Development of a new generation of bone cement using nanotechnology

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Abstract

A new generation of bone cement with mechanical properties significantly higher than that of commercially available acrylic bone cements are strongly desired in order to ensure the long term clinical performance of the cemented arthroplasty. Currently commercial acrylic bone cement formulations contain micron-sized particles of either $BaSO_4$ or ZrO_2 to provide radiopacity, however these particles lead to a deterioration in mechanical properties. In this work, we have introduced nanosized fibrous and tubular titania (TiO_2) particles with high aspect ratio, in the acrylic polymer matrix which not only provides radiopacity, but also acts as a reinforcing agent for the cement. The challenge for preparing nanocomposite is the agglomeration of the nano fillers in the polymer matrix which leads to poor performance of the composite. We have presented a novel method of functionalizing titania nanostructure in order to avoid the nanophase agglomeration when it is blended with the polymer matrix.

Methacrylic acid (MA), a functionalization agent that can chemically link TiO_2 nanomaterials and polymer matrix, was used to modify the surface of titania using a Ti-carboxylic coordination bond. Then, the double bond in MA was copolymerized with methyl methacrylate (MMA) to form a TiO_2-PMMA nanocomposite. In order to enhance the adsorption of carboxylic group of methacrylic acid on titania surface, the pH of the reaction medium has also been adjusted taking into account the amphoteric nature of the naturally occurred hydrated titania surface. A control material was also synthesized consisting of 6% commercial $BaSO_4$ embedded in a PMMA matrix. Fracture toughness and dynamic and static elastic moduli of the nanocomposites were evaluated in the wet condition. Experimental composites containing commercial barium sulfate particles have also been subjected to all these characterization for a comparative study with the experimental composites.

Composites with functionalized titania nanotubes and nanofibers were shown to possess significantly higher fracture toughness and tensile moduli, compared to the composites containing commercial $BaSO_4$ at $p<0.05$. High interfacial area of nanotubes and fibers promote the adhesion between the functionalized nanofillers and surrounding polymer matrix in allowing an external load to be effectively transferred to the nanofillers from the polymer matrix resulting in producing tougher and stiffer cements. More specifically, composites with nanotube exhibits stronger mechanical properties than that of composites with nanofibers. The improved mechanical properties are due to the higher aspect ratio and ability of the hollow nanotubes to mechanically interlock with the polymer matrix.

Introduction

Acrylic bone-cement is currently the only material used for anchoring cemented arthroplasties to the contiguous bones.[1] In this application the main functions of the cement are to transfer body weight and service loads from the prosthesis to the bone and /or increase the load-carrying capacity of the prosthesis-bone cement-bone system.[1] In a joint replacement surgery it is vital for the bone cement to be radiologically detectable. Most acrylic bone cements are rendered radiopaque by the addition of heavy metal salts of barium or zirconia as a contrast medium.[2] A major disadvantage associated with the addition of heavy metal salts is the phase separation due to the incompatibility of highly polar, ionic radiopaque substances with low polarity resin, which in turn lead frequently to degradation of physical and mechanical properties of the cement.[3] Radiopacifying agents that are compatible with the polymer matrix is an alternative route for achieving radiopacity in organic polymer without compromising its mechanical properties.[4]

In this work we have used nano-sized TiO_2 fibers and tubes as reinforcing agent in the poly(methyl methacrylate) (PMMA) matrix which are biocompatible and possess a certain level of radiopacity.[2] In order to compatibilize them with polymer matrix we have functionalized them by using methacrylic acid (MA), which has both a carboxyl group for coordination to the nano-titania,[5, 6] and a vinyl group for subsequent polymerization.[7] In addition, the functionalization has been enhanced by varying the pH of the reaction environment. It has been found that the extent of functionalization varies with pH of the reaction medium with a maximum of 10wt% at pH 5.5 and a minimum of 2.9wt% at pH 3.85 for the case of TiO_2 nanofibers, while the TiO_2 nanotubes yield 10wt% functionalization at pH 5.0.

The purpose of this research was to evaluate the mechanical properties of PMMA based composites reinforced with TiO_2 nanostructures having fibrous and tubular morphologies. Moreover, the effect of extent of functionalization of nanofibers on the mechanical properties of the composites as well as a comparative study of the mechanical properties of the experimental composites with nano-titania and commercial barium sulfate particles have also been conducted in this work.

Experimental Section

Materials. TiO_2 nanofibers were synthesized by a direct sol-gel technique in supercritical carbon dioxide in accordance with the procedure explained in the previous work of our group.[8] TiO_2 nanotubes were synthesized by an alkaline hydrothermal method in an autoclave with a Teflon lined high-pressure stainless steel vessel equipped with electrical resistance and temperature control.[9]

2-propanol, Methacrylic Acid (99.99%, Sigma-Aldrich) and MMA monomer (95.9 wt %) containing a butanediol dimethacrylate cross-linker (4 wt %) and activator (0.1 wt %) were used as received (Ivoclar Vivadent). PMMA beads (99.2 wt %, Ivoclar Vivadent) having an average particle diameter of 57.5 μm (as measured by laser diffraction using a Malvern Mastersizer 2000) with a free radical initiator BPO (0.8 wt %) were used as received.

Functionalization of Titania Nanostructures. The as-prepared TiO_2 nanofibers and nanotubes were calcined at 600 and 400 ºC respectively to impart crystallinity and thermodynamic stability.[10] In order to functionalize the surface of the n-TiO_2, 0.1 g of calcined titania powder was dispersed in 35 mL of 2-propanol with the aid of ultrasonic agitation, followed by reacting with 3 mL of methacrylic acid at 80-85 °C for 24 hours with constant stirring. During the reaction the pH of the medium was measured to be 3.85 in the case of nanofibers and 4.5 in the case of nanotubes. In order to increase the extent of functionalization, the same reaction has been carried out with the medium having pH 5.5 and 5.0 for nanofibers and tubes respectively adjusted by adding few drops of potassium hydroxide solution in the reaction mixture prior to the reaction.

Preparation of TiO_2-PMMA Nanocomposite. TiO_2-PMMA nanocomposites were prepared by bulk polymerization free-radical technique as mentioned in our previous work.[7] Nanocomposite specimens with 2 and 6 wt% titania nanofillers were prepared and kept in distilled water at 37 °C for seven days before evaluating the mechanical properties.

Characterization.

The FTIR spectra were collected using KBr pellet form with a Bruker IFS 55 FTIR instrument with an attached MCT detector. Scanning electron microscopy (SEM) were recorded using a LEO 1530 instrument without gold coating. Transmission electron microscopy (TEM) was studied using a Philip CM10 operated at 80 KV. Thermogravimetric analysis (TGA) was performed using a Q500 TA instrument from 25 to 600 °C at a heating rate of 20 °C/min under nitrogen atmosphere. The NTP fracture toughness was determined using the method developed by Ruse et al.[11] Triangular prism specimens (n=12) (6mmX6mmX12mm) were produced. Testing was conducted using an Instron 2519-107 at a crosshead speed of 0.1 mm/min. The tensile moduli of the nanocomposite specimens was determined by the diametral tensile strength (DTS) method.[12, 13] Disc specimens (n=12), 4.6 mm in diameter and 2 mm in thickness, were produced and testing was conducted using an Instron 2519-107 at a crosshead speed of 2 mm/min. The tensile modulus was determined from the slope of the elastic portion of the stress-strain curve.

Results and Discussion

FTIR. The FTIR spectra of both the calcined and the functionalized TiO_2 nanofillers (fibers and tubes) are shown in Figure 1. In Figure 1(a) the absence of any peak from 1300-1800 cm^{-1} indicates the absence of any organic groups on the titania surface. In Figure 1(b) the very strong bands at 1546, 1444 and 1414 cm^{-1} are due to the bidentate coordination between titanium atoms and the carboxylic groups of methacrylic acid.[14]

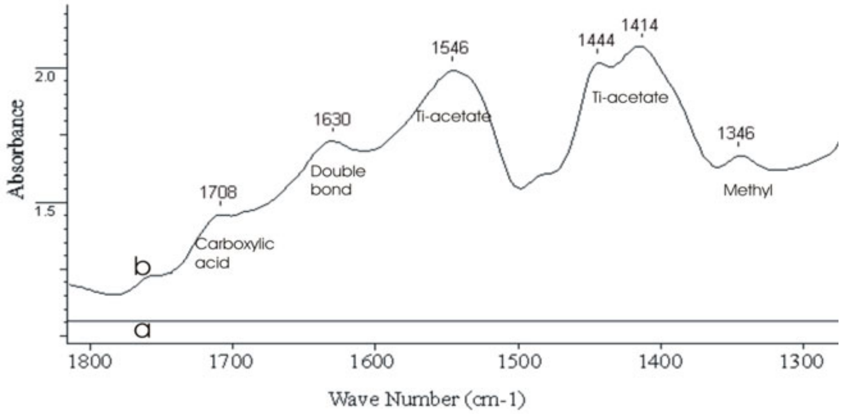

Figure 1. FT-IR Spectra: the non-functionalized (a) and functionalized (b) titania nanofillers.

TGA. The extent of functionalization of the TiO_2 nanofibers and nanotubes have been evaluated by thermogravimetric analysis(TGA). Figure 2 shows the thermal weight loss of nonfunctionalized and functionalized titania nanofibers. The nonfunctionalized titania does not exhibit any weight loss while the functionalized titania show 2.9 and 10 % weight loss which correspond to their extent of functionalization of 2.9 and 10 %. Similar results were obtained for functionalized TiO_2 nanotubes.

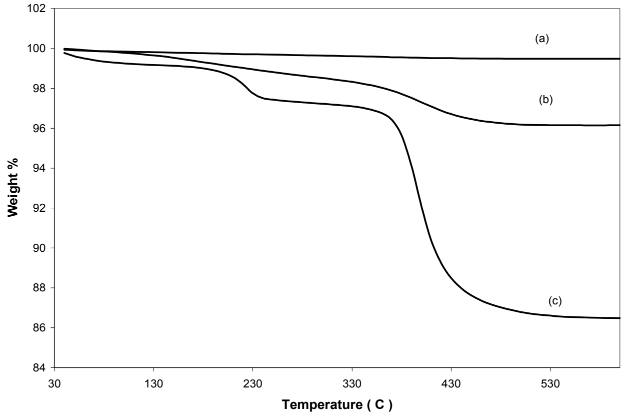

Figure 2. TGA: extent of functionalization. (a) non-functionalized TiO_2 nanofibers; (b) 2.9 wt% functionalized TiO_2 nanofibers and (c) 10 wt% functionalized TiO_2 nanofibers.

Electron Microscopy. The physical morphology of the functionalized TiO_2 nanofibers, nanotubes and commercial $BaSO_4$ particles used in this work are shown in Figure 3 a, b and c. These micrographs show that TiO_2 nanofibers and tubes, following functionalization, preserve their fibrous and tubular shape respectively. (Figure 3 a, b), while commercial $BaSO_4$, as received, exhibits irregular shape morphology, (Figure 3 c).

The SEM images of the fracture surfaces of the nanocomposites loaded with 6 wt% functionalized TiO_2 nanofibers and nanotubes are shown in Figure 3 d and e while Figure 3 f shows the PMMA composite loaded with 6wt% $BaSO_4$. The functionalized TiO_2 nanofibers and tubes show strong adhesion with the PMMA matrix, while the $BaSO_4$ particles are loosely embedded in the matrix and surrounded by a number of pores.

