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Fabrication of PGS/$CaTiO_3$ Nano-Composite for Biomedical Application

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Abstract

Biodegradable elastomeric materials are gaining extensive attention in the field of soft tissue engineering. Poly (glycerol sebacate) (PGS) is a novel biocompatible elastomer in this scope. However this polymer has poor mechanical properties especially when the molar ratio of glycerol is higher than sebacic acid. Calcium Titanate ($CaTiO_3$) is a biocompatible ceramic with some degrees of piezoelectricity, which is in favor of cell growth. In this study; Calcium Titanate is synthesized at nano-scale by sol-gel method and dispersed into as-synthesized PGS pre-polymer in weight-ratio of 5:95 for $CaTiO_3$ and PGS, respectively. This waxy material was cured to achieve the final product. The molar ratio of glycerol and sebacic acid for the synthesis of PGS was 1:0.8, respectively. X-ray diffraction (XRD) test confirms successful synthesis of $CaTiO_3$ and the nano-scale of crystals are approved by transmission electron microscopy (TEM) Image. Fourier transform infrared (FTIR) spectroscopy has revealed a chemical bond between the two phases after addition of ceramic into pre-polymer. Distribution of $CaTiO_3$ nano-structures in the polymeric matrix is shown by Scanning Electron Microscopy (SEM).

Keywords: *Elastomer, Poly(glycerol sebacate), Calcium Titanate, Nano-composite.*

1. INRODUCTION

Over the past few decades, there has been expanding efforts to develop biodegradable elastomeric materials for high-demanding clinical applications [1]. For numerous biomedical uses in the field of tissue regeneration such as heart and tendon tissue engineering and nerve conduits, complete elastic deformation is of high importance [2]. Although biodegradable thermoplastics such as poly(lactic acid) (PLA), poly(glycolic acid)(PGA) and poly(caprolactone) (PCL) have been used with some extents of success, it seems mechanical incompatibility which rises from their plastic deformation is a key point in cases that are subjected to failure [3]. Poly(polyol sebacate) (PPS) polymers are a novel family of elastomers introduced for biomedical applications which have exhibited high potentials for nerve and cardiovascular tissue engineering. Among this family; poly(glycerol sebacate) (PGS) is more investigated both in-vivo and in-vitro [4]. This biodegradable elastomer undergoes surface degradation and its degradation products are inherently found in specific metabolic pathways [5]. But this elastomer suffers from poor mechanical strength and lack of bioactivity which limits its biomedical use [6]. There has been many efforts to surmount this hurdle through incorporation of materials such as bioactive glass [7], cellulose [8] and carbon nanotubes

[9] into PGS polymeric network for hard tissue regeneration, but the practical use of PGS in soft tissue is still far from reliability.

It is well established that piezoelectric materials are inversely capable of accelerating and enhancing the process of tissue regeneration [10]. In this regard, calcium titanate is a biocompatible ceramic with perovskite structure which is its origin for manifesting piezoelectricity [11]. In this study, $CaTiO_3$ is synthesized at nano-scale and added to as-synthesized PGS pre-polymer in weight ratio of 5:95 respectively in order to render the elastomer more electrically active. The final product has been compared with the elastomeric PGS in term of synthetic differences.

2. MATERIALS AND METHODS

2.1. Materials

Titanium isopropoxide with 97% purity was purchase from Sigma-Aldridge. Calcium nitrate tetrahydrate, Glycerol, Ethanol with purity of higher than 99% and Sebacic acid with 99% purity were all purchased from Merck.

2.2. Characterization

The microstructure of $CaTiO_3$ was examined by a PHILIPS/CM120 transmission electron microscope (TEM).

X-ray diffraction (XRD) of final product and its components were carried out with X-ray diffractometer (BRUKER/ D8 ADVANCE), Cobalt target, 2θ range from 10° to 80°.

Fourier transform infrared (FT-IR) was executed by using infrared spectrometer (Jasco/ FTIR-6000). Attenuated total reflection mode was utilized in the mid-infrared region of 4000–650 cm^{-1} and recorded with a resolution of 0.96 cm^{-1}.

The distribution of ceramic powder in a cross section of the final material was characterized by an environmental scanning electron microscope (PHLIPS/XL30).

