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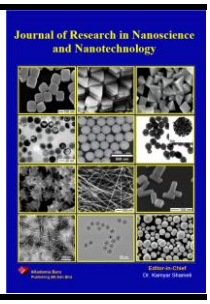

Facile Fabrication of Polysaccharide Nanocomposites Using Ionic Gelation Method

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ABSTRACT

Polysaccharide-based nanomaterials with significant biocompatibility and physiochemical features have been widely analyzed in modern biomedical nanotechnology. Chitosan-coating is an advantageous procedure to provide several pharmacological characteristics of chitosan on the reinforcement. Here, we fabricated polysaccharide nanocomposites using the facile ionic gelation method and sodium tripolyphosphate (TPP) cross-linker. The polysaccharide nanocomposites comprised natural cellulose and chitosan as reinforcement and coating agents, respectively. From the image of the scanning electron microscope, the nanocomposites indicated almost spherical dimensions with sizes below 60 nm. Results from X-ray powder diffraction and Fourier-transform infrared spectroscopy showed multifunctional properties of the nanocomposites related to both cellulose and chitosan. Therefore, the ionic gelation method is potentially appropriate to synthesize the polysaccharide nanocomposites for medically-related applications.

Keywords:
Polysaccharide; Chitosan; Ionic Gelation Method; Nanocomposites

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1. Introduction

In biomedical application, the popular polymers as biocompatible coating agents are polyvinyl pyrrolidine (PVP) polyvinyl alcohol (PVA), polyethylene glycol (PEG), polyethylenimine (PEI), gelatin, starch, albumin, alginate, chitosan, and natural cellulose [1-3]. Chitosan is an attractive polysaccharide and has a production above 100 million tons, annually [4]. It might be derived from abundant natural biopolymer chitin and is a green-based amino-polysaccharide containing -(1-4)-linked d-glucosamine and *N*-acetyld-glucosamine in deacetylated and acetylated form, respectively [5]. The most abundant polymer on earth is natural cellulose, which can be distributed throughout nature in plants, animals, algae, fungi, and minerals. However, the major source of cellulose is plant

fiber [6]. Cellulose contributes approximately 40% to the carbon fraction in plants, serving as structuring element within the complex architecture of their cell walls. Natural cellulose and nanocellulose based materials have been applied widely in therapeutic excipients, which carboxymethyl cellulose, methyl cellulose, ethyl cellulose, and many different cellulose are also analyzed for oral, topical, implantation, and injectable forms. Properties, including crystallinity, surface chemical reactivity, less toxicity, proper mechanical strength, rheological and barrier characteristics and proper specific surface area. Therefore, these fabulous characteristics can lead to obtain structured products of ''nanoenabled'' as well as ''nano-enhanced'' with diverse applications such as drug delivery vehicles for anticancer treatment, advanced composite materials, and rheological modifier [7]. Of this, several studies have aimed to pinpoint synthesis and structural analysis of various nanoparticles and nanocelluloses for biomedical applications [8-13].

In order to produce layer-by-layer chitosan-based nanocomplex and nanoparticles (NPs), ionic gelation approach as an organic solvent-free solution, quick, and facile method indicated high efficiency and low toxicity [14]. This approach uses the phosphate groups of sodium tripolyphosphate (TPP) as a physical crosslinking agent, which has more benefits compared to other methods such as emulsifying and chemical crosslinking agents. For example, this method has less toxicity to the organs and no destruction to the structure of the loaded-drugs in chitosan NPs. Polysaccharide blends are vital to construct advanced complexes in numerous applications [15]. The blend of degradable polymers can merge the desirable properties of the polymers [16]. In addition, the crosslinking procedure might considerably improve physiochemical characteristics of the polysaccharide nanocomplex [17]. In biomedical applications, the most common antimicrobial coating material on cellulose is currently chitosan for composite fabrication with suitable biodegradability and water-rich structures [18]. Chitosan coating on natural cellulose is possibly facile since both polysaccharides have a very similar structure. In addition, the complex of chitosan and natural cellulose has intermolecular interactions, because of H-bonds and Van der Waals forces [19]. Most significantly, chitosan-cellulose nanocomplex or composites have shown a great swelling and water absorption capability. Thus, the biocompatibility, biodegradability, and physiochemical characteristics of cellulose and also chitosan can be modified when cellulose as a matrix and chitosan as a coater contributed in synthesis of polysaccharide nanocomposites. For biomedical application, the coating agent such as polysaccharide may decrease a blockage in the blood vessels. Particularly, high colloidal stability polysaccharide-based therapeutic agent can improve blood circulation to be delivered to targeted tissue.

In this present study, polysaccharide system of chitosan-cellulose nanocomposites was fabricated by the ionic gelation method and using TPP as a cross-linker. The physiochemical properties of the synthesized polysaccharide nanocomposites were evaluated by X-ray powder diffraction (XRD), Fourier-transform infrared spectroscopy (FTIR), and scanning electron microscopy (SEM).