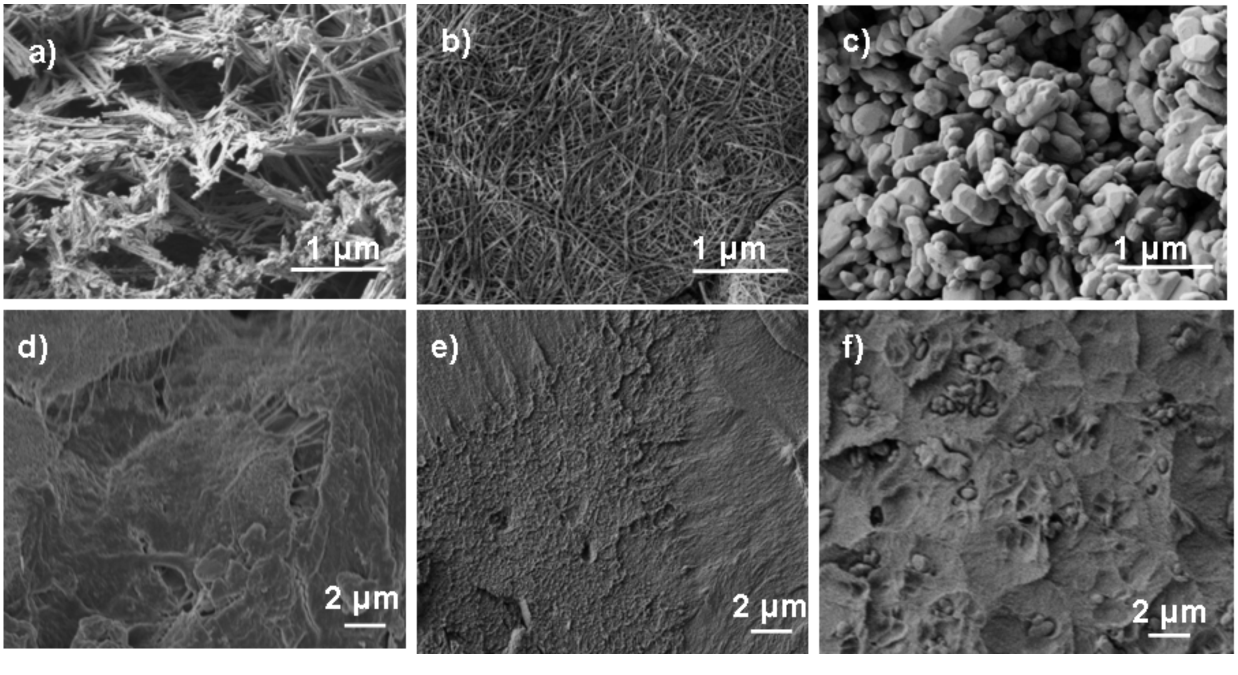

Figure 3. SEM: (a) Functionalized TiO_2 nanofibers; (b) functionalized TiO_2 nanotubes; (c) as received commercial $BaSO_4$ particles; (d) Fracture surface of 6 wt% functionalized TiO_2 nanofibers-PMMA composite; (e) Fracture surface of 6 wt% functionalized TiO_2 nanotubes-PMMA composite (f) Fracture surface of 6 wt% $BaSO_4$-PMMA composite.

Functionalization provides organophilicity to the TiO_2 nanofibers and tubes which resulted in strong adhesion of the nanofibers with the PMMA matrix (Figure 3 d and e), while $BaSO_4$ particles exhibited only a weak adhesion with the matrix (Figure 3 f).

In order to examine the microstructures and nanofiller distribution within the nanocomposites TEM analysis were conducted. Figure 4 shows TEM images of PMMA composites with 3 wt% functionalized nanofibers (a) and nanotubes (b).

