Functionalization of Magnetic Hollow Spheres With (3-Aminopropyl)Triethoxysilane for Controlled Drug Release

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Direct functionalization strategy has been employed to modify the surface of the magnetic hollow spheres (MHS) with (3-aminopropyl)triethoxysilane (APTES) for controlled drug release. The MHS were prepared by the solvothermal method and characterized by X-ray diffraction, field emission scanning electron microscopy (FE-SEM), Fourier transform infrared spectroscopy, and vibrating sample magnetometer. The FE-SEM study shows that MHS have a size of ~200 nm and are made up of smaller nanoparticles (NPs) having average size of ~20–25 nm. MHS exhibits a superparamagnetic behavior with a saturation magnetization of 74 emu/g at room temperature. The direct functionalization of MHS with APTES provided an efficient loading of model anticancer drug Camptothecin (CPT). The drug release study performed at pH of 7.4 showed 30% of CPT release in a controlled way after 4 h.

Index Terms— **Functionalization, magnetic hollow spheres (MHS), magnetic nanoparticles (MNPs), targeted drug delivery.**

I. Introduction

A NUMBER of advanced drug delivery systems (DDS) have been developed to improve the therapeutic efficacy and bioavailability of poorly water-soluble drugs [1]–[6]. Presently, many micro and nanoscale organic and inorganic drug carriers such as micelles, liposomes, mesoporous particles, polymers, metal and metal oxide nanoparticles (NPs) have been reported [3]–[9]. However, many of these systems have biocompatibility issues, related to the toxicity and strong interaction with serum proteins, which causes occasional rapid blood clearance and hepatic removal [10]. Among the variety of nanodrug carriers, magnetic NPs (MNPs) are most important due to their intrinsic magnetic properties at nanoscale, better stability in physiological fluids, and lower toxicity profile toward normal cells. The unique feature of MNPs is that they can be translocated at the target site by an external magnetic field, which can be employed for the targeted DDS [11]–[13]. Magnetic hollow spheres (MHS) can be the most promising potential candidate for the development of efficient DDS. The higher outer surface area along with the inner accessible voids within hollow spheres can provide higher loading capacity of the drug on the outer and inner surfaces of MHS [14].

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To link the drug or any biological entity to MNPs, appropriate surface modification of MNPs is required. The various polymer coatings such as polyethylene glycol [15]–[17], dextran [18]–[20], and chitosan [21], [22] have been routinely explored for surface modifications of MNPs. MNP-silica core–shell structure has also been widely used as a drug carrier system [1], [3]–[6], [21], [22]. However, such coating of MNPs with a nonmagnetic material may lead to decrease in its magnetic properties, limited drug storage capacity, and time-consuming synthesis protocols, which hinder them from being high-performance carriers in targeted DDS [1], [5], [18], [23]. (3-aminopropyl)triethoxysilane (APTES) is the most commonly used alkoxysilane linker for surface modification of MNPs due to its terminal amino groups. Generally, to link APTES the silica-coated MNPs or mesoporous silica NPs have been used [24], [25]. We have adopted a strategy to directly functionalize MHS with APTES, which avoids the use of nonmagnetic coatings and retains its magnetization. The direct functionalization of APTES on MHS offers several advantages over silica-coated MNPs. Direct linking of APTES can weaken the interparticle magnetic interaction and prevent the particle agglomeration providing increased colloidal stability. It also provides amino functional groups, which can be used for the bonding of different bioactive complexes, drug or anti-body [26], [27]. Camptothecin (CPT) is a water-insoluble anti-tumor drug isolated from the oriental tree *Camptotheca accuminata* [28]. CPT is well known for its anti-cancerous activity against different human cancers by inhibition of cellular enzyme deoxyribonuclic acid