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Sunny Skaria[a]; Scott R. Schricker[a]
[a] College of Dentistry, The Ohio State University, Columbus, OH

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Synthesis and Characterization of Inorganic-Organic Hybrid Materials Derived from Polysilsesquioxanes (POSS)

SUNNY SKARIA** and SCOTT R. SCHRICKER*

The Ohio State University, College of Dentistry, Columbus, OH

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This article describes two synthetic strategies of biodegradable multi-arm star polymers with a polyhedral oligomeric silsesquioxane (POSS) core. The goal is to develop synthetic strategies towards reinforced biodegradable polymers that can potentially be used in hard tissue engineering. The polymers were characterized including a preliminary evaluation of the cytotoxicity of the POSS-hybrid polymers and the POSS core. A core first strategy employed the ring opening polymerization of ε–caprolactone and/or L-lactide using $Sn(Oct)_2$ as the catalyst and octa hydroxy silsequioxane as the initiating core. The arm first strategy utilized an esterification reaction between octaanhydride functionalized POSS (POSS-SA) molecule and hydroxyl functionalized polyesters. The hybrid polymers were characterized with FTIR, ^{1}H, ^{13}C, ^{29}Si NMR, GPC and thermal analysis. The POSS-polymer ratio can be tailored to obtain polymers with different handling properties, from a solid to a viscous liquid. Preliminary cell toxicology studies of octakis hydroxy POSS and hybrid polymers were evaluated using Myoblast (C2C12 cells) and human osteoblast cells (MG63). The studies indicated that there is no significant cell toxicity exhibited by these POSS derived materials demonstrating their potential use as biomaterials.

Keywords: Silsesquioxanes, scaffold, synthesis, star polymer, biocompatibility

1 Introduction

This work describes the synthesis and characterization of a biodegradable organic-inorganic hybrid nanocomposite that can act as a reinforced scaffold for hard tissue engineering. Utilizing versatile synthetic strategies can lead to materials with a wide variety of properties consisting of the same basic components. For instance, varying the arm length of these hybrid star polymers yields materials that range from liquids at room temperature to solids. Mechanical properties are key parameters in the design of tissue engineering scaffolds for bone and hard tissue regeneration. Several studies have shown that scaffold stiffness influences cellular behavior (1–9). Most polymeric scaffolds do not have the mechanical properties of bone, therefore, it is important to develop synthetic strategies to create reinforced synthetic scaffolds. These scaffolds have a star geometry with a polyhedral silsesquioxane (POSS) core and either poly-lactic acid (PLA) or polycaprolactone (PCL) arms. Initial cytotoxicity assays suggests that the scaffold and its POSS component are biocompatible and non-toxic.

Several strategies have been employed to increase the strength of tissue engineering scaffolds. Matching the initial strength of the scaffold to the bone allows for stress-transfer and weight bearing loads across the defect. Furthermore, reinforced scaffolds will aid in maintaining mechanical properties as the scaffold degrades. The most common is the addition of a filler such as hydroxy appatite to reinforce the scaffold (10-13). The major drawback to this methodology is that filled polymers have reduced processability. This is particularly important if in vivo curing or processing is desired.

Our strategy employs a star-polymer motif with a polyhedral silsesquioxane core. The POSS core will provide mechanical reinforcement, the hybrid design and star geometry will yield a highly functional material that can be easily processed. Previous work has described a poly caprolactone-POSS star polymer (14,15), but our work extends this strategy to create both a core first and arm first strategy. The arm first synthesis uses an octa-anhydride POSS core and is the first example of this functional POSS core. In addition, a cell culture model using an osteoblast and myoblast cell lines, provide preliminary evidence for the biocompatibility of the polymer and POSS core.

*Address correspondence to: Scott R. Schricker, The Ohio State University, College of Dentistry, 3001Q Postle Hall, 305 W. 12th Ave., Columbus, OH 43210, Tel. (614) 688-3367; Fax: (614) 292-9422; E-mail: schricker.1@osu.edu

**Sunny Skaria, Pulpdent Corporation, 80 Oakland Street, Watertown, MA 02471-0780, Tel. (617) 926-6666; Fax: (617) 926-6262; E-mail: skariasunny@gmail.com

Aliphatic polyesters such as polycaprolactone and polylactic acid are of considerable interest due to their potential biomedical applications such as tissue engineering scaffolds, bone fracture fixation and as drug release carriers (16,17). There is a great deal of interest in the synthesis of multi arm-star PCLs and polylactides (PLA) which employ, tri, tetra, octa and multifunctional initiators as well as dendron cores (18,19). The star geometry leads to easily processable functional polymers due to a lower viscosity profile and high number of functional groups compared to linear analogs (20). Star polymers containing a precise number of arms are synthesized either by the core first approach (21) or by the arm first strategy (22). The core first method employs multifunctional core molecule which act as initiator whereas the arm first method uses attaching of the pre-formed polymers to a central core in a later stage. The former method has been more popular due to the availability of a large number of core molecules and the elimination of a fractionation step required in the arm first method to remove excess linear chain polymers.

Polyhedral oligomeric silsesquioxanes are unimolecular organic-inorganic hybrid materials that are used as building blocks for sophisticated structures such as dendrimers and liquid crystals (23-29). Many derivatives of POSS are known because the organic component of POSS can contain a wide variety of functional groups. Methacrylate, epoxy, vinyl, amine and isocyanates allow POSS to be incorporated into both thermoplastic (30-33) and thermoset polymers (29,34). In addition, silane functionalized POSS undergoes a hydrosilation reaction with allyl alcohol to yield a hydroxy functionalized POSS, which acts as an initiator for cationic ring-opening polymerization (35). The hydrosilation reaction is widely used to add functionality to a POSS core due to the mild conditions and good tolerance of functionality (24,35,36).

POSS has also been incorporated into a variety of biocomptable materials such as dental composites and denture base materials (37,38). A poly(ethylene oxide) functionalized POSS was synthesized by the reaction of octa silane POSS with allyl PEG in presence of platinum catalyst (36). Recently hybrid-POSS-polycaprolactone star polymers were synthesized from silsesquioxane cores and have been evaluated as potential biomaterials (14,15,39,40). Kannan et al. reported that POSS-polyurethane nanocomposites exhibit better mechanical, and greater thromboresistance properties compared to their respective polymers (41). However, little is known about the biocompatibility of POSS compounds. Materials that are not designed to be biodegadable still have the potential to release POSS through mechanical and chemical degradation. Therefore it is important to begin to explore the affect of POSS on biological systems.

