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Synthesis of BiOI nanoparticles toward potential contrast applications

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Abstract: The use of heavy metal-containing nanoparticles as potential X-ray contrast agents for the medical imaging of the human body, predates the advent of iodinated compounds because of their high X-ray attenuation power. Among the investigated heavy metals for contrast agents, Bi is the heaviest stable nonradiative metal element with a very high X-ray attenuation coefficient. There have been very few attempts to make hydrolytically stable CT (Computerized Tomography) active nanoparticles; Bismuth tends to form chalcogens among which Bi_2S_3 has been investigated to be used for a prospective CT contrasting agent. The said synthesis has given ultra-small nanoparticles, but they are hydrolytically unstable giving off a foul smelled toxic gas H_2S over time. However, the colloidal solution of BiOI NPs withstands mild acidic conditions, whereas the Bi_2S_3 is not stable in acidic condition. In this preliminary study, a unique decelerated hydrolytic procedure was developed for synthesizing biocompatible and ultrasmall PVP (polyvinylpyrrolidone) coated BiOI nanoparticles which are having a nearly spherical structure with an average size of ~2.7 nm. The phase purity and crystal structure of these prepared materials was determined by X-ray powder diffraction using bulk materials. The synthesized compound has a layered structure and is hydrolytically stable at neutral pH. Hence, the prepared BiOI nanoparticles can be an ideal material for potential CT contrast agents.

Keywords: biocompatible, contrast agents, nonradiative, X-ray attenuation coefficient

Introduction

In the case of searching possible solution for increasing imaging efficiency and blood circulation time to increase the time windows for imaging, the use of nanoparticles (NP) as contrast agents has been reported as one solution. So far, a variety of heavy metal containing nanoparticles like Iodine, Gold, Bismuth, Bromine, Platinum, Thorium, Yttrium, Tungsten, Cesium, and Palladium has been reported as potential X-ray contrasting agents for the medical imaging of the human body. Among these heavy metals, bismuth is the heaviest stable nonradiative metal element with a very high X-ray attenuation coefficient. Generally, these Bi containing compounds are having very low solubility in an aqueous solution, and they are considered to be nontoxic compared to the other heavy metals like Hg, Tl, and Pb. However, the investigations carried out for some metallic elements with high X-ray attenuation power, except Bi based compounds have reported many deleterious effects that are either short term acute or chronic effects in nature [1].

It is important to note that for *in vivo* biomedical applications all injectable contrast agents should be excreted from the body completely in a reasonable period of time. Thus, the potential nanoparticles agents should be ultrasmall in diameter ($d < 3.0$ nm) to allow renal excretion. In that case, the investigations should be set up to search for bismuth compounds that are hydrolytically stable and which can be prepared as ultrasmall nanoparticles as

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particulate CT contrast agents that are biocompatible and renal clearable[2].

The BiOI nanoparticles were reported as useful X-ray contrast agents because they contain heavy elements, Bi (Z = 83) and I (Z = 53) with higher X-ray attenuation coefficients. Thus, we describe a simple one-step aqueous solution route for preparing biocompatible and ultrasmall BiOI nanoparticles which can be developed as an efficient CT contrast agent [3, 4].

Methodology

Synthesis of PVP coated BiOI nanoparticles

An aqueous solution of 1.0 mM $Bi(NO_3)_3$ (400 mL at pH ~2.7) containing 2g of polyvinylpyrrolidone (average MW = 40000) was mixed slowly with a solution of 20 mM NaI (20 mL) under stirring at room temperature. After the mixture had been stirred for 30 min, aliquots of 10 mL were mixed with an equal amount of acetone and centrifuged at 10000 rpm for ~15 min, which resulted in the formation of a pellet of nanoparticles in each centrifuge tube. The pellets of nanoparticles were redispersed in ~10 mL of distilled water by sonication and separated again by the addition of an equal volume of acetone and centrifugation.

Synthesis of bulk BiOI materials

An aqueous solution of 1.0 mM $Bi(NO_3)_3$ (400 mL at pH ~2.7) was added slowly with a solution of 20 mM NaI (20 mL) while being vigorously stirred at room temperature. After the mixture had been stirred for 8 h at room temperature, the product was washed by the addition of water twice followed by the addition of acetone twice. The product was dried in the air at room temperature for 24 hrs.

Results and Discussion

In this investigation, BiOI nanoparticles coated with PVP were synthesized targeting to use as CT contrasting agent. Once the particles were synthesized, various analytical techniques were employed to characterize the BiOI nanoparticles prior to use *in vivo* experiments. As usual, transmission electron microscopic (TEM), and High angle angular dark field (HAADF) images were taken to determine the size and the approximate morphology of the BiOI NPs and shown in the Figure 1A and 1B correspondingly. In order to determine the average particle size, randomly selected more than hundred particles were used to generate the histogram of particle size distribution as shown in Figure 1D. It was revealed that the average BiOI nanoparticles size is ~2.7 nm. As can be seen in the histogram, the synthesized NPs are ultrasmall and nearly monodisperse which assure renal clearance of the NPs after use as CT contrasting agent. The HR-TEM and HAADF images presume to conjecture that BiOI NPs are quasi spherical, and the particles are well separated. The presence of annular electron diffraction rings in the selected area electron diffraction (SAED) map (Figure 1C) revealed that the synthesis procedure of BiOI NPs yields polycrystalline particles.