3. EXPERIMENTAL

3.1. Synthesis of $CaTiO_3$

The experimental method employed for synthesis of CaTiO3 was as follows: (CaNO3.4H2O) and titanium (IV) isopropoxide were used as precursors of calcium and titanium respectively. The two precursors dissolved in ethanol separately at room temperature in the Ca/Ti=1:1 molar ratio. Then titanium precursor solution added dropwise to the other solution under intense stirring. A minor quantity of deionized water was added to the solution in order to activate titanium precursor; which immediately caused the solution turn white and opaque. Under temperature of 50° C and medium rate of rotation this sol gradually converted into a viscous gel. This gel dried at 200◦ C for 2 h and then annealed at 750◦ C for 1 h.

3.2. Synthesis of PGS

The conventional method for synthesis of PGS consists of two steps. Primarily by poly-condensation of glycerol and sebacic acid in 1:0.8 molar ratio respectively; PGS pre-polymer was achieved. This reaction was processed at 125° C and under slow flow of nitrogen gas. After 24 h the material cooled down at room temperature and the dough-like pre-polymer reached. The pre-polymer dissolved in tetrahydrofuran (THF) at weight ratio of 1:1. Then 5 wt% of pre- synthesized $CaTiO_3$ gradually added to the solution under vigorous rotation of magnetic stirrer. The addition of ceramic drastically boosts the viscosity of solution to the threshold of pausing the magnet if the speed of rotation would not be fast enough. This slurry also mixed ultrasonically for optimized

dispersion. The resulted slurry heated up to 50° C under rapid stirring until entire evaporation of THF.

3.3. Fabrication of Elastomeric Samples

For second stage of the reaction, the slurry casted into dishes with 2 mm thickness and cured at 140°C under vacuum of 40 Torr to increase crosslink density of the product. A batch of intact pre-polymer was cured under the aforementioned condition for comparison.

4. RESULTS AND DISCUSSIONS

4.1. XRD Analysis and TEM

Figure 1 shows XRD spectra of PGS/$CaTiO_3$ composite vis-a-vis its composing materials

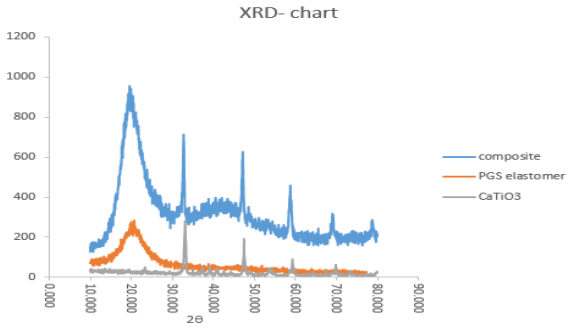

Figure 1. *XRD spectrum of the final material in comparison to its components.*

at room temperature. The apparent flattened peak for the elastomer is typical of all amorphous polymers. The same peak is observed for the composite beside all corresponding long peaks of $CaTiO_3$. No sign of new peaks in the spectrum of the composite indicates that no new crystallized phase is produced. We see a main diffraction peak around 21° for both elastomeric samples which ascends after addition of ceramic. This offers that the degree of polymer is higher in the nanocomposite network [12].

The size of the grains which is ascertained by Debye-Scherrer's formula is 49 nm. This result is also confirmed by TEM image which is shown in figure 2.