2. Materials and Methods

2.1. Materials

Acetic acid glacial (CH_3COOH) (98%), chitosan (low molecular weight, 190,000–310,000 degree of acetylation), Tween-80 and TPP were all purchased from Sigma Aldrich (St. Louis, MO, USA). 5FU, 99%, 5-Fluoro-2,4(1H,3H)-pyrimidinedione (ACD CODE MFC D00006018) with a molecular weight of 130.08 g/mol was purchased from ACROS ORGANICS part of Thermo Fisher Scientific, Branchburg, NJ, USA. The chemicals were used without further purification. All glassware used was washed with distilled water and dried before used.

2.2. Synthesis of Polysaccharide Nanocomposites of Chitosan-Cellulose (C-C NCs)

Fabrication of rice straw cellulose was explained earlier in our previously published studies [20, 21]. Ionic gelation technique was used to synthesize layer-by-layer of polysaccharide system of chitosan-cellulose nanocomposites (C-C NCs) [22]. First, a 250 mL beakers contained 80 mL mixture solution of 1.0% acetic acid and 0.250 g of chitosan powder (low molecular weight). Then, 2% (*v*/*v*) of Tween-80 as a stabilizer was respectively added to each solution and mixed gently for 45 min to obtain the chitosan solutions. After that, 0.125 g cellulose was mixed with the prepared chitosan solution and homogenized vigorously at 9000 rpm for around 7 min. The 0.50 g of TPP cross-linker was dissolved in 15 mL deionized water and added dropwise to the cellulose chitosan solution with the continuously vigorous stirring of the homogenizer for another 45 min. The mixture solution was washed with distilled water and centrifuged three times at 2500 rpm for 7 min at 25 °C. Finally, the C-C NCs sample was freeze-dried for 16 h and stored at −4 °C for further analysis.

2.3. Characterization

XRD (Philips, X'pert, Cu Ka) at an ambient condition was used to evaluate the structure of the samples. The sample was compressed between two smooth glass films and the XRD analysis was carried out in dispersion 2 angles of 5°– 80° at a step size of 0.02° with 2 s/step as scanning rate using a voltage of 45 kV, a Ni-filtered Cu K radiation (=1.5406 A)° and a filament current of 40 mA. FTIR spectroscopy (ThermoNicolet, Waltham) determined the chemical and super-molecular structural analysis of the samples under an ambient condition. First, crushing and mixing of the sample with KBr at a ratio of 1:100 *w*/*w* to prepare a transparent pellet and the spectra of the plate was evaluated under a transmittance mode in a range between 4000 cm^{-1} to 400 cm^{-1} with a 4 cm^{-1} resolution and an accumulation of 128 scans. The SEM images were taken via using an Electro-Scan SEM instrument (model JSM 7600 F SEM). A low-acceleration voltage (10 kV) was used to prevent the degradation of the sample.

3. Results and Discussion

The ratio of the components in the polysaccharide composites is a significant concern to obtain desirable size and physiochemical properties. The ratio between the chitosan powders to TPP cross-linker was optimized as 1:2 (*v*/*v*). We use cellulose and chitosan with the ratio of 1:2 to fabricate the polysaccharide composites. In a spate research, 2.0% (*w*/*v*) chitosan, 1.2% (*w*/*v*) carboxymethyl-cellulose, and 1.0% (*w*/*v*) scleroglucan were used to synthesize a nanocomposite hydrogels that the SEM images of this sample was not spherical with uniform structure[23]. Furthermore, the chitosan did not display uniform coating structure on the carboxymethyl-cellulose, possibly because of unsuitable ratio between the cellulose, scleroglucan, and chitosan. Investigations by Samy et al. (2020) used the 1:1 ratio of chitosan and cellulose and epichlorohydrin cross-linker that this composite indicated SEM size more than 100 nm [24]. In our research, thus, the effective synthesis of C-C NCs with spherical size below 60 nm was due to blending the appropriate ratio of chitosan coating agent and cellulose matrix with vigorous homogenizing, which dropwise adding TPP advantageously *acted as* a crosslinking agent.

3.1. X-ray Powder Diffraction Analysis

Figure 1 shows the XRD results of C-C NCs. As the sample containing natural cellulose, it exhibited the diffraction peaks approximately at 2θ = 15°, 22° and 35°, similar to the normal cellulose-I structure [25]. The highest crystalline area was shown at 22° with a sharp intensity, showing the

sufficient crystallinity of cellulose. C-C NCs indicated a pattern related to both cellulose reinforcement and chitosan coater with peaks approximately at 2θ = 22° and 15°, which is in a good agreement with the JCPDS card no. 04-0784. Noticeably, the peak at 15° is an overlapping peak between cellulose and chitosan. The C-C NCs showed a decrease crystallinity peaks, due to presence of the TPP cross-linker to abate the crystallinity. The XRD results could show the successful fabrication of polysaccharide nanocomposites containing cellulose reinforcement and chitosan coating agent.

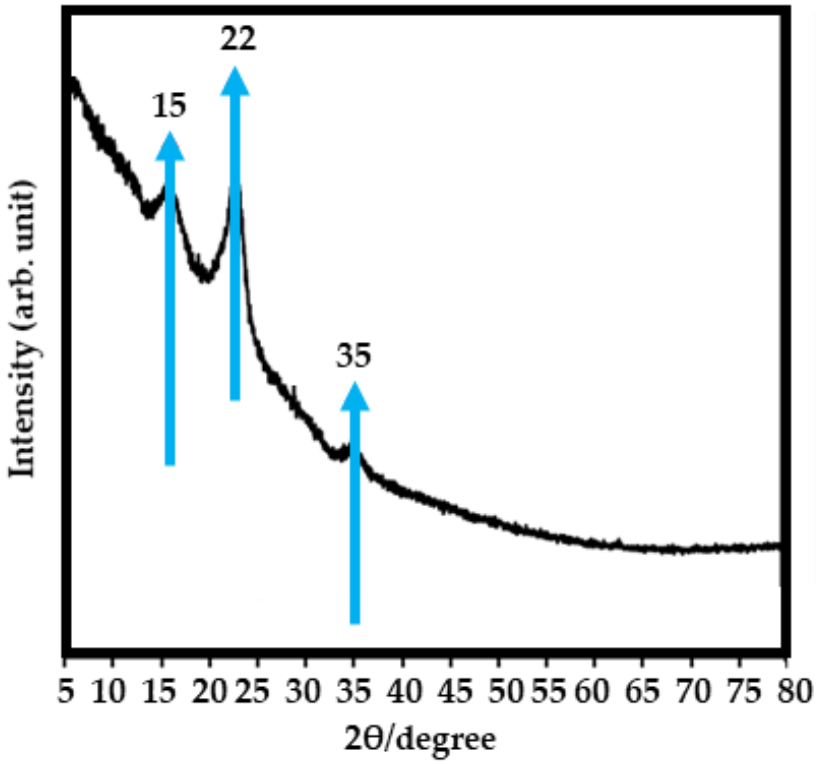

Figure 1. XRD spectra of polysaccharide nanocomposites of C-C NCs.

3.2. Fourier-Transform Infrared Spectroscopy

The FTIR findings of C-C NCs is indicated in Figure 2, showing contribution of OH or NH and changes in the sugar ring, Van der Waals forces, dipole moments and hydrogen bonds [26]. Furthermore, the CO stretching vibration at 1628 cm^{-1} could be owed to an appropriate interaction between the drug and its nano-carrier. It stated that the amine groups of chitosan with carbonyl groups of natural cellulose may cause formation of functional groups of imines with carbon-nitrogen double bond. Therefore, the above FTIR results identified the chemical structure of the polysaccharide nanocomposites.

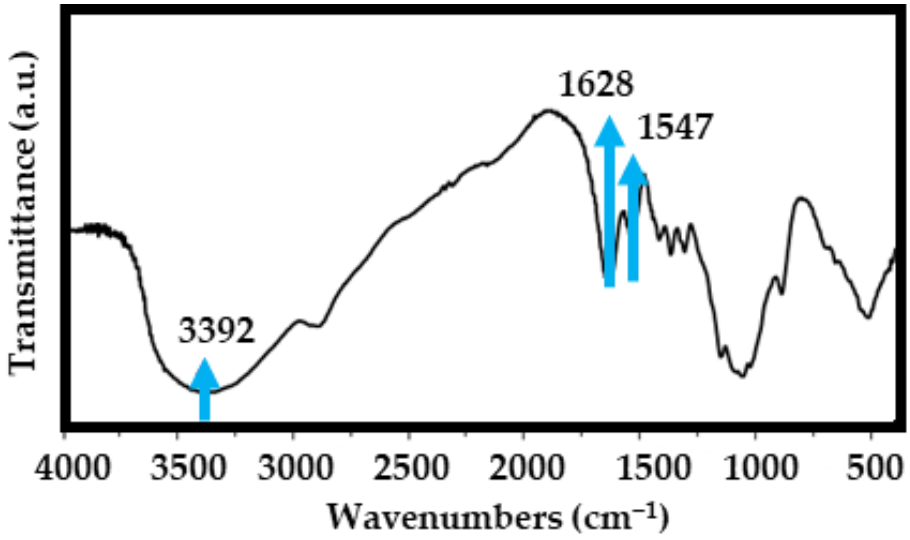

Figure 2. FTIR results of polysaccharide nanocomposites of C-C NCs.

