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LETTER

Facile synthesis of β-cyclodextrin-grafted solid silica nanoparticles

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Abstract

In this work, a simple and reliable method for the synthesis of β-cyclodextrin (β-CD)–grafted silica nanoparticles (SiNPs) is developed. The synthetic protocol included postsynthesis functionalization of silica nanoparticles with aminopropyl trimethoxysilane (APTES) followed by the condensation of the amino groups with imidazole carbamate ester of β-CD. The activated β-CD (carbamate ester) was prepared by reacting it with carbonyldiimidazole (CDI). The grafting of (β-CD) on SiNPs was confirmed by ATIR-IR, DLS, and TGA analyses. The method developed can be easily reproduced with any other oxide nanoparticles for the preparation of β-CD-grafted nanoparticles.

KEYWORDS

β-cyclodextrin, grafting, hybrid nanoparticles, silica nanoparticles, surface modification

1 | INTRODUCTION

The cyclodextrins (CDs) are cyclic oligosaccharides made of 1,4 linked glucopyranose subunits.[1] The glucopyranose subunits are joined together by oxygen bridges and this structure forms hydrophilic outer surface and lipophilic central cavity.[2] The main characteristic property of CDs is their ability to form inclusion complexes with several compounds especially with drug molecules.[3] The drugs which are insoluble in water when complexed inside the hydrophobic cavity of CDs they form a soluble complex hence CDs are used to improve the solubility of drugs.[4] In addition, the CDs are also used extensively in various other applications such as food, cosmetics, and chromatography.[5] There are three main cyclodextrins, namely α-, β-, and γ-cyclodextrin. Out of these, the β-CD is the most common CD in pharmaceutical formulations, and it is the most studied CD for drug delivery applications.

The grafting of β-CD molecules on the surface of nanoparticles produces hybrid core-shell nanomaterial which combines the inclusion complex formation property of β-CD and the intrinsic property of the nanoparticle on which it is grafted. Therefore, a continued interest to prepare β-CD-grafted nanoparticles is observed. Some representative examples of the β-CD-grafted materials include the synthesis of β-CD-grafted magnetic nanoparticles for drug delivery,[6,7] β-CD-grafted TiO_2 nanoparticles for improved dispersability in polymer nanocomposites,[8] β-CD-grafted barium titaniate nanoparticles for improved colloidal or dispersion stability,[9] and β-CD-grafted chitosan nanoparticles for drug delivery.[7,10] The previous works reported in the literature about grafting of β-CDs on various nanoparticles used multistep and complicated synthetic protocols. So, there is a need to develop new, fast, and efficient method for rapid and reliable grafting of β-CDs on nanoparticles. For this purpose, in the present work, a relatively simple, short, and reliable method for grafting of β-CD on silica nanoparticles by preparing the carbamate ester of β-CD and its grafting on amino-functionalized silica nanoparticles (SiNPs) is developed. The importance of the work lies in the fact that the synthetic protocol developed can be easily reproduced with any other oxide nanomaterials to prepare β-CD-grafted nanoparticles.

2 | EXPERIMENTAL

2.1 | Materials

The chemical reagents and solvents β-cyclodextrin, carbonydiimidazole, (3-Aminopropyl)triethoxysilane (APTES), cyclohexane, propylamine, and dimethylformamide were purchased from Sigma-Aldrich and used as received. Commercially available silicon dioxide powder (referred as SiNPs) having hydrodynamic diameter of 74 nm were used as the starting material.

2.2 | Instruments and methods

The ATR-FTIR spectra were recorded with Perkin Elmer spectrometer operated at room temperature with nominal resolution of detector of 2 cm^{-1}. An advanced ATR baseline correction was applied to all spectra in the range of 4000 to 600 cm^{-1} region. Thermogravimetric analyses (TGA) were carried out on a Q500 model from TA Instruments by heating samples in alumina pans at a rate of 10°C/min up to 600°C in a nitrogen flow and from 600 to 800°C in air. The hydrodynamic diameters of AgNPs were measured using nano particle analyzer Nanoplus (Particulate systems Norcross, GA, USA) instrument. A 0.1 w/v suspensions of the particles were prepared and sonicated for at least 30 minutes before the analysis. The transmission electron microscopy (TEM) images were taken with a JEOL 2011 instrument operating at 300 kV and equipped with a LaB6 filament.

2.3 | Synthesis of amino-functionalized SiNPs

SiNPs (2 g) were taken in a single-neck round-bottom flask, and to it, 40 ml of cyclohexane was added, and the suspension was stirred for 5 minutes. Then, aminopropyl trimethoxysilane (APTES) 1000 microliters was added to the suspension followed by 100 microliters of *n*-propylamine. The suspension in the flask was stirred at room temperature for 30 minutes, then at 60°C for another 30 minutes. The amino-functionalized SiNPs were recovered by centrifugation and washed three times with acetone to remove nongrafted MPS and other impurities. Each time, the particles were separated from the liquid by centrifugation. The particles were then dried in oven at 40°C for several hours.

