Synthesis and Characterization of Hybrid Polymers as Bioactive Ceramics for Bone Regeneration

Alaa M. Ayed[1] Ali S. Ismail[2]*
[1]Department of Chemistry, College of Education for Pure Sciences, University of Anbar, Ramadi, Iraq
[2]Department of Chemistry, College of Education for Pure Sciences, University of Anbar, Ramadi, Iraq.
Email: alaamohammed945@gmail.com
Email: sami@uoanbar.edu.iq

Abstract
Herein, an organic–inorganic hybrid bioactive polymer, namely, random hybrid bioactive ceramic copolymer (EMA-*co*-TMSPMA-*co*-HPMA), for bone regeneration is synthesized and characterized. An organic–inorganic hybrid biopolymer gel (EMA-*co*-TMSPMA) was first prepared as a polymer base for the bioactive polymer. Both polymers are intended for bone regeneration. Both polymers are prepared from ethyl methacrylate, 3-(trimethoxysilyl)propyl methacrylate, and hydroxypropyl methacrylate through free-radical polymerization using benzoyl peroxide as the initiator in the presence of a $CaCl_2$ solution that released Ca^{+2} ions to stimulate the formation of surface apatite $CaO–SiO_2$ via the sol–gel method. Fourier transform infrared spectroscopy was used to confirm the skeletal structure of the polymers. FT-IR spectra showed that all the obtained bands corresponded to the chemical composition of the polymers. Further, chemical structures of the polymers were analyzed using X-ray diffraction to confirm the formation of an apatite layer through the binary system $CaO–SiO_2$ on the surface of the polymer. Thermogravimetric analysis and derivative thermogravimetric analysis were performed for the random hybrid ceramic bioactive copolymer to understand its thermal stability. By synchronizing these results with the gravimetric derivative, a peak of the mass-loss temperature of the polymer was found.
Keywords: hybrid, bioactive polymer, bone regeneration, apatite layer, methacrylate, hybrid ceramic.

Introduction

During the Vietnam war, specifically in 1969, the first bioactive glass was prepared by Professor Larry Hench from the University of Florida, USA, at the request of a colonel in the US Army. Hench knew that the previously used materials included minerals and polymers that could be infused with bones. Most of these materials did not have chemical or biological links with bones, and thus, triggered fibrosis after transplanting with the bone tissue. Therefore, Hench developed a biodegradable bioactive glass with a high calcium content. The composition of the prepared bioactive glass had different proportions of raw materials and it was named the $Na_2O–CaO–SiO_2–P_2O_5$ system. At that time, Hench's bioactive glass was called bioglass 45S5 but was later renamed to 45S5 to indicate its composition. One of the characteristics of 45S5 is that it forms strong unbreakable bonds with bones. The efficiency of 45S5 is attributed to its attachment to the bones via the formation a hydroxycarbonate (HCA) apatite layer on the glass surface. [1] It is believed to be close to the bone tissue, and it interacts with the collagen fibers in the host bone. Then, the bioglass dissolves in the bone matrix because of the decomposition of silica and calcium ions and the presence of hydrophilic groups in the glass. This discovery led to the establishment of the fields of bioactive glass and ceramics, and many novel materials were prepared with different compositions of bioactive glass and ceramics [1-4]. Afterward, studies continued to use methacrylate monomers with inorganic monomers containing silica for preparing bioactive ceramics because the resulting polymer exhibited excellent mechanical properties. Notably, most of the published studies in this field used methyl methacrylate monomers as an organic component with methacrylate monomers, and it contains silica or silicone compounds such as tetraethyl orthosilicate (TEOS), dimethyldiethoxysilane (DMDES), and vinyltrimethoxysilane as inorganic components. To delve deeper into the biologically active glass bone regeneration scaffolds that can be considered artificial bone scaffolds that stimulate the regeneration of new bone despite the difficulty of conducting clinical application due to its mechanical properties that do not reach high hardness and therefore are almost fragile and not compatible with the high Young model[5-12].

To achieve the main conditions for preparing artificial bone scaffolds, it is necessary to synthesize materials exhibiting high bone bonding strength between the surface of these scaffolds and the bone defects when

doi.org/10.31838/hiv23.02.215 Received: 08.10.22, Revised: 16.11.22, Accepted: 23.12.22

implanted. It can be reinforced in Ca^{2+} ions to form an apatite layer CaO–SiO_2 as a binary system. This support enables the development of bone scaffolds as bone substitutes exhibiting a biological activity and stiffness similar to that of natural bone, particularly if a hybrid organic–inorganic polymer containing an apatite layer is prepared or in the presence of a simulated body fluid or so-called Kokubo solution[13-14].

An early study on using copolymerization to prepare hybrid polymers for bone regeneration focused on preparing a polymer for in vivo applications, where Justin J. Chung [15-17], and he could prepare a hybrid polymer structure from copolymers methyl methacrylate and 3-(methacryloxy)propyl methacrylate through several methods. The synthetic strategy started with controlled polymerization, followed by the preparation of copolymers methyl methacrylate and 3-(trimethoxylyl)propyl methacrylate through reversible addition fragmentation chain transfer and group transfer polymerization to produce well-defined polymers.