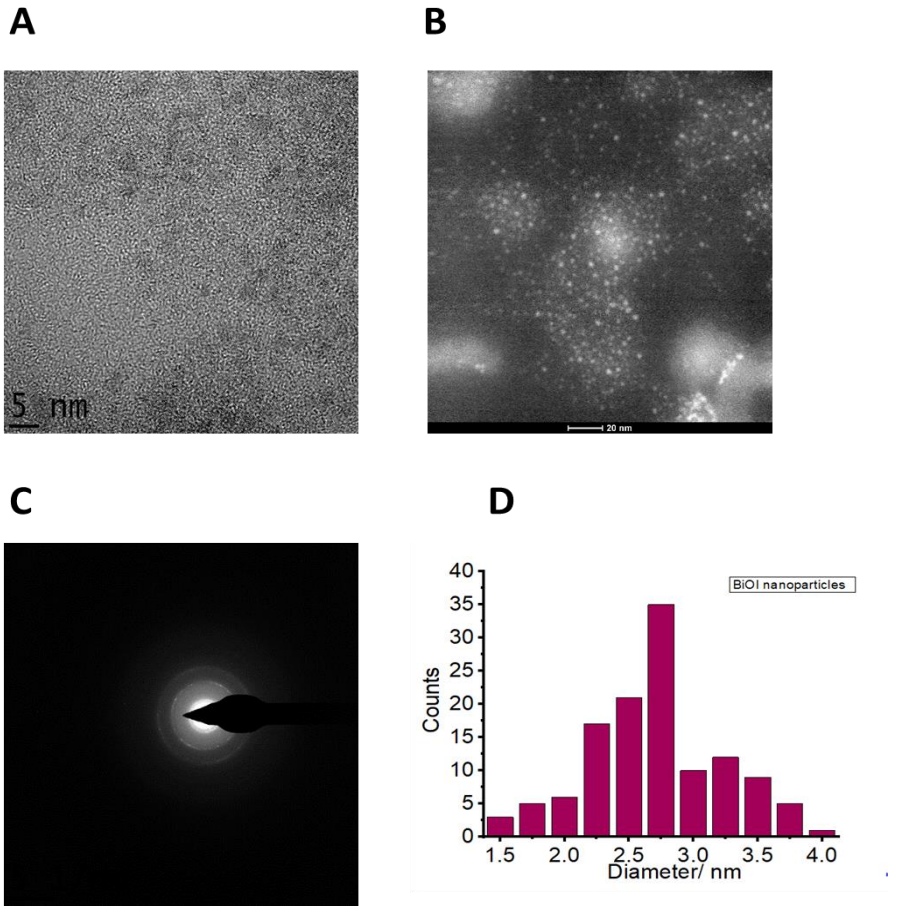

Figure 1. Transmission microscopic studies, **(**A**)** HR-TEM images, (B) Z-contrast HAADF images, and (C) SAED map, and (D) histogram of size distribution.

Further, semiquantitative elemental analysis performed using EDX (Energy-dispersive X-ray) showed that the NPs are composed of Bi and I (Figure 2). Further, it was implied the Bi:I ratio in NPs likely to be 1:1 as were seen for the bulk BiOI sample. However, various of X-ray scattering power of elements limit the ability of EDX spectroscopy to be used for quantitative EDX analysis. Thus, powder X-ray diffraction analysis needs to be used to verify the exact phase identity of both bulk and coated NPs.

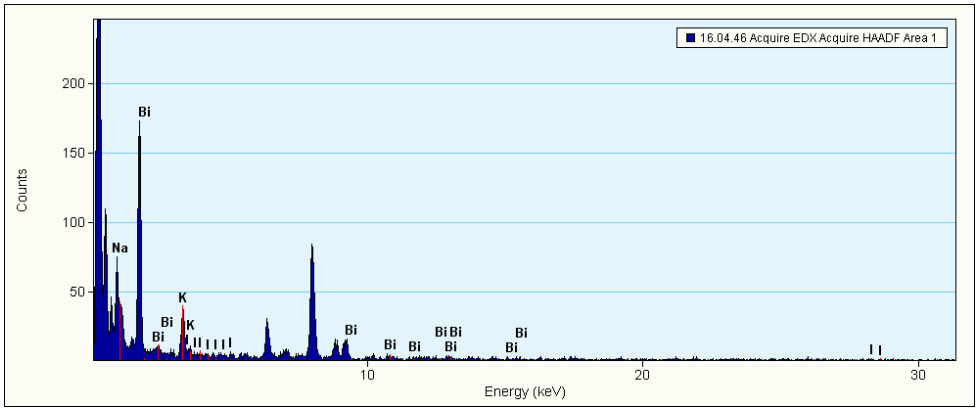

Figure 2. Energy-dispersive X-ray (EDX) spectrum for PVP coated BiOI nanoparticle.