2.4 | Synthesis of β-CD-grafted SiNPs

β-CD (1 g, 0.88 mmol) was dissolved in 10 ml of dry DMF, to it, 0.143 g of carbonyldiimidazole (CDI, 1 mole equivalent to β-CD) was added, and the solution was kept under magnetic stirring at 20°C for 2 hours. A suspension of 1 g of amino-fucntionalized silica nanoparticles was prepared in 5 ml dry DMF. This suspension of particles was added drop by drop to the solution of activated β-CD. The condensation reaction was continued for 12 hours at 20°C to 25°C. At the end of the reaction, the particles were recovered by centrifugation and washed two times with fresh DMSO to remove all nongrafted β-CD. Finally, the particles were washed two times with acetone and then dried in oven at 40°C to 50°C for several hours.

3 | RESULTS AND DISCUSSION

The synthetic protocol followed for the preparation of β-CD-grafted SiNPs is shown in Figure 1. The postsynthesis surface functionalization of SiNPs with APTES was carried out by using the alkoxysilane grafting protocol (Figure 1 A). On the other hand, β-CD was reacted with carbonyldiimidazole (CDI) in DMF solvent to prepare the carbamate ester of β-CD with CDI (Figure 1B). The amino-functionalized SiNPs were then condensed with carbamate ester of β-CD to obtain the β-CD-grafted nanoparticles (Figure 1C). The grafting of β-CD on the surface of nanoparticles was confirmed by ATR-IR spectroscopy. The IR spectra of all samples are shown in Figure 2A (A-D) while zoom of the upper region is showed in Figure 2B). The important spectrum D showed the combined peaks of β-CD and silica framework from the nanoparticles. The spectrum C of β-CD showed the characteristic peaks at 3290 to 3400 cm^{-1} due to the O—H group stretching and the peak at 2890 cm^{-1} due to C—H asymmetric/symmetric stretching. In addition, the peaks at 1144 and 1039 cm^{-1} were due to C—H overtone stretching, and the main peak at 1081 cm^{-1} was due to C—O