Wie et al. [8] studied the thermal stability, density, and hardness of the polyacrylate–SiO_2 hybrid glassy polymer synthesized from polymer 3-(trimethoxysilyl)propyl methacrylate (TMSPMA) and comonomer methyl methacrylate through free-radical polymerization using benzoyl peroxide (BPO) as an initiator and TEOS as a silica network via the sol–gel method, depending on organic and inorganic components. Wie et al. [8] found that the thermal stability of the hybrid glassy polymer increased with increasing the molar ratio of TMSPMA, and the density and hardness of the polymer could be increased by increasing the content of SiO_2 in the hybrid polymer through heat treatment of materials at 200°C, and the density to hardness ratio of the hybrid polymer reached 16% without any degradation of the polymer structure.

Herein, an organic–inorganic hybrid polymer (EMA-*co*-TMSPMA) was prepared using ethyl methacrylate (EMA) and 3-(methoxylyl)propyl methacrylate monomers and BPO as an initiator through free-radical polymerization. Using the sol–gel method, first, a gelatinous polymer was prepared, and then, a bioactive ceramic polymer was prepared by introducing a third monomer, namely, hydroxypropyl methacrylate, containing the hydrophilic OH group to reinforce the polymer matrix with an apatite layer.

Experimental Section

Methodology

The linear hybrid copolymer (EMA-co-TMSPMA) was prepared via one-pot polymerization of an organic monomer (EMA) with an inorganic monomer (TMSPMA). EMA (0.0858 mol, 9.80 mL) and TMSPMA (0.0072 mol, 1.8 mL) were added to a Schlenck flask, followed by the addition of 20 mL of ethanol as a solvent. The flask was closed tightly, and then BPO (0.5 mL) was injected in the flask under an N_2 atmosphere. The beaker was immediately placed in an electric oven at 70°C for 3 h to start polymerization. While the beaker was in the oven, $CaCl_2$ (0.03 mol, 3.00 mL) was added to the flask. After the heating process, the hybrid polymer was dried for two weeks at room temperature to form a bulk gel. Figure 1 shows the preparation of hybrid linear polymer EMA-*co*-TMSPMA.

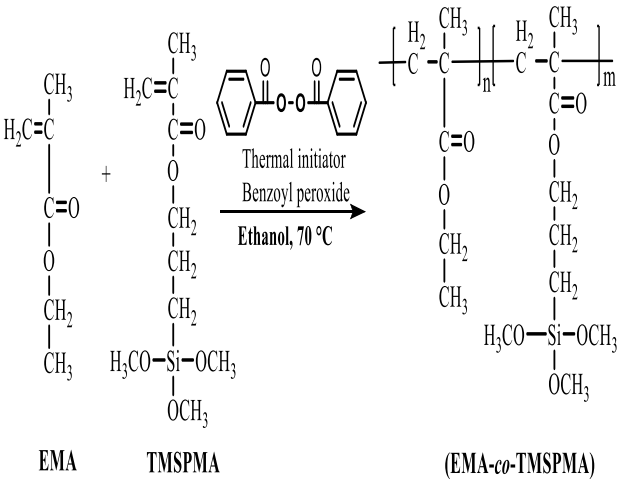

Figure 1. Synthetic route of hybridized gel polymer EMA-co-TMSPMA.

Then, a second random bioactive hybrid polymer was prepared in a flask using the same volumes of EMA and TMSPMA as the first polymer but with a third monomer, hydroxypropyl methacrylate (0.055 mol, 8.00 mL), which provided a hydrophilic polymer matrix in the hybrid and also helped form silanol group (Si–OH) aggregates. Then, BPO (0.5 mL) was injected into the flask under an N_2 atmosphere. The beaker was immediately placed in an electric oven at 70°C for 3 h to start polymerization. While the beaker was in the oven, $CaCl_2$ (0.03 mol, 3.00 mL) was added to the flask, which formed an apatite layer CaO–SiO_2. The layer is formed when the hybrid is combined with calcium chloride by dissolving calcium ions with bioactive glass in the presence of the silanol group (Si–OH) in the silica gel formed on the surface. This led to the incorporation of calcium ions (Ca^{2+}) and the Si–OH group into a binary system (CaO–SiO_2). Figure 2 shows the reaction for preparing solid hybridized polymer EMA-*co*-TMSPMA-*co*-HPMA.

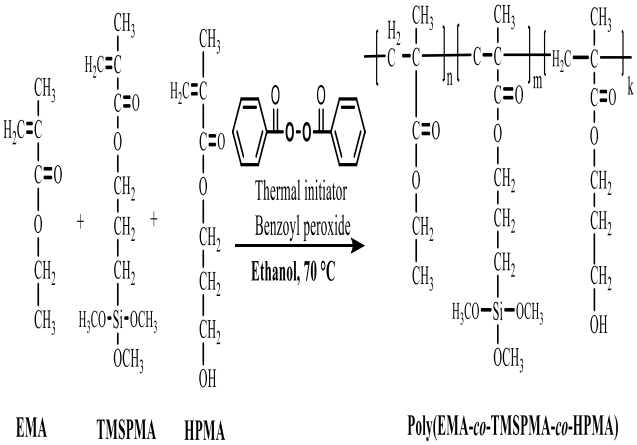

Figure 2. Synthetic route of hybridized polymer (EMA-co-TMSPMA-co-HPMA).

Figure 3 shows an image of a sample of hybridized solid hybrid polymer EMA-*co*-TMSPMA-*co*-HPMA synthesized via the route in Figure 2.

Figure 3. Image of a sample of the hybridized solid hybrid polymer (EMA-co-TMSPMA-co-HPMA)

Results and Discussion

The Fourier transform infrared (FT-IR) spectrum of hybrid copolymer (gel) (EMA-*co*-TMSPMA) shows that it contains Ca^{2+} ions. Figure 4 shows the FT-IR spectrum of the gelatinous polymer presