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Chemical Modification of Hydroxyapatite Nanocrystals by Poly(2-hydroxyethyl methacrylate) through a Facile Surface Initiated RAFT Polymerization

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***Abstract*-A hybrid nanomaterial of poly(2-hydroxyethyl methacrylate) (PHEMA) and hydroxyapatite nanocrystals (HAPs) was successfully synthesized by in situ surface-initiated reversible addition fragmentation chain transfer (RAFT) polymerization upon employing grafting from strategy. The HAP was first modified with S-benzyl S-trimethoxysilylpropyltrithiocarbonate in one-step process to afford RAFT agent-immobilized HAP (HAP-RAFT). Subsequently, surface initiated radical polymerization of HEMA was carried out with the HAP-RAFT in the presence of 2,2'-Azobisisobutyronitrile (AIBN) initiator. The physical, chemical structure, and thermal property of the HAP NCs, HAP-RAFT PHEMA-g-HAP nanocomposites were exclusively investigated by Fourier Transformed Infrared (FT-IR) Spectroscopy, Field Emission Scanning Electron Microscopy (FE-SEM), Energy Dispersive X-Ray (EDX), X-ray diffraction (XRD) and Thermogravimetric analysis (TGA).**

***Keywords*-Hydroxyapatite, PHEMA, graft polymerozation, surface-initiated RAFT polymerization**.

I. INTRODUCTION

The fabrication of novel materials with fascinating properties and improved performance is a continuously expanding research interest which covers subjects ranging from chemistry, physics, biology, to material science [1-3]. To date, hydroxyapatite nanocrystals (HAP NCs), with the chemical formula of $Ca_{10}(PO_4)_6(OH)_2$, has the great advantage of being able to bond directly to a biologically active calcium phosphate ceramic that is used in surgery to replace and mimic bone as its chemical composition is close to that of natural bone; furthermore, its ceramic forms exhibit osteoinductive properties [4-6]. For many applications, the control of surface functionality is a key for controlling the nanoparticle's interaction with biological species, self-assembly dispersion and compatibility with polymeric materials [7-9].

Of various modification approaches, grafting of organic polymers on HAP surface has gained much focus as it allows achievement of synergistic characterisitics derived from each component. Consequently, in attempts to improve the interfacial adhesion, the surface of HAP NPs has been modified with a variety of coupling agents and polymers via chemical reaction with hydroxyl groups on the HAP nanocrystals surface. Recently, reversible addition chain fragmentation transfer (RAFT) polymerization is known as one of the most successful ''controlled/living'' polymerization methods that have been developed [10-14]. Several groups have demonstrated that RAFT is very versatile and tolerant of a wide range of functional groups present in the monomer, solvent, or initiator. RAFT has been adopted to prepare a wide range of architectures, including block, star, gradient and statistical copolymers, as well as well-definded macromonomers [15-17]. This technique has some advantages over the conventional radical polymerization in terms of controlling polymer architecture, molecular weight and molecular weight distribution. In addition, it allows introduction of functional groups to the inorganic surface for polymerization with complex structures under mild reaction conditions, without using many reaction steps and metal catalyst.

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PHEMA is a common polymer widely utilized in various bio-medical processes, e.g. as bone cement for fixing total hip prostheses to give suitable mechanical properties to the material. It exhibits a number of advantageous properties such as high oxygen permeability, good mechanical properties, favorable refractive index value, feasible functionality via a conversion of end hydroxyl groups on side chains. [18-20]. Moreover, the hydrophilicity basically from the hydroxyl functional groups makes it bio- and blood-compatibility and highly resistant to degradation. Therefore, the biocompatibility and functionalization ability of HAP nanocrystals can be greatly improved by introducing a monolayer with well-defined high density PHEMA to their surface. In this work, we have applied RAFT technique to graft the poly(2-hydroxy ethyl methacrylate (PHEMA) from the HAP nanocrytals, which employed a one-step direct anchoring of preferably RAFT agent group to the HAP surface followed by the polymerization of HEMA in the presence of in the presence of 2,2'-Azobisisobutyronitrile (AIBN) initiator

II. EXPERIMENTAL DETAILS

A. Materials

S-benzyl S- trimethoxysilylpropyltrithiocarbonate (BTPT) was prepared according to the procedure described elsewhere [21]. 2-Hydroxyethyl methacrylate (HEMA) was passed through a column of basic alumina to remove inhibitors. 2,2'-Azobisisobutyronitrile (AIBN) was re-crystallized with ethanol and tetrahydrofuran (THF) was dried over CaH_2 and distilled before use. Hydroxyapatite particle (HAP), all solvents were used as received. All of the above chemicals were purchased from Sigma-Aldrich.