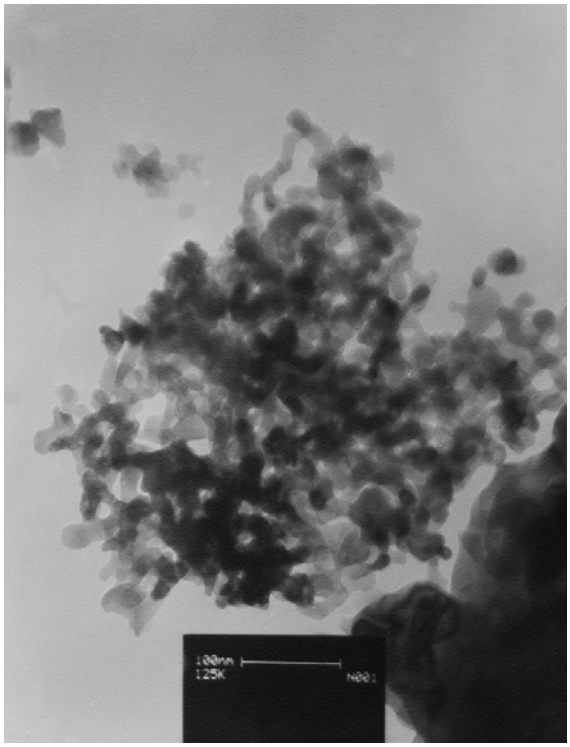

Figure 2. *TEM image of synthesized $CaTiO_3$ after annealing at 750°c for 1 h.*

4.2. FTIR Analysis

Figure 3 shows FTIR spectrum of crosslinked product in comparison to pure PGS. Formation of esteric bonds is authenticated by its robust peak at 1732 cm^{-1}. A twin ridge around 2900 cm^{-1} is originated from the methylene groups and the bulgy swells near 3460 cm^{-1} indicates the hydrogen bonds of hydroxyl agents. Since hydrogen bonds account for hydrophilicity of PGS, even superior hydrophilicity is expected for the composite due to broader intense peak. In comparison to pure PGS, there is a tiny crest at 1575 cm^{-1} for composite which suggests

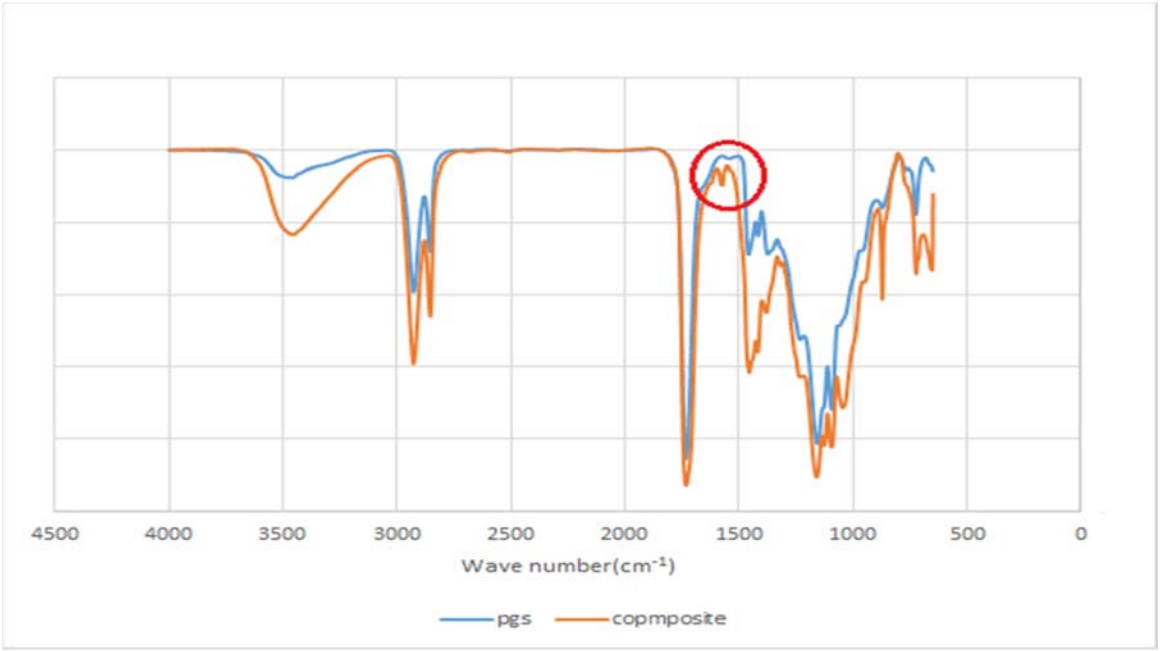

Figure 3. *FTIR spectrum of PGS/$CaTiO_3$ in comparison to PGS. The red circle shows metallic carboxylate bond.*

formation of metallic carboxylate bond. This is attributed to stretches of calcium carboxylate from hydrolyzed calcium ions by carboxylic agents of sebacic acid molecules which have remained intact. This bond is also responsible for the dramatic change of viscosity after addition of ceramic. During the process of synthesis the following reaction carries out between the two starters:

$$2\ \text{—COOH} + CaO \longrightarrow (\text{—COO}^-)_2Ca^{+} + H_2O$$

This reaction has also been referenced in the study of Liang et al which investigated PGS/Bioglass® composite [7]. The reaction has occurred due to presence of Ca^{2+} ion in the structure of Bioglass and the bond has been mentioned as responsible for boosting mechanical strength and elastic module, while lowering biodegradation rate of elastomer as well [7].

4.3. Distribution Evaluation

Achievement of uniformity in structure is of high importance in fabrication of nanocomposites. Nano-scale materials are prone to agglomeration in the process of blending due to high surface to volume ratio [13]. In this study pre-polymer solution in THF was used as dispersing media to neutralize elevated viscosity that had risen from the noted chemical bond. To bring ultrasonic bath into play is also essential to attain a stable suspension with plausible dispersion. Figure 4 shows SEM image of the product in backscattered mode which shows qualitative distribution of $CaTiO_3$ in its polymeric environment. In case of using pure pre-polymer as dispersing media, SEM images revealed apparent agglomerated areas of the ceramic phase. The image is not provided here.

5. CONCLUSION

In this work we have successfully synthesized and characterized $CaTiO_3$ powder by sol-gel method. TEM obviously shows particles of this product at nano-scale. PGS with molar ratio of 1: 0.8 has also been synthesized. Using these both, A PGS/$CaTiO_3$ composite with 5% weight ratio of ceramic nano-structure is presented. The degree of polymer rises after ceramic insertion in the polymer network which offers that the ceramic is well-homogenized in the matrix at nano-scale. A chemical reaction has occurred between the two phases. However this does not sacrifice ester bonds in polymer network and the level of ester bonds in the composite remains at the same level as for intact polymer. The reaction between the two phases can modify some properties of this product such as mechanical properties, biodegradation kinetics, hydrophilicity and as a result its cyto-compatibility in comparison to its pure matrix. Experimental analysis to approve these conjectures is currently under investigation.

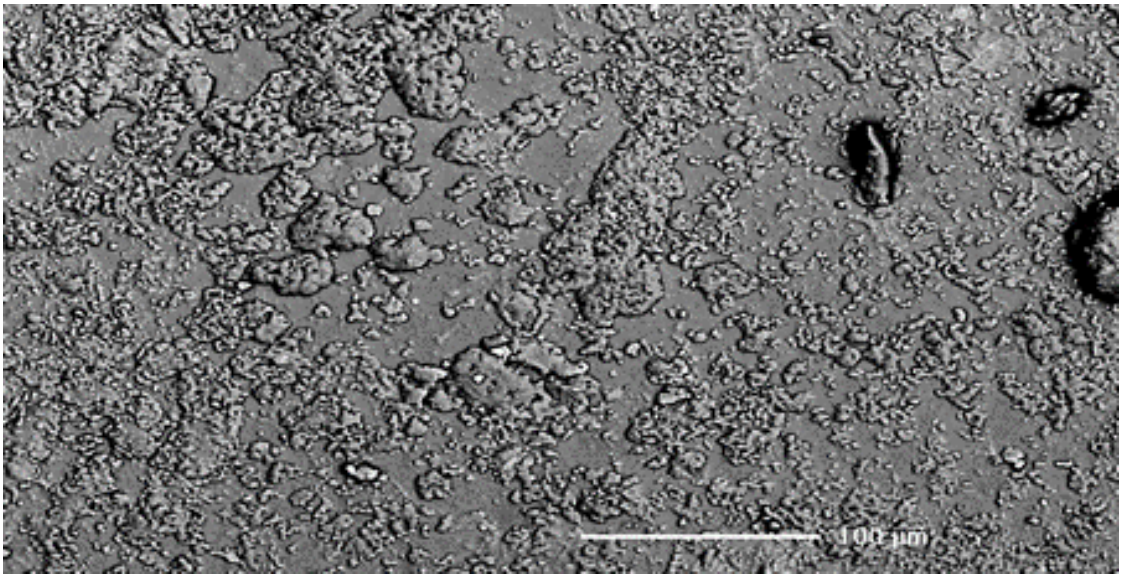

Figure 4. *SEM image of a cross section of final composite in backscattered mode; brighter points display presence of ceramic particles*

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