The presence of the PVP coating around the BiOI NPs was confirmed using the FTIR spectrum. As shown in Figure 3, the characteristic peaks at ~1661 nm^{-1} for C=O stretching validated the functionalization of BiOI NPs with PVP presumably through intermolecular hydrogen bonding. This analysis further confirmed that PVP coating cannot be removed or stripped off from the NP surface by prolonged dialysis against distilled water or sedimentation by centrifugation in water/acetone mixture.

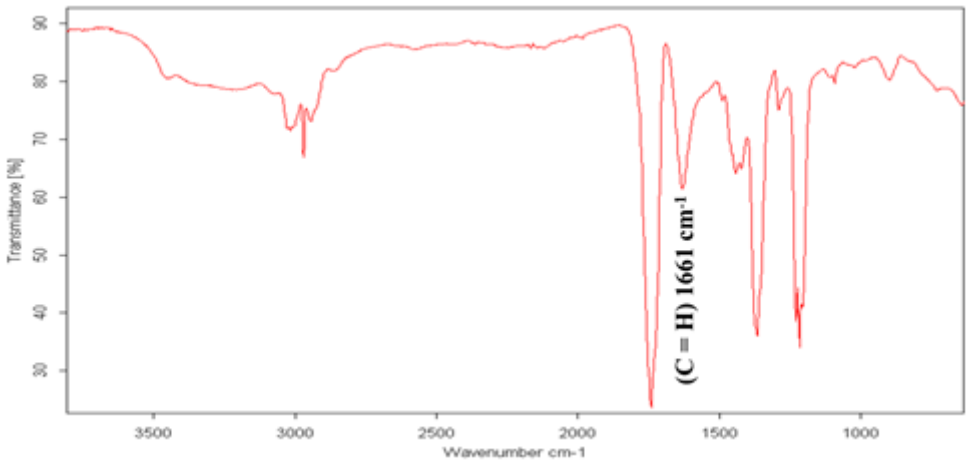

Figure 3. The FTIR spectrum of PVP coated BiOI nanoparticles

The particle phase and purity of synthesized BiOI bulk samples were evaluated by powder x-ray diffraction (XRD) analysis. The observed XRD patterns of the samples revealed that the product obtained from the slow aqueous hydrolysis reaction was phase pure and all the detectable peaks in these patterns could be readily indexed in space group P4/nmm, which indicates that BiOI is isostructural with BiOCl.

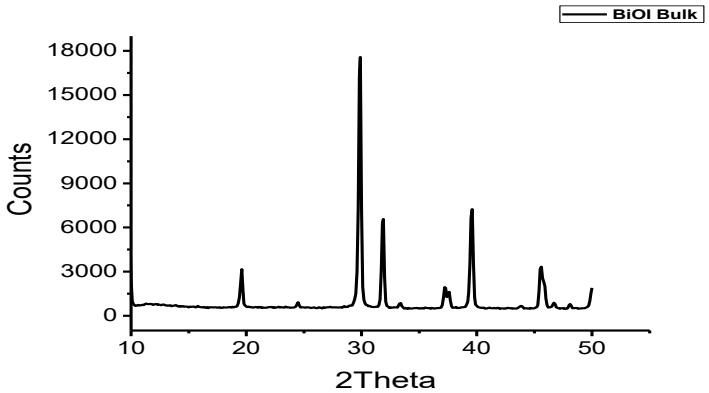

Figure 4. Powder XRD patterns of bulk BiOI sample

The atomic parameters of the BiOCl structure were used as the initial parameters in the Rietveld refinement performed using GSAS software. The final refinement included 54 atomic coordinate and isotropic displacement parameters refined against 148 reflections within a 2θ angular range of 7-109º, which yielded a = 3.99399 (4) Aº, c = 9.15486 (8) Aº, V = 146.038 (2) A^{o3}, ρ_{calc} = 8.002 g/cm^3 and converged at R_{wp} = 3.6% and R_p = 2.7%.

The structure of BiOI is composed of layers of BiOI perpendicular to the c direction. Five alternating I-Bi-O-Bi-I sublayers are present within each BiOI layer and the O layer is situated at the center of the double sandwich. The Bi layer is cushioned by an O layer from the bottom and capped by an I layer from the top. Each O atom shows tetrahedral geometry whereas each Bi atom is eight coordinated. Every Bi atom is coordinated by four O atoms from a tetragonal base and four I atoms from a tetragonal cap which forms a square antiprism.

Conclusion

The prepared PVP coated BiOI NPs can be a potential candidate for CT contrast agents because of their ultrasmall size of ~2.7nm and strong X-ray attenuation coefficient. The product was phase pure and NPs were nearly spherical structures with a layered structure. Hence, prepared BiOI NPs could be developed as an efficient CT contrast agent.

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