B. Immobilization of RAFT agent onto the HAP NCs

The HAP NCs (1 g) were silanized by BTPT (1 g) upon stirring them in a mixed solution of 40 mL of ethanol. The mixture was then stirred for over night, heated to 80°C under N_2. HAP-RAFT nanocrystals were purified by washing several times with THF. After filtration, the particles were dried at room temperature.

C. Synthesis of PHEMA-g-HAP Nanocomposites via Surface-Initiated RAFT.

0.2 g of HAP-RAFT, 1 g of HEMA, 0.012 g of AIBN, 8 mL of methanol and a Teflon-coated stir bar were placed in a 25 mL round flask equipped with a reflux condenser. The flask was purged with nitrogen, heated to 80°C and kept stirring. At the end of the reaction, the viscosity increased dramatically. After 4 hrs, the flask was cooled to room temperature and the reaction mixture was precipitated in diethy ether. The product was filtered and dried in a vacuum oven. The polymer product was diluted in toluene to obtain the PHEMA grafted HAP free from the unbound polymer and centrifuged to collect the PHEMA-*g*-HAP.

D. Instrumentation

The changes in chemical bonds were studied by Fourier Transformed Infrared (FT-IR) Spectroscopy by Tensor 37 spectrophotometer (Bruker, Germany) in the frequency range of 4000-400 cm^{-1} with a resolution of 4 cm^{-1} and 16 scans. The crystallographic state of functionalized HAP nanocrystals was determined by a Philips X'pert-MPD system diffractometer (Netherlands) with Cu Kα radiation. The morphology and elemental analyses of the hybrids were investigated by using Field Emission Scanning Electron Microscopy (FE-SEM) equipped with JOEL JSM-7600 (USA) Energy Dispersive X-Ray (EDX) spectrometer (Hitachi TM3000 and Oxford SwiftED3000).

III. RESULTS AND DISCUSSION

The chemical bonds of RAFT agent and HEMA chains on the HAP surface were studied by using FT-IR spectroscopy. The FT-IR spectra of the HAP nanocrystals, the surface functionalized HAP (HAP-RAFT) and PHEMA-*g*-HAP nanocomposites are shown in Fig. 1. For the HAP nanocrystals, the absorption strong bands at 1092 and 1059 cm^{-1} are related to stretching vibrations of phosphate group; the bands at 634, 603 and 572 cm^{-1} are responsible for deformation vibrations of phosphate group; the absorption band at 3570 cm^{-1} can be ascribed to free hydroxyl group stretching vibration in crystal lattice of the HAP phase. In the FT-IR spectrum of HAP-RAFT (Fig. 1B), the introduction of BTPT to HAP surface can be confirmed via the peak of C-H asymmetric and symmetric stretching vibrations of propyl group at 2930 and 2838 cm^{-1}. Upon polymerization, a new peak appeared at around 1725 cm^{-1} indicating the characteristic carbonyl (C=O) double bond stretching present in the PHEMA-g-HAP (Fig. 1C). In the FT-IR spectrum of PHEMA-*g*-SiO_2, the broad absorption band at 3419 cm^{-1} is due to the O-H stretching. The absorption bands at 1160-1225 cm^{-1} might come from the stretching vibrations of -C-O- in the ester groups. All the results indicate that PHEMA chains were successfully grafted to the surface of HAP particles through surface modification by RAFT strategy.

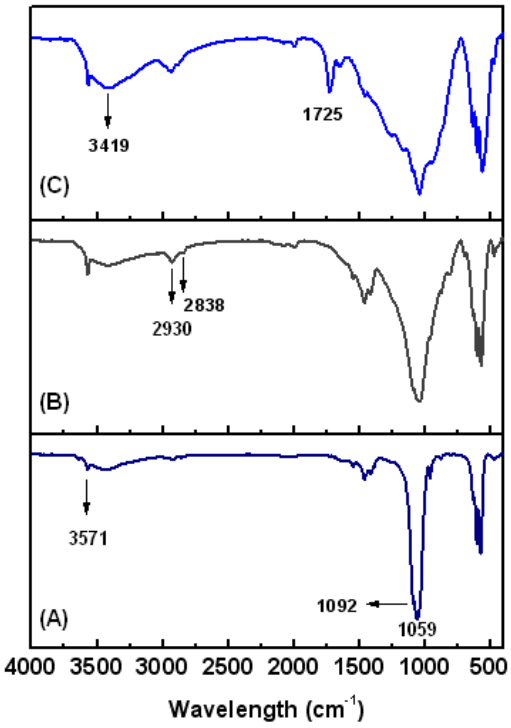

Fig. 1. FT-IR spectra of (A) HAP nanocrystals, (B) HAP-RAFT, and (C) PHEMA-*g*-HAP nanocomposites

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In order to better understand the chemical composition of the prepared nanocomposites, EDX spectra of pristine HAP nanocrystals and PHEMA-*g*-HAP nanocomposites were recorded as shown in Fig. 3. The existence of carbon, oxygen, phosphorus, and calcium in HAP NCs can be clearly seen in Fig. 2A. The BTPT immobilized on the surface of HAP particles could offer a condensation reaction to produce a stable initiator monolayer. As expected, significant peaks of carbon, oxygen, phosphorus, calcium, silica, and sulfur were observed for HAP-RAFT (Fig. 2B). It is noteworthy that the presence of characteristic S peak on the HAP-RAFT reveals successful attachment of active RAFT agent to the HAP surface, as susceptible to initiate subsequent polymerization. The EDX spectrum of PHEMA-*g*-HAP nanocomposites shows the presence of carbon, oxygen, phosphorus, calcium, silica, and sulfur elements (Fig. 2C). These characterization results prove the successful grafting of the PHEMA on the surface of HAP nanocrystals via RAFT polymerization

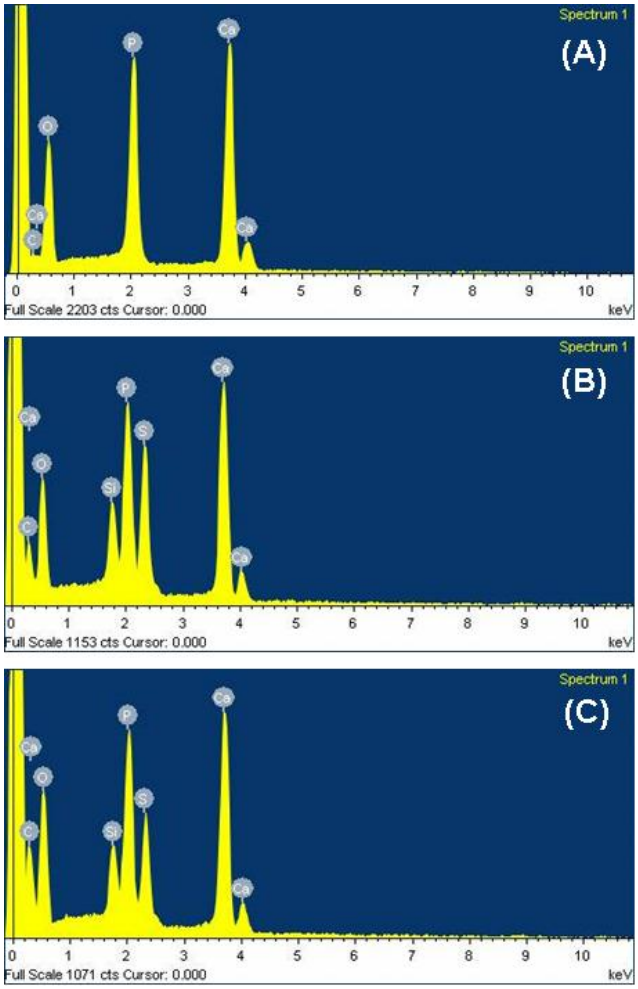

Fig. 2. EDX spectrometric analysis of (A) HAP nanocrystals, (B) HAP-RAFT, and (C) PHEMA-*g*-HAP nanocomposites

The physical structure and morphology of PHEMA-*g*-HAP nanocomposites were next investigated by XRD and SEM. Surface-initiated RAFT is an efficient way to realize the covalent immobilization of polymer chains on the surface of inorganic particles. However, as a surface modification route, the chemical reaction usually should not change the bulk properties or original crystalline state and intrinsic properties of the HAP nanoparticles. In this study, XRD technique was used to characterize the crystallinity of the HAP NCs, HAP-RAFT and PHEMA-*g*-HAP. The HAP NCs exhibit several sharp peaks at 2θ of 26°, 29°, 32–34°, 40°, and 46–54° attributable to the crystalline nature of HAP nanocrystals (Fig. 3A). It is clearly seen that the main constituent phase of the composite is crystalline HAP. As shown in the Fig. 5B and 5C, the characteristic diffraction peaks of the (002), (102), (211), (300), (202), (310), (222), (213), and (411) crystal planes of HAP-RAFT and PHEMA-*g*-HAP nanocomposites remained almost the same upon modification with RAFT agent and grafting of polymer chains, proving that the grafting reaction did not induce any change in the crystalline phase of HAP nanocrystals.

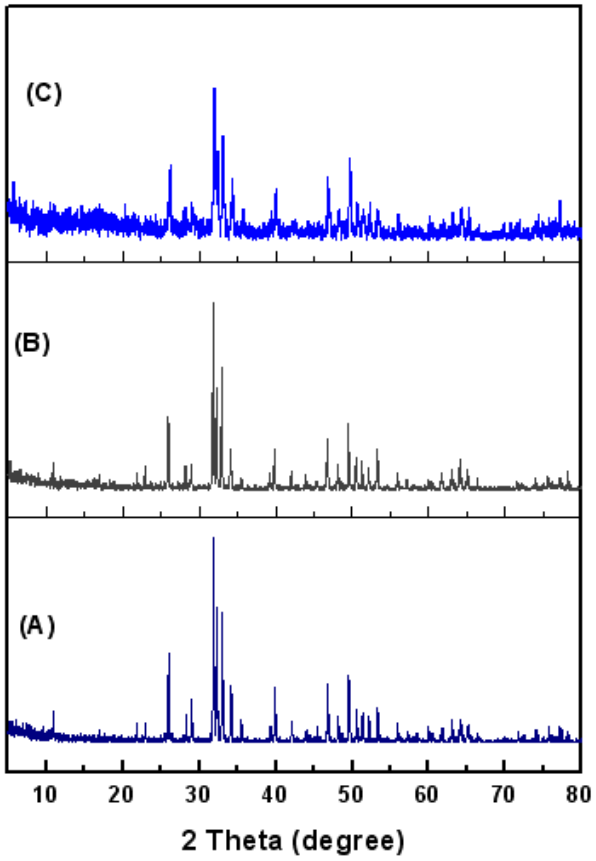

Fig. 3. X-ray diffraction curves of (A) HAP nanocrystal, (B) HAP-RAFT and (C) PHEMA-*g*-HAP nanocomposites

The morphology of pristine HAP NCs, HAP-RAFT and PHEMA-*g*-HAP nanocomposites are shown in Fig. 5. There is a similarity in crystalline structure of the needle-like HAP NCs and HAP-RAFT (Fig. 5&5B). However the immobilization of PHEMA onto HAP surface can be distinguished by taking a closer look onto Fig. 5C. However, as the PHEMA brushes were anchored onto the surface of the HAP nanocrystals, the needle-like particles were encapsulated by a thin film (i.e. the aggregation of polymer brushes). The nanoparticles aggregated together and the presence of the polymer layer is relatively prominent in the SEM image. These are futher morphological evidence for succesful grafting of PHEMA brushes from HAP nanocrystals.

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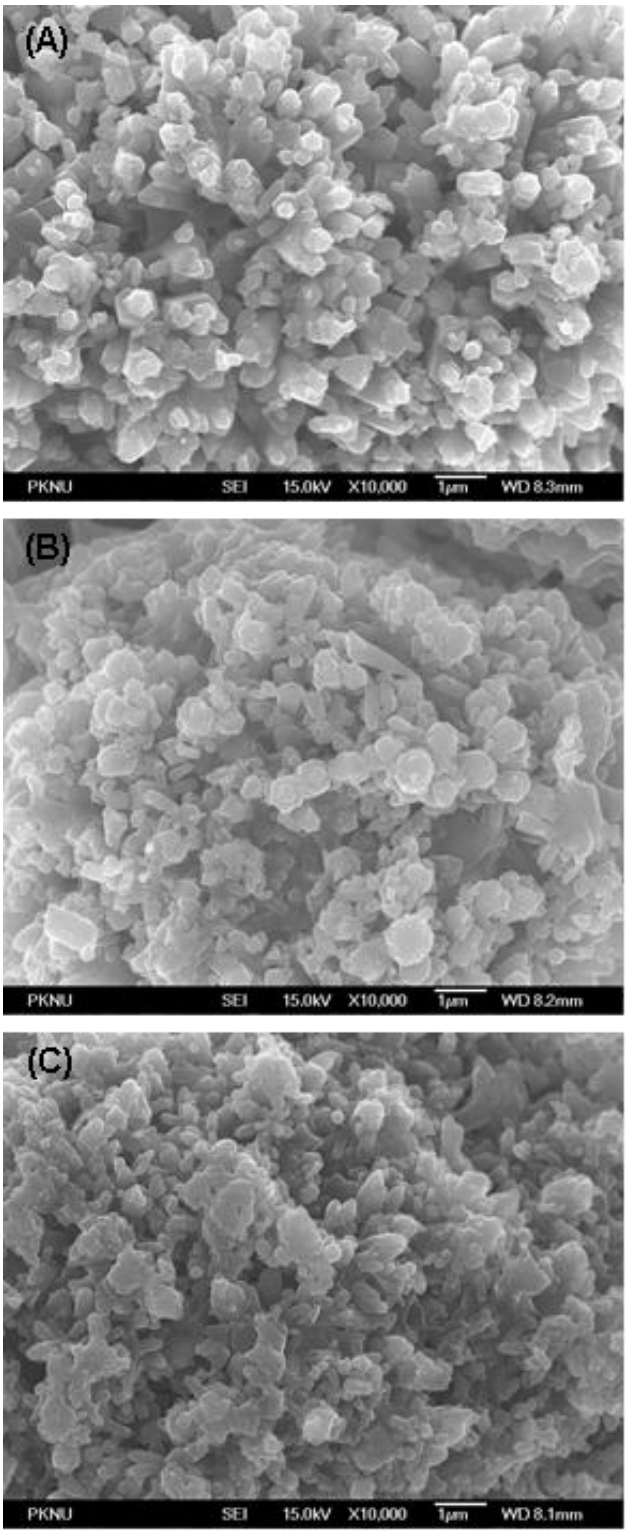

Fig. 5. FE-SEM images of (A) HAP nanocrystal, (B) HAP-RAFT, (C) PHEMA-*g*-HAP nanocomposites.

IV. CONCLUSIONS

Poly(2-hydroxyethyl methacrylate) (PHEMA) grafted hydroxyapatite nano-crystals (HAP NCs) was synthesized by SI-RAFT using *grafting from* approach. The chemical functionalization of HAP nanocrystals by biocompatible PHEMA was investigated by FT-IR, EDX while the phase compositions and morphology of synthesized nanocomposites were studied using XRD and FE-SEM. A moderate degree of functionalization of HAP particles by PHEMA was determined by TGA results. Keeping the above findings into accounts, it can be concluded that the RAFT technique could be applied to synthesize a cascade of hybrid materials in material science and nanotechnology with increasing complexity based on hydroxyapatite nanocrystals.

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