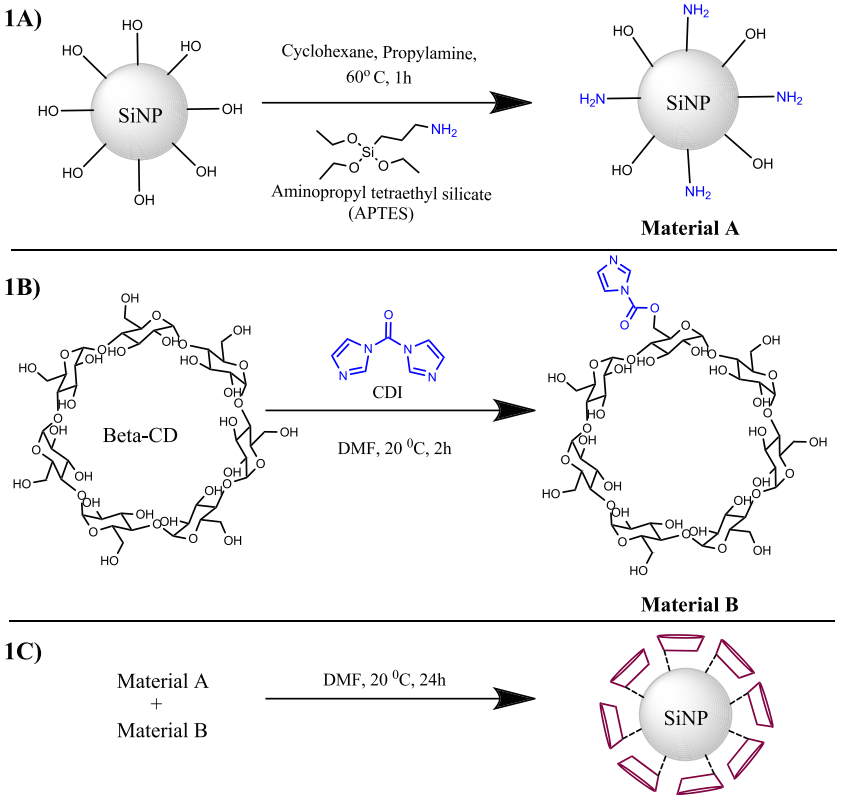

FIGURE 1 Synthesis protocol for the preparation of β-CD-grafted SiNPs

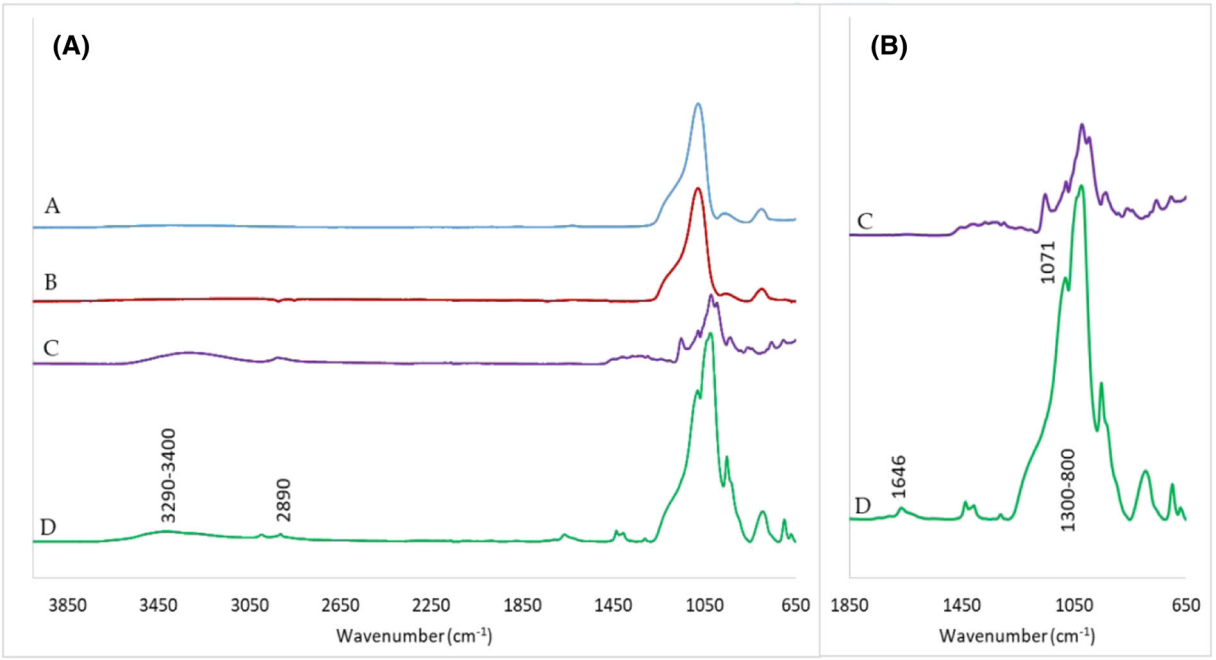

FIGURE 2 A, ATR-FTIR spectra of (A) bare, (B) amino-functionalized, (C) β-CD, and (D) β-CD-grafted SiNPs. B, Zoom of spectra C and D

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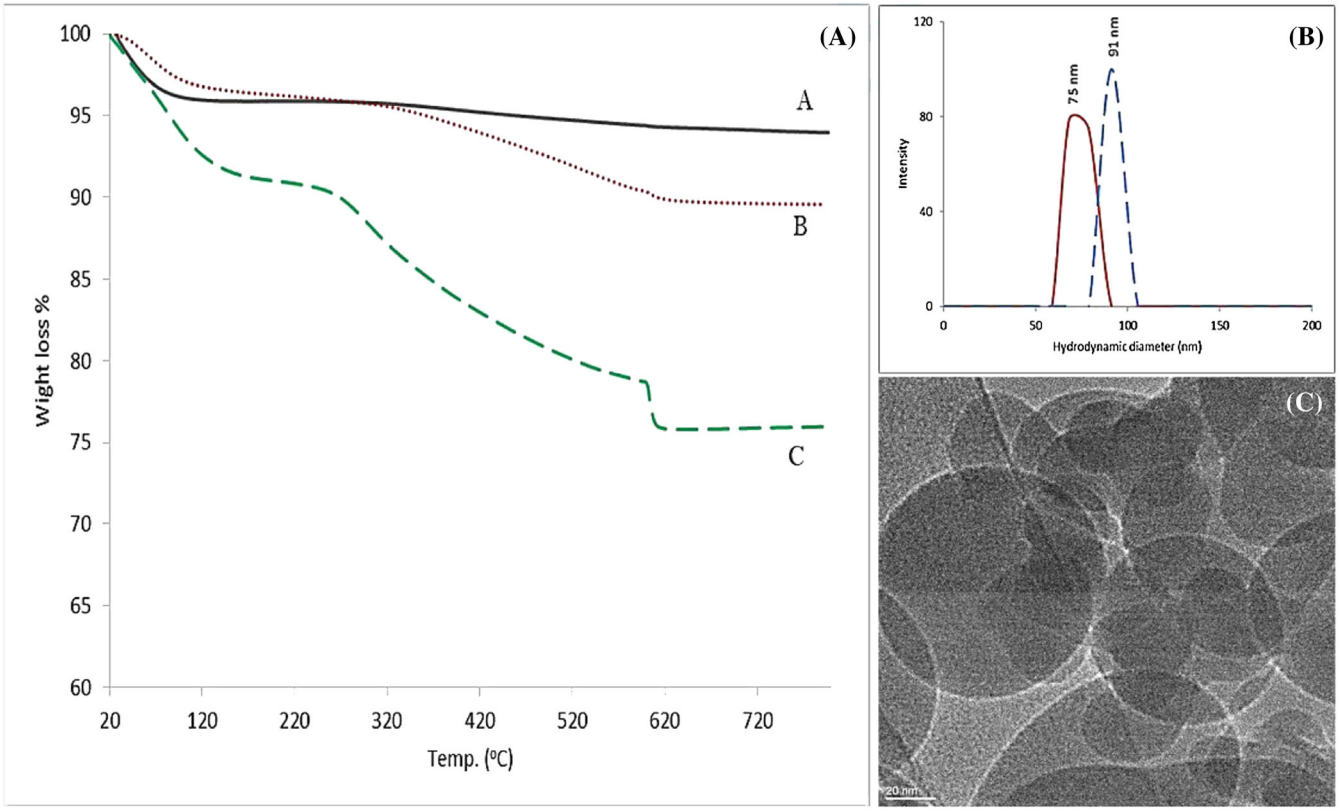