This work will describe both and arm first and core first synthesis of polycaprolactone and polylactic acid star polymers with a POSS core. The ring opening reaction between the anhydride and the hydroxyl functionalized polyester arm yields a carboxylic group that allows further functionalization. The core first polymerization results in terminal hydroxy groups yielding a highly functional material. We further evaluated the cytotoxicity of the star polymers and POSS core with a cell culture model. Human osteoblast (MG63) and mouse muscle (C2C12) cell lines were cultured on the polymer were evaluated to determine the suitability of these materials as future tissue engineering scaffolds.

2 Experimental

Octa silane POSS was obtained from Hybrid Plastics, MS, USA, ε-caprolactone was purchased from Aldrich Chemical, WI, and used after distillation over CaH_2. L-lactide and the catalyst stannous octoate ($Sn(Oct)_2$), allyl alcohol, Karstedts catalyst (3 Wt.% $Pt(dvs)_2$ in Xylene), N,N-dimethyl aminopyridine (DMAP) and 1,3-dicyclohexylcarbodiimide (DCC) were purchased from Aldrich Chemical, WI, and used as received. Allyl succinic anhydride was purchased from TCI Chemicals, USA. Solvents used in the reactions were purified by distillation. Octakis (3-hydroxypropyldimethylsilyloxy) octasilsesquioxane (POSS-HP, III) was synthesized (Fig. 1) using a known method. Briefly, octasilane-POSS (I) underwent a direct hydrosilylation of allyl alcohol (II) according to a literature procedure (35). Linear monofunctional polycaprolactones (PCL-OH) were synthesized by general laboratory procedure using n-butanol as the initiator and $Sn(Oct)_2$ as the catalyst (42).

2.1 Preparation of Octakis (Propenyl Succinicanhydrido) Polyhedral Oligomeric Silsesquioxane (POSS-SA, V)

To a two-neck oven dried round bottom (RB) flask, 8.0 g (7.85 mmole) of octasilane-POSS (I) was weighed and was dissolved in 60 mL toluene. To this, 10 mL (70 mmole) of allyl succinic anhydride (IV) was added (Fig. 1). The solution was purged with dry nitrogen. Karstedts catalyst (0.05 mL) was then added at room temperature and the reaction was continued for 4 h at 60°C. The reaction was monitored by FTIR for the disappearance of Si-H bond at 2139 cm^{-1}. After completion of reaction, 10 mg PPh_3 was added and stirred for 1 h to deactivate the catalyst. The reaction mixture separated into two phases and bottom layer containing the product was removed and concentrated under reduced pressure. The residue was dissolved in excess ethyl acetate and the polar catalytic impurity was removed by precipitation with n-hexane. Finally, the pure white solid product was obtained after re-crystallization in 7:3 CH_2Cl_2-isopropanol in 89% (15.0 g) yield. Melting point 74°C (determined by DSC). FTIR (cm^{-1}): 2955; 2867; 1863, 1783; 1459; 1414; 1087. ^{1}H-NMR ($CDCl_3$; δ ppm): 3.1 & 2.6 (m, 2H; C$\underline{H}_2$-COO and 1H C$\underline{H}$ COO); 1.6-2.0 (m, 2H, C$\underline{H}_2$-CH); 1.5 (m, -C$\underline{H}_2$-CH_2); 0.6 (t, 2H, Si C$\underline{H}_2$-); 0.1 (Si C$\underline{H}_3$). ^{13}C-NMR ($CDCl_3$; δ ppm):

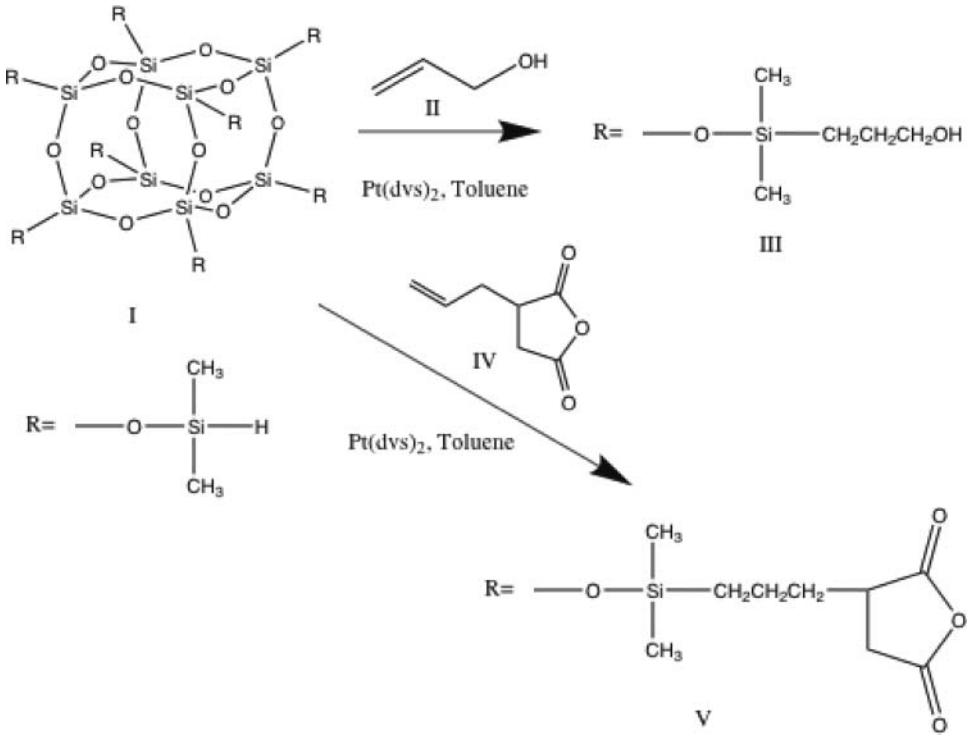

Fig. 1. The synthesis of the octahydroxy and octaanhydride core molecules.

174 (CH-C=O); 170 (CH_2-C=O); 40 (CH-C=O); 34.2 (CH_2-C=O); 34.1(CH_2-Succinic Anhydride); 20.35 (-CH_2-); 17.12 (Si-CH_2-); 0.32 (Si-CH_3).