3.3. Scanning Electron Microscopy (SEM)

Figure 3a-b demonstrate the SEM image, average diameter histogram, and schematic of polysaccharide nanocomposites of C-C NCs, respectively. An average size of C-C NCs was estimated to be 57.01±3.4 nm. The size of chitosan is strongly attributed to the ratio between the TPP cross linker and the chitosan. It was reported [27], that the chitosan and TPP with a ratio around 1:2 could cause the formation of chitosan NPs with suitable physiochemical and morphological characteristics thus, it was applied in our research. It is worth to mention that the layer-by-layer synthesis could led to proper coating of cellulose reinforcement by chitosan with desirable distribution and low agglomeration. This was similarly found in different investigations [28, 29]. It can be understood from the SEM image that the natural cellulose was entangled within the almost spherical chitosan NPs; therefore, C-C NCs mainly showed the spherical shape. The SEM analysis could prove that the ionic gelation method was successful to fabricate polysaccharide nanocomposites with desirable nanodimension and morphology.

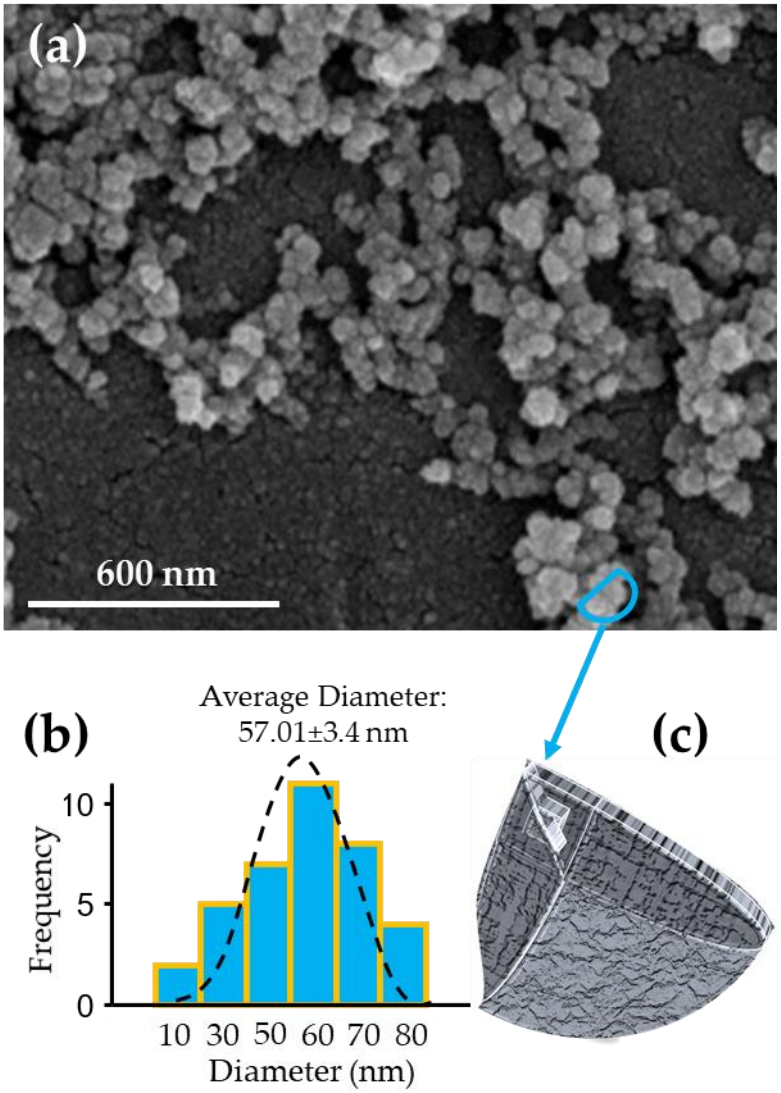

Figure 3. (a) SEM image, (b) average diameter histogram, and (c) schematic of polysaccharide nanocomposites of C-C NCs.

4. Conclusions

The polysaccharide system of C-C NCs was fabricated by using the ionic gelation method. Since TPP can crosslink chitosan with cellulose at multiple points, C-C NCs showed a uniform and nanosize structure. The ratio between the chitosan to TPP cross-linker was 1:2 (v/v) whereas, using 1.0% acetic acid, and 2% (v/v) Tween-80 led to the synthesis of C-C NCs with desirable physicochemical properties. Further, we use cellulose and chitosan with the ratio of 1:2 to obtain the composites with a size below 60 nm, as indicated in the SEM images. The composites indicated the XRD and FTIR peaks related to the chitosan cross-linked cellulose. Therefore, this study demonstrates the low cost, facile, and eco-friendly polysaccharide composites for various biomedical applications.

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