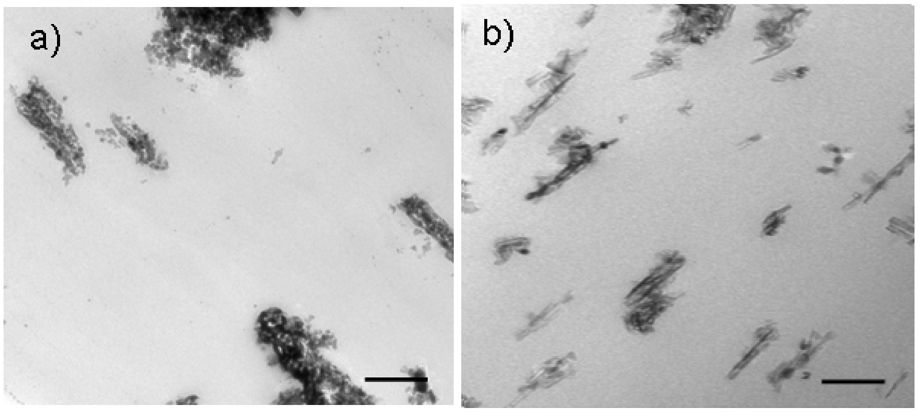

Figure 4. TEM:(a) 3wt% TiO_2 functionalized nanofiber-PMMA composites; (b) 3wt% TiO_2 functionalized nanotubes-PMMA composites. (scale bars are in 100 nm)

From Figure 4 a it is observed that while there are several individual particles distributed throughout the polymer matrix, most are clumped together in bundles. The bundles are in the nanosize range, and are uniformly dispersed throughout the polymer matrix. Fig 4 b shows the functionalized titania nanotubes in PMMA matrix where the 10 nm sized tubes are uniformly dispersed.

Tensile Modulus. The tensile modulus of the composites is mainly affected by the interfacial adhesion between the inclusions, i.e. TiO_2 nanofibers, nanotubes or $BaSO_4$ particles, and the polymer matrix.[7] Figure 5 shows the comparison of the tensile modulus values between nanocomposites reinforced with commercial $BaSO_4$ and experimental TiO_2 nanofibers having 0, 2.9 and 10% functionalization and nanotubes having 10% functionalization in the wet condition. As some commercial bone cements contain 6wt% radiopacifiers, we introduced 6wt% commercial $BaSO_4$ fillers into the PMMA matrix to prepare the composite. The nanocomposite reinforced with 2wt% TiO_2 nanofibers and nanotubes having 10wt% functionalization exhibited the highest value of tensile modulus, which was significantly higher than that of unfilled PMMA matrix, and the composites reinforced with $BaSO_4$ and TiO_2 nanofibers having 2.9wt% functionalization at $p=0.05$.