2.2 Preparation of POSS-star Polycaprolactone (for PPCL10, Core first Approach)

In a typical synthesis, PPCL10 (Table 1) was prepared using the following procedure. POSS-HP (0.5968, 0.4 mmol) was placed in an oven dried 50 mL two-neck RB flask equipped with a reflux condenser and magnetic stirrer and was dissolved in ε-caprolactone (3.42 g, 32 mmole). To this, 5 mL of dry toluene and 20 mg of the catalyst $Sn(Oct)_2$ was added via syringe under nitrogen atmosphere and was placed in a pre heated oil bath of temperature 110°C and the reaction was allowed to proceed for 8 h (Fig. 2). The reaction was cooled and the viscous polymer was dissolved in minimum amount of dichloromethane and was precipitated twice from cold methanol. Yield: 3.7g (92%). FTIR (cm^{-1}): 3535 (O-H); 2939 (C-H); 1732 (C=O); 1166 (C-O); 1089 (C-O-). ^{1}H-NMR ($CDCl_3$; δppm): 4.1 (24H; CH_2-OCO), 3.6 (2H, CH_2-OH); 2.35 (21H, CH_2COO); 1.8–1.4 (72 H, -CH_2-CH_2 -of PCL and from Core), 0.6 (2H, Si-CH_2), 0.06 (6H, Si-CH_3).

Table 1. Synthesis of Multi-arm star POSS-PCL and POSS-PLA

Polymer	*(M)/I*	*Mn (GPC)*	*Mn(NMR)*	*PD*	*Tm °C*	*Tc °C*
PPCL5	5	3448	6200	1.8	15.1	20.8
PPCL10	10	7864	10500	2.2	40.9	14.5
PPCL20	20	13780	19600	1.7	48.0	20.6
PPCL40	40	28262	36500	2.1	51.3	18.8
PPCL80	80	47260	68600	2.4	52.1	23.9
PPCL150	150	59270	86800	1.3	53.5	30.9
PPLA5	5	2565	4280	2.6	n.d.	22.2
PPLA20	20	9632	11800	3.2	138.0	45.3

2.3 Preparation of POSS-Star Polylactides (for PLLA20, Core First Approach)

In a typical synthesis PLLA 20 (Table 1) was prepared using the following procedure. POSS-HP (0.3 g, 0.2 mmol) and L-lactide (4.6 g, 31.9 mmol) were weighed in an oven dried flask and was purged with nitrogen. The reactor was placed in a preheated oil bath of temperature 130°C and was stirred magnetically. After complete dissolution of the core molecule in the lactide melt, 20 mg $Sn(Oct)_2$ was added via syringe under nitrogen atmosphere and allowed to react for 8 h. The polymer obtained was dissolved in dichloromethane and precipitated in methanol. Yield: 4.7 g (96%). FTIR (cm^{-1}): 3508 (O-H); 2994 (C-H); 1748 (C=O); 1454 (C-H); 1090 (C-O), 846. ^{1}H-NMR ($CDCl_3$; δppm): 5.1 (10H, CH_3-CH), 4.4 (1H, terminal CH-OH); 4.0 (2H, CH_2-OCO); 1.4–1.8 (34H, CH_3 of PLA and POSS core), 0.6 (2H, Si-CH_2), 0.06 (6H, Si-CH_3).

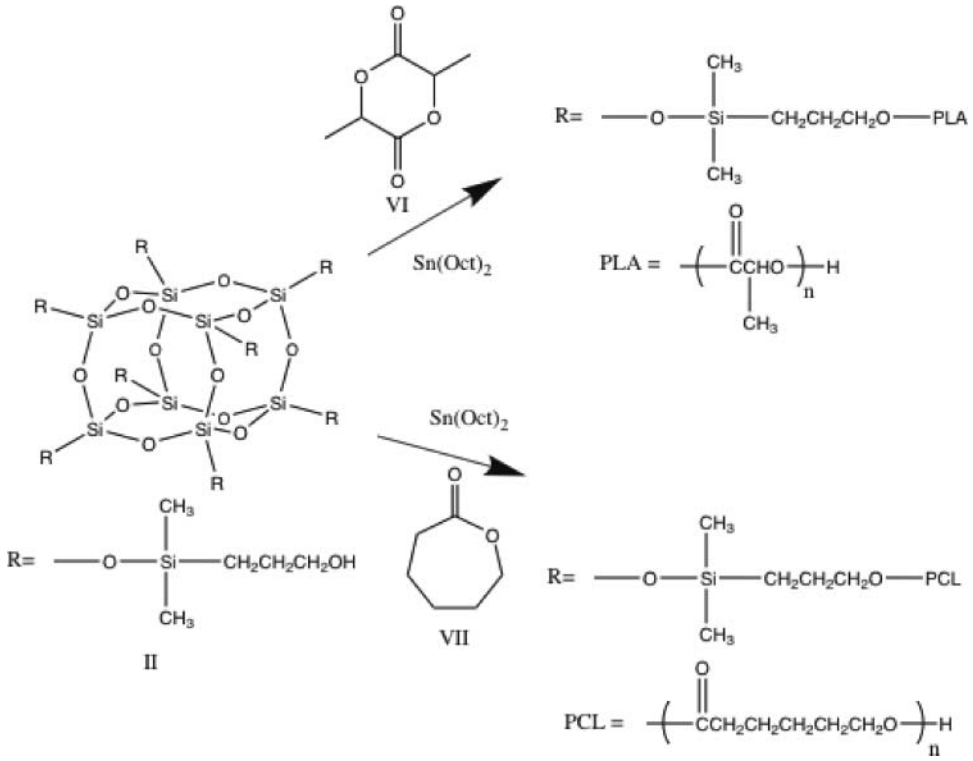

Fig. 2. The core first synthesis of the polycaprolactone and polylactic acid star polymers.

2.4 Preparation of Multi-Arm Star POSS-Polycaprolactones (Arm First Strategy)

In an oven dried flask, POSS-SA (V), (43 mg 0.02 mmol), 800 mg of PCL-OH (0.16 mmol, Mn approx. 5000) and a catalytic amount of dimethyl amino pyridine (DMAP, 20 mg) was dissolved in 20 mL dry 1,4 dioxane (Fig. 3). The reaction was allowed to proceed for 12 h at 70°C, then concentrated and dried under vacuum at 40°C. The residue was further dissolved in 20 mL of dry dichloromethane. To this, 850 mg of PCL-OH and 10 mg DMAP were added was stirred under nitrogen followed by 80 mg (0.388 mmols) of N,N′-dicyclohexylcarbodiimide (DCC). The reaction was allowed to react for another 16h. The dicyclohexyl urea (DCU) formed was filtered off, and the multi arm-star polymer was obtained by selective precipitation from methanol. Yield: 1.1g (67%). FTIR (cm^{-1}): 2990 (C-H); 1732 (C=O); 1454; 1090 (C-O). ^{1}H-NMR ($CDCl_3$; δ ppm): 4.1 (-C$\underline{H}_2$-OCO), 2.35 (-C$\underline{H}_2$COO); 1.8–1.4 (-CH_2-CH_2 -of PCL and from Core) 2.9-1.2 (very minor peaks from the succinyl group), 0.9 (CH_3, butyl) 0.6 (Si-C$\underline{H}_2$), 0.06 (Si-C$\underline{H}_3$).

2.5 Measurement and Techniques

2.5.1. *Nuclear magnetic resonance spectroscopy (NMR)*

^{1}H and ^{13}C-NMR were recorded in deuterated chloroform ($CDCl_3$) on a Bruker 250 MHZ spectrometer. Inverse gated ^{1}H decoupling ^{29}Si NMR was obtained in $CDCl_3$ solution using tetramethyl silane (TMS) as the internal standard.

2.5.2. *Gel permeation chromatography (GPC)*

GPC analysis was carried out at 25°C using THF as eluant at a flow rate of 1 mL/min with a Polymer Labs PLgel MIXED-E (300 × 7.5 mm) (Polymer Laboratories, MA) size-exclusion chromatography column. A dual detector set-up with a Wyatt Technology miniDAWN multi-angle laser light scattering detector, and a Shimadzu refractive index detector were used to collect the data. The analysis was performed with the Astra 4.70 (Wyatt Technology, CA) software package.

2.5.3. *Fourier transform infrared spectroscopy (FTIR)*

FTIR spectra were recorded on a Perkin Elmer Spectrum One spectrophotometer (Perkin-Elmer, MA) as a neat film on KBr.

2.5.4. *Differential scanning calorimetry (DSC)*

Differential scanning calorimetry was carried out on a TA DSC Q 100 series (TA Instruments, DE) with a heating rate of 10°C/ minute under nitrogen atmosphere. Thermogravimetric (TGA) analysis was recorded on a Perkin-Elmer TGA instrument at a heating rate of 20°C/minute in the range of 30–600°C under nitrogen atmosphere.

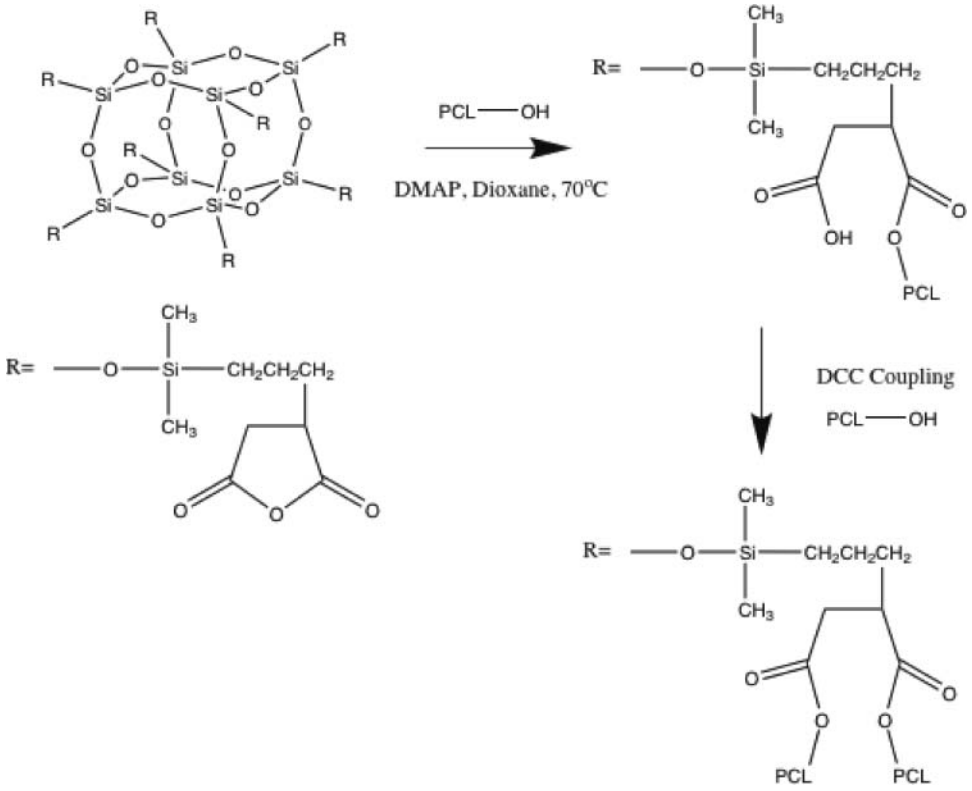

Fig. 3. The arm first synthesis of the polycaprolactone and polylactic acid star polymers.

2.6 Cytotoxicity/Cell Viability Experiment

Human osteoblast (MG63) and mouse muscle cells (Myoblast C2C12 cells) were kindly provided by Dr. Sudha Agarwal (College of Dentistry, The Ohio State University). Always passages of 2-4 were used for the cytotoxicity experiment. The cytotoxicity of the POSS derived materials was determined after incubation with fibroblast and osteoblast cell lines. The cells were maintained in Dullbeco's Modified Eagle Medium (DMEM) and supplemented with 10% fetal bovine serum (FBS), antibiotics (penicillin and streptomycin) and incubated in 5% CO_2 incubator at 37°C. To determine cell cytotoxicity, well plates were seeded at a density of 2×10^4cells/well in 24 well plates at 37°C in 5% CO_2 atmosphere. After 24 h, the medium in the wells was replaced with fresh medium and 5 mg of POSS derived material or a solution of POSS derived materials in dimethyl sulfoxide (DMSO) (50 μL of 10 wt% solution) were added to the well. After 24 h (or 48 h) the detached cells in the medium were stained with trypan blue and counted using hemocytometer where as the cells attached were counted after staining with trypan blue. The relative cell viability (%) related to controlled wells containing cell culture medium was calculated from the number of living and dead cells in the medium and in the plate.

3 Results and Discussion

3.1 Core Synthesis

The synthesis of octakis allyloxy-POSS by the hydrosilylation reaction of octa silane POSS (I) with allyl alcohol (II) using Karstedts catalyst in toluene was described in detail by Laine et al. (35) We have adopted a similar experimental procedure (Fig. 1) for the synthesis of the POSS core molecule, Octakis(3-hydroxypropyldimethylsilyloxy) octasilsesquioxane (POSS-HP, III). As reported previously, the reaction was exothermic, which in turn raised the temperature of the reaction medium to reflux. The reaction proceeded very smoothly and a nearly quantitative conversion was obtained in 30 minutes. The progress of the reaction was monitored by FTIR for the disappearance of the Si-H bond at 2139 cm^{-1}. The hydrosilylation of POSS-octa silane with allyl succinic anhydride also occurred in the presence of Karsted's catalyst in toluene (Fig. 1). A slightly higher temperature of 60°C was required to complete the reaction. There was no significant heat liberation (exotherm) was observed for the hydrosilylation reaction between POSS and allyl succinic anhydride indicating slower reaction kinetics. The product was obtained as a white solid with a melting point of 74°C and a glass transition temperature of –3.98°C as determined by DSC. The absence of an FTIR

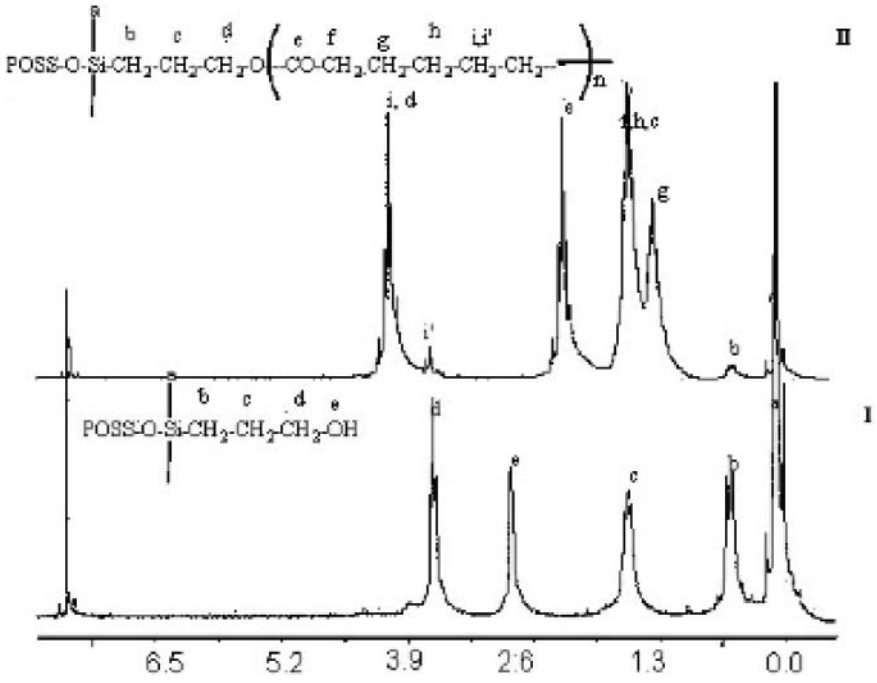

Fig. 4. ^{1}H-NMR spectra of the POSS-HP core (I) and the polycaprolactone star polymer (II).

stretch corresponding to a COOH group (at 1722 cm^{-1}) demonstrates that there was no hydrolysis of the anhydride groups under the present experimental conditions.

3.2 Core First Preparation of the Star Polymers

Polycaprolactones and polylactides are generally synthesized by the ring opening polymerization (ROP) of cyclic lactones or lactides using an organometallic catalyst such as tin ethyl hexaoate ($Sn(Oct)_2$) in the presence of a hydroxyl functional initiator. The ROP of lactones using ($Sn(Oct)_2$) are known to occur in pseudo-living pathway and the molecular weight of the polymers depends on the monomer/initiator ratio (42). The multi-arm star polymers were generated by the ROP of lactide (VI) or ε-caprolactone (VII) in the presence of octahydroxy core molecule using $Sn(Oct)_2$ as the catalyst. The core molecule was soluble in either ε-caprolactone or molten lactide allowing polymerization in bulk. The reaction is depicted in Figure 2. Star polylactides were synthesized in bulk whereas star polycaprolactone was synthesized in solution of toluene and ε-caprolactone (50/50 V/V) in order to reduce the viscosity of the reaction mixture.

The polymerization of lactide was conducted at a temperature of 130°C while that of ε-caprolactone at 110°C. A polymerization reaction temperature for the star-polycaprolactone above 130°C resulted in gelation of the polymer. This may be attributed to either the transesterification of the ester bonds or side reactions occurring at the core initiator molecules facilitated by the organometallic catalysts used in the polymerization. All the polymerization reaction was carried out for 8 h for the optimum conversion and the yields of the polymers were more than 90% in all cases. As noted in the literature, (18,43) the monomer-catalyst ratio does not have any significant effect on the molecular weight of the polyester, so all the polymerization reactions were conducted at a constant monomer-catalyst molar ratio of 400:1. The arm lengths and the molecular weights of the polymers were adjusted by controlling to the ratio of initiating hydroxyl groups to the monomer.

3.3 ^{1}H-NMR

NMR (^{1}H) spectroscopy was used to estimate the relative concentration of POSS unit in the polymer and the degree of polymerization of the caprolactone and or lactide arms (Table 1). The number of caprolactone repeat units in the PCL polymer was calculated from the ratio of the integrals of the (-C$\underline{H}_2$-O-CO) methylene which appeared at 4.08 ppm to that of Si-C$\underline{H}_2$ methylene belonging to the core molecule appears at 0.6 ppm. Similarly, the chain lengths of the polylactides were determined from the ratio of C$\underline{H}$ peak at 5.1 ppm to the Si-C$\underline{H}_2$ peak at 0.6 ppm. The absence of resonances due to the CH_2-O$\underline{H}$ group of the core molecule at 2.6 ppm indicates that all the hydroxyl terminals of the POSS core (POSS-HP) initiated a polymerization reaction. New resonances due to the esterification of terminal C$\underline{H}_2$OH group of POSS core molecule were observed at 3.9–4.1 ppm and overlap with signals from PCL chains. This change is accounted for in the estimation of the DP of polycaprolactone arms. Assuming that all the

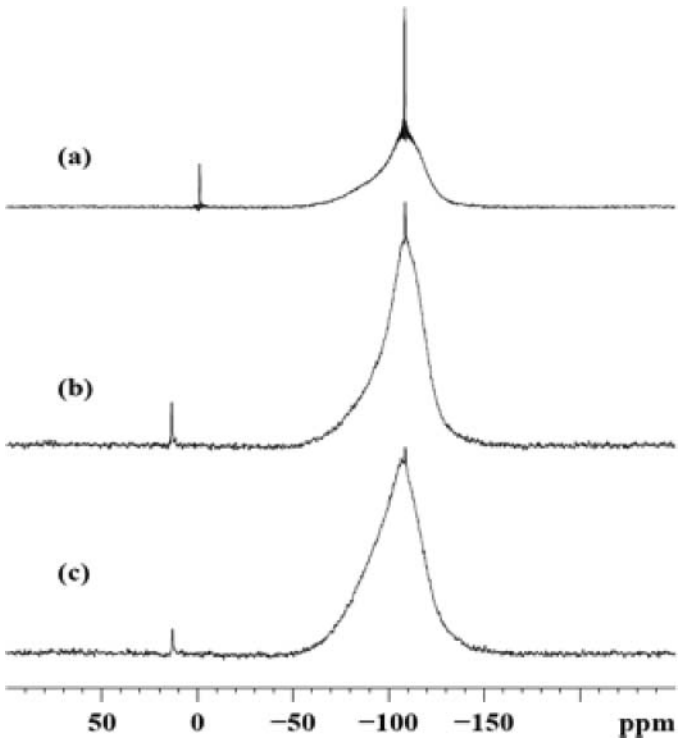

Fig. 5. ^{29}Si NMR spectra of (a) Silane POSS. The peak at -1.4 ppm corresponds to (O-Si$(CH_3)_2$-H and the broad peak at -110 ppm corresponds to (Si-$(OSi)_4$) (b) POSS-HP. The peak at 12.9 ppm and -110 ppm corresponds to (O-Si$(CH_3)_2$-CH_2 and Si-$(OSi)_4$) respectively (c) polycaprolactone star polymer. The same peaks from the POSS-HP are observed in this spectra. No peaks corresponding to Si-OH (99-100 ppm), which would result from a backbiting reaction, are observed.

hydroxyl end groups of the core molecule initiated the ring opening polymerization of the respective monomers, the average chain lengths of each arm can be determined. Thus, the estimation of the POSS content and arm lengths were determined from the ratio of resonances at 0.6 ppm (Si-CH_2) to that of caprolactone chains at 4.1 ppm or at 2.5 ppm. The ^{1}H-NMR spectrum of the polymers is presented in Figure 4. In the case of polylactides, new resonances were detected for the group POSS-CH_2-OC=O at 4.1 ppm and the resonance due to terminal CH-OH was observed at 4.5 ppm. The estimated arm lengths of the star polymers from the ^{1}H-NMR data were in accord with the expected result from the monomer-initiator ratio in the feed.

3.4 ^{29}Si NMR

It is known that POSS-HP compounds can undergo cleavage due to back biting reaction of the hydroxyl groups on the silyloxy group of POSS core in polar media. Laine and coworkers (35) have detailed the backbiting reaction of POSS-HP in polar solvents like methanol resulting the formation of silanol group in the core molecule with the liberation of 2,2 dimethyl 1-oxa silacyclopentane. We have conducted ring opening polymerization reaction of ε-caprolactone and the reaction was studied by ^{29}Si NMR for possible detection of Si-OH group in order to investigate whether any backbiting reactions occur in the polymerization reaction. The silicon NMR spectrum of octa silane POSS has a characteristic chemical shift at –1.4 ppm (O-Si$(CH_3)_2$-H) and at –110 ppm (Si-$(OSi)_4$). Similarly the silicon NMR spectrum of POSS-HP, and hybrid polymer POSS-PCL, has a chemical shift values at 12.9 ppm and -110 ppm corresponds to (O-Si$(CH_3)_2$-CH_2) and (Si-$(OSi)_4$) respectively. The absence of a peak in the 99–100 ppm range indicate the absence of Si-OH groups in the core. This demonstrates that there was no backbiting under the polymerization conditions. The silicon NMR spectra are presented in Figure 5.

3.5 Arm First Preparation of the Star Polymers

The possibility of preparing multi-arm star polymer by arm first strategy has also been explored. Monohydroxy polycaprolactones of controlled molecular weight were prepared by initiating PCL polymerization in presence of n-butanol using $Sn(Oct)_2$ as the catalyst. We used the anhydride-nucleophile esterification chemistry to attach polymer chains to the POSS core. The hydroxyl terminated PCL arms were attached to POSS core through a reaction with POSS-SA in 1,4 dioxane in the presence of a catalytic amount of DMAP at 70°C. The ring opening reaction between anhydride units and hydroxyl functional reagents generates compounds with carboxylic functional compounds. The carboxylic acid groups were then further catalytically esterified by DCC coupling reaction to generate a sixteen arm POSS-PCL. The reaction is presented in Figure 3. The removal of any unreacted PCL-OH arms from the star polymer was attained by selective precipitation of the star polymer in hexane and methanol. FTIR spectroscopy and ^{1}H NMR spectrum of the multi arm star polymer did not show presence of any terminal CH_2-OH peaks that clearly indicates the absence of any unattached linear polymer in the star polymer. The successful grafting of PCL chains onto POSS cores are further evidenced from the FTIR, NMR and GPC studies.

3.6 Molecular Weight Characterization

The molecular weight of the polymers was measured by GPC using THF as eluant. The GPC results show a high molecular weight shoulder possibly due to aggregation, with a polydispersity value ranging from 1.3-2.5. The high molecular weight shoulder suggests aggregation and polymer functionalized POSS molecules have shown aggregation behavior in solution (44,45) The low polydispersity of the polymers can be explained by the pseudo-living character of the polymerization. Though the $Sn(Oct)_2$ initiated ROP is not strictly living, it is known to generate

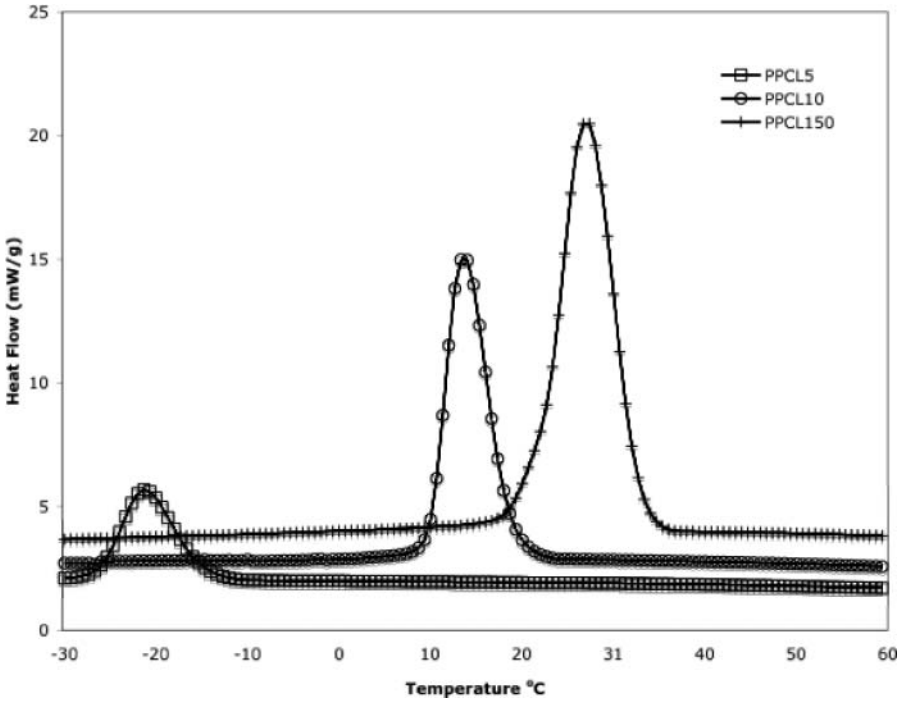

Fig. 6. Crystallization temperature as measured by DSC. PPLC5 polycaprolactone star polymer with an arm length of 5 repeat units; PPCL10 arm length of 10 repeat units; PPCL150 arm length of 150 repeat units.

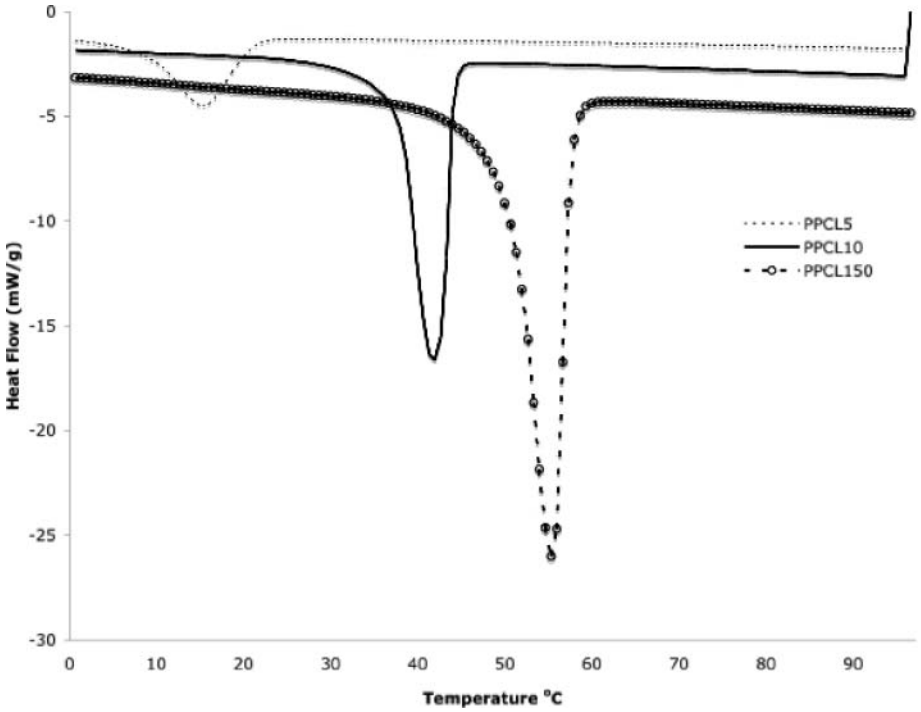

Fig. 7. Melting temperature as measured by DSC. PPLC5 polycaprolactone star polymer with an arm length of 5 repeat units; PPCL10 arm length of 10 repeat units; PPCL150 arm length of 150 repeat units.

polymers with narrow molecular weight distributions, good molecular weight control and quantitative yields (46). The molecular weight obtained by NMR is much higher than that obtained with GPC and is attributed to the spherical structure of star shaped polymers which posses a different hydrodynamic volume compared to that of linear polystyrene standards we used for calibration. The molecular weights and the polydispersity of the polymers are presented in Table 1. The GPC chromatogram of multi arm star PCL prepared by arm first strategy did not show any characteristic retention volume corresponding to linear PCL.

3.7 Thermal Characterization of the Star Polymers

Due to the spherical molecular architecture of the star polymers, it is known that these polymers exhibit different physico-chemical properties compared to their linear analogues. The DSC thermograms of the polymers show a unimodal melting endothermic peak, Tm as well as an exothermic crystallization peak, Tc. The thermal properties of the star polymers are reported in Table 1. The typical DSC scans of POSS-PCL star polymers are presented in Figures 6 and 7. From the table it is clear that the multi-arm star polymer show decreased Tm and Tc compared to the linear analogues. Multi-arm star polymers and branched polymers are generally exhibit lower Tm and melting viscosity values compared to their linear analogues (20,39). Polymers prepared by arm first strategy also showed a similar trend, exhibits lower melting points (54.8°C) compared to the individual arms we have used in the synthesis, PCL-OH (58.2°C), despite of the dramatic increase in the molecular weight. The optical microscopy of the PPCL150 and PPCL40 showed similar spherulite structure (not shown) as of linear polycaprolactone.

Thermogravimetric analysis (TGA) was used to evaluate the thermal stability of the multi-arm star polymers as well as the residual POSS content of the polymer. TGA of POSS-HP and POSS-PCL polymers were recorded in the range of 30–600°C at a heating rate of 20°C/min under nitrogen atmosphere. The core molecule and the multi-arm star polymers have similar degradation profiles as expected. For the control linear polycaprolactone, initial thermal degradation was started around 250°C and complete degradation was observed at 550°C. The thermograms are presented in Figure 8. POSS-HP has a residual silica content of 56% which is lower than the theoretical POSS content of POSS-HP (64.8%), based on the assumption that all the silicon present in core POSS molecule has been converted to silicon dioxide. In an earlier study, Laine et al. also reported a lower residual ceramic content in POSS-HP molecule, which is probably attributed to the partial loss of silicon by the possible backbiting reactions yielding a volatile 2,2 dimethyl 1-oxa silacyclopentane (35).

The residual silica content of PPCl10 is 8.53% instead of 9.01% and that of PPCL20 is 4.75 instead of 4.86. The

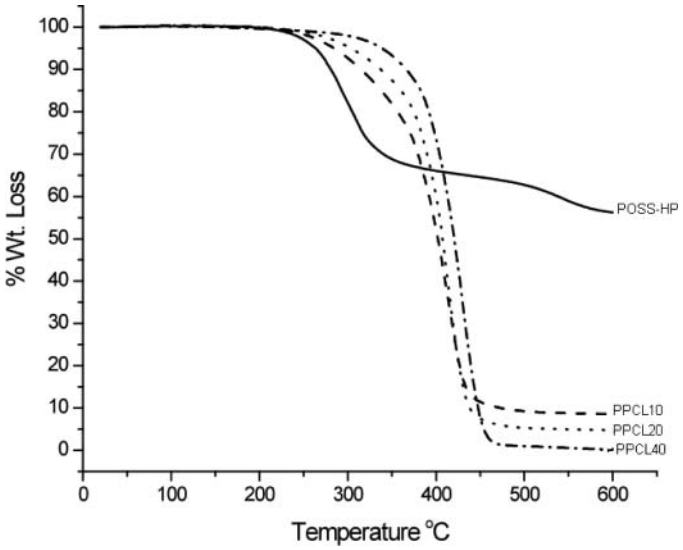

Fig. 8. Degradation temperature as measured by TGA. POSS-HP is the Hydroxy POSS core, PPLC10 polycaprolactone star polymer with an arm length of 10 repeat units; PPCL20 arm length of 20 repeat units; PPCL40 arm length of 40 repeat units.

TGA data supports the claim that there is no significant backbitting reaction during polymerization or unreacted hydroxyl groups. Either the backbitting reaction or free core hydroxyl groups would result in less residual silicon. The ^{1}H and ^{29}Si NMR provide further evidence that very little backbitting took place.

3.8 Cell Viability Studies

In order to investigate the cytotoxicity of these polymers, we have conducted the cytotoxicity experiments for two different cell lines the C2C12 rat muscle myoblast cells and the MG63 human osteoblast cells. The results are presented in Figure 9. The results are normalized to that of control experiment which is set at 100%. We have not observed any significant reduction in the number of living cells compared to the control. Our results show that the studied cells are viable in presence of the POSS hybrid material. Any observed toxicity of the polymers could be due to degradation products or from the leaching of low molecular weight soluble components. As these polymers are insoluble in the cell culture media, we have also conducted experiments with polymer solutions in DMSO. Though the POSS-PCL and POSS-PLA polymers precipitated in the cell media, a dispersion of the core (POSS-HP) was obtained. Both experiments are comparable and did not show any significant toxicity towards these cell lines. As we do not fully understand the degradation of POSS derived materials, a more detailed investigation is needed.

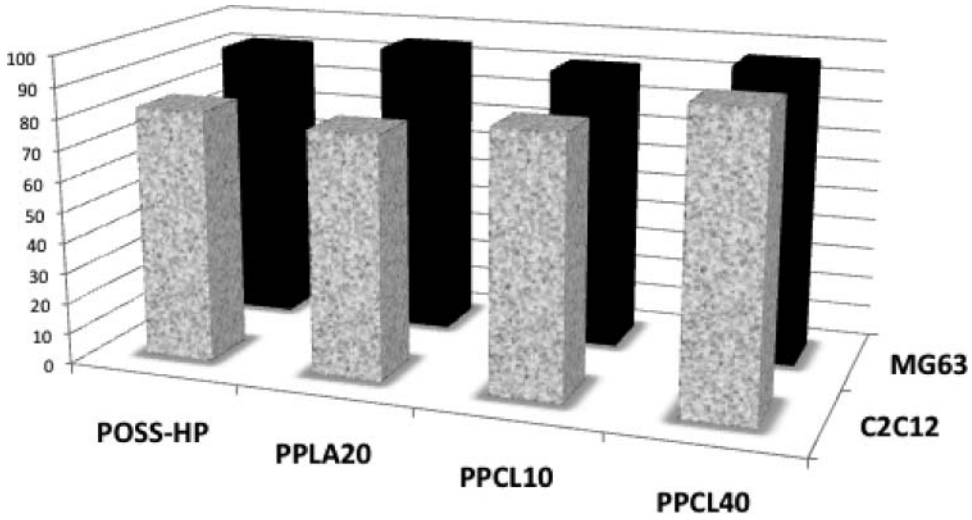

Fig. 9. Percentage of Surviving Cells Compared to Control. MG63 are a human osteoblast (MG63) cell line, C2C12 are a mouse muscle cell line (Myoblast C2C12 cells). The cells were grown on POSS-HP, hydroxy POSS core; PPLA20 polylactic acid star polymer with an arm length of 20 units; PPLC10 polycaprolactone star polymer with an arm length of 10 repeat units; PPCL40 arm length of 40 repeat units.

4 Conclusions

Multi-arm star polycaprolactone-POSS hybrid polymers were prepared by core first approach and by arm first strategy. The synthesized multi-arm star polymers exhibit lower Tm and Tc values corresponding to their linear analogues which further indicate the branched architecture of the polymer. The arm lengths of the polyester chains could be tailored by controlling the amount of ε-caprolactone and POSS-HP in the feed. The calculated amounts of POSS in the hybrid polymers are in accordance with theoretical ratios. The functionalization of POSS anhydrides with hydroxyl polymers is a versatile modification technique for modification of POSS. POSS-SA could be used for the synthesis of multi-arm polymers and thus, could judiciously tailor the properties of hybrid polymers. The preliminary cytotoxicity experiments with these hybrid polymers show there is no significant cell toxicity exhibited by these materials towards C2C12 and MG63 cell lines. We are now investigating the development of POSS containing biomaterials for soft and hard tissue scaffolds.

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