FIGURE 3 **A**) TGA curves of (A) bare, (B) amino-functionalized, and (C) β-CD-grafted SiNPs. **B**) Hydrodynamic diameter of amino-functionalized-SiNPs (solid line) and β-CD-grafted SiNPs (dashed line). C, TEM image of the particles.

stretching.[11] The FTIR spectrum of the β-CD-grafted SiNPs showed intense peak between 1300 and 800 cm^{-1} due to the inter-intra tetrahedral fundamental vibrational modes of the silica framework (Si—O—Si) which was also clearly visible in the bare SiNPs spectrum A.[12,13] In addition to the peaks of silica, the spectrum D also showed the peaks attributed to C═O stretching of the amide group at 1646 cm^{-1} and the peak due to C—O stretching at 1071 cm^{-1}.[14,15]

The successful grafting of the β-CD on the surface of the SiNPs was further confirmed by dynamic light scattering (DLS) and thermogravimetric analysis (TGA). The quantitative grafting of β-CD on the particles was calculated from the results of TGA analysis. As seen in Figure 3A, the bare SiNPs showed 6% weight loss (Curve A) upon programmed heating up to 800°C mainly due to evaporation of the adsorbed water. The percentage weight loss of the amino (APTES)–functionalized SiNPs sample (Curve B) was 11%, indicating 5% by weight grafting of the APTES on the bare SiNPs. While the percentage weight loss of the β-CD-grafted SiNPs (Curve C) was 24% which indicated 13% grafting by weight of the β-CD on the amino-functionalized SiNPs. The average hydrodynamic diameter (HD) of the bare SiNPs was 74 nm, which upon APTES grafting, was increased to 75 nm. Instead, upon β-CD-grafting, the HD of the particles was further increased to 91 nm (Figure 3). The polydispersity index values for APTES-grafted and β-CD-grafted SiNPs were 0.39 and 0.26, respectively. This indicated the increase in colloidal stability of the SiNPs upon β-CD grafting due the formation of the shell of β-CD molecules (refer to Figure 1) around the particles which minimizes the particle-particle interactions. The TEM image of the hybrid particles is shown in Figure 3C in which discrete SiNPs with spherical shapes can be seen. The alkoxysilane (APTES) grafting process to prepare the amino-functionalized nanoparticles and their subsequent condensation with carbamate ester of β-CD with CDI are simple and reproducible steps and involves relatively simple organic chemistry to prepare β-CD-grafted nanomaterials with various potential applications.

4 | CONCLUSION

In conclusion, a simple and reliable method for the preparation of β-CD grafted solid SiNPs is developed. The grafting of the β-CD on the surface of the particles was confirmed by using three main instrumental characterization techniques,

viz IR, DLS, and TGA. The results confirmed the successful grafting of the β-CD on the SiNPs. This method can be easily reproduced with various oxide nanoparticles for the preparation of β-CD-grafted nanoparticles.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

AUTHOR CONTRIBUTION STATEMENT

All authors contributed to the work.

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