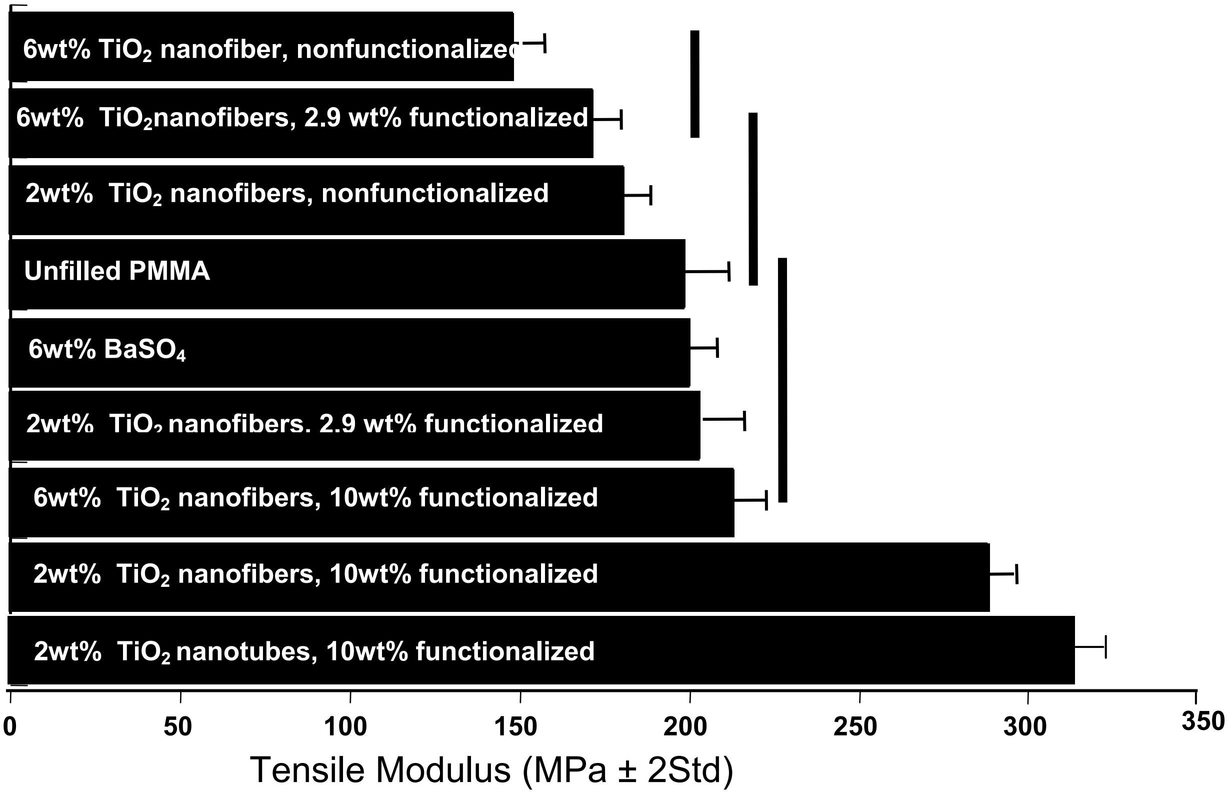

Figure 5: Tensile modulus of composites reinforced with TiO_2 nanofibers, nanotubes and $BaSO_4$ in wet condition (P=0.05). (A solid line connects those values which are not significantly different at $P = 0.05$)

The increase in functionalization enhances the organophilicity of the hydrophilic TiO_2 nanofibers and nanotubes, improving the dispersion of the nanofillers in the organophilic PMMA polymer matrix. Hence, the nanocomposites reinforced with 2wt% nanotubes and 10 wt% functionalization exhibited the highest values of tensile modulus which is 30% higher than the nanocomposite reinforced with 2% TiO_2 nanofibers having 10% functionalization. High aspect ratio and hollow internal structure of the nanotubes not only allows high interfacial area for chemical adhesion with the matrix through its outer surface but also mechanical interlocking with the polymer chain through its inner surface. Furthermore, the incorporation of 6wt% $BaSO_4$ did not have any significant effect on the tensile modulus of the composite, as this value is not significantly different from that of the unfilled PMMA matrix or non-functionalized TiO_2 nanocomposite, p=0.05. It should be noted that when comparing the nanocomposites reinforced with 6wt% TiO_2 nanofibers to those with 2wt% nanofibers (at either % functionalization), the tensile modulus was significantly lower, p=0.05. This may likely be due to agglomeration of the TiO_2 nanofibers at the higher % loading.

Fracture Toughness. Fracture toughness is defined as the energy absorbed by the material prior to crack propagation.[1, 15] Hence, fracture toughness is a very important material property for experimental bone cement which is also affected by the morphology, dispersion and extent of functionalization of its radiopacifying fillers. Figure 6 shows the fracture toughness of the composites reinforced with 6wt% $BaSO_4$ nanocomposites with 2 and 6 wt% of TiO_2 nanofibers having different extents of functionalization, nanocomposites with 2 wt% TiO_2 nanotubes having 10% functionalization, as well as the unfilled PMMA matrix in the wet condition. It can be seen that the nanocomposite reinforced with 2wt% TiO_2 nanotubes having 10wt% functionalization exhibited significantly higher fracture toughness values amongst all other composites and unfilled PMMA at p=0.05 which is obviously due to the stronger and greater adhesion of the polymer matrix with the functionalized nanotubes than any other nanofillers and particles used in this work.

