advanced cancer treatment relies on the optimum choice of carriers for targeted drug delivery (TDD) and controlled drug release [2,3]. Many chemotherapeutic agents are delivered by TDD to enhance the therapeutic efficacy of drugs [4–8]. For TDD, various kinds of drug carriers have been explored, including gold nanoparticles, silica nanoparticles, polymeric micelles, and magnetic nanoparticles (MNPs) [9–13]. The controlled release of drugs from MNPs has received considerable attention. MNPs are biocompatible and colloidally stable nanocarriers [14,15]. MNPs possess unique magnetic properties and can be translocated at the targeted site under the influence of the magnetic field. The drugs can be released in a cancerous environment in a controlled manner under the influence of pH [16], temperature [17], and certain enzymes [18–20]. Magnetic nanoparticles are widely explored in biomedical and pharmaceutical applications such as magnetic resonance imaging [21,22], biosensors [23], tissue repair and imaging [24], cancer therapy [25], targeted drug delivery [26], hyperthermia [27], and antibacterial activities [28–30]. MNPs have also been used as photoluminescence [31] and photocatalytic degradation of dyes [32].

To load the MNPs with an anticancer drug, the surface of the MNPs needs to be functionalized with small molecules [33] or polymers [34,35]. For this various organic and inorganic compounds have been grafted on MNPs such as alginate [36–40], polyethylene glycol (PEG) [41,42], polyvinyl alcohol (PVA) [43,44], dextran, chitosan [45], silica [46–48], metal-organic coating [49–51], and metal oxides or sulfides [52–54]. Among these, chitosan is a natural polyaminosaccharide which possess distinct chemical and biological properties [55–59]. In its linear polyglucosamine chains, chitosan has reactive amino and hydroxyl groups, required for chemical modifications [58,60–62]. Chitosan is

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https://doi.org/10.1016/j.jpcs.2020.109749
Received 16 July 2020; Accepted 6 September 2020
Available online 8 September 2020
0022-3697/