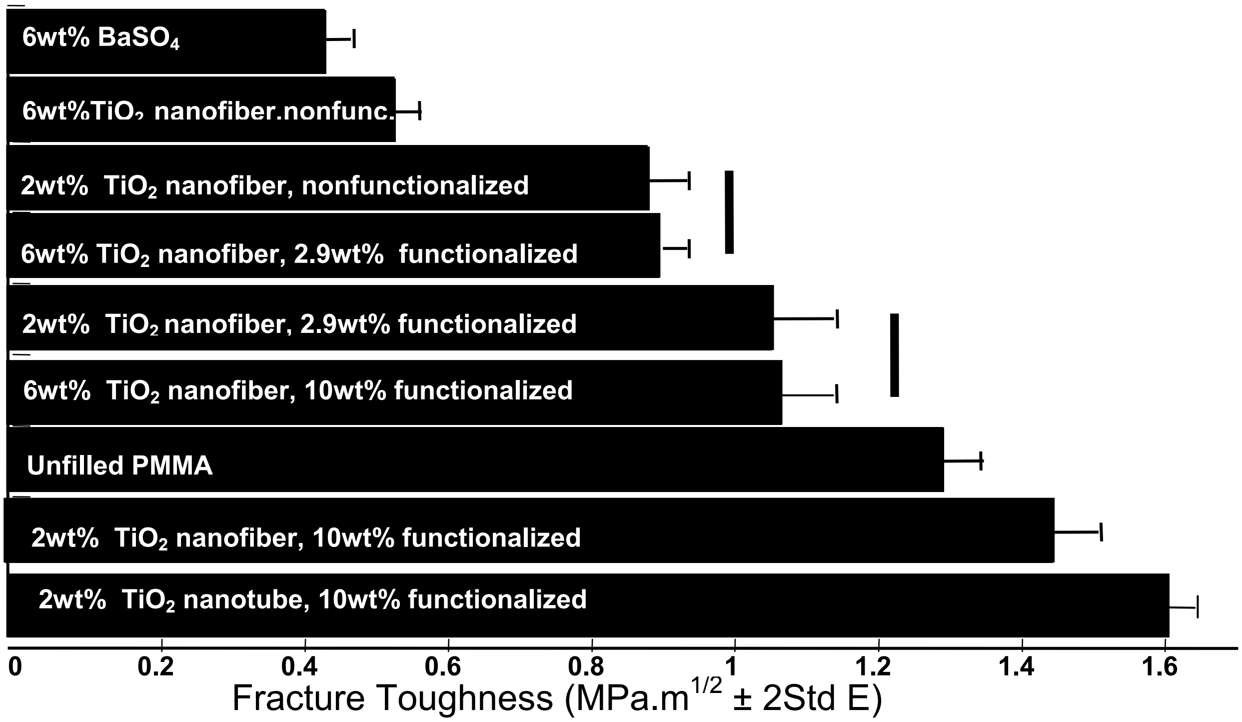

Figure 6: Fracture toughness of composites reinforced with TiO_2 nanofibers, nanotubes and $BaSO_4$ in Wet condition (p=0.05).

As shown in Figures 6, the composite with 6wt% $BaSO_4$ exhibited a significantly lower value of fracture toughness compared to the TiO_2 nanocomposites, as well as the unfilled PMMA matrix. Being incompatible with the organophilic PMMA matrix, the clumps of $BaSO_4$ particles resulted in the generation of pores which acted as stress concentrators and sites for initiating crack propagation during tensile loading on the composite. This is also reflected by the SEM image of the fracture surface of the composite as shown in Figure 3 (f).

Conclusions.

TiO_2-PMMA nanocomposites with chemical bonding between the filler and polymer matrix were synthesized using the coupling agent methacrylic acid. The coordination of methacrylic acid to the TiO_2 nanofiller was confirmed by IR spectra. An excellent distribution of the filler in the polymer matrix was observed from electron microscopy. It has also been observed that with the extent of functionalization the physical and mechanical properties of the composites also increased. After analyzing the mechanical properties, it has been found that the composites with functionalized TiO_2 nanotubes exhibited significantly higher elastic moduli and fracture toughness than those with functionalized nanofibers and commercial $BaSO_4$ particles at $p<0.001$. In order to evaluate the efficacy of the experimental nanocomposites as bone cement, radiopacity, rheology and osteoblast cellular response will be studied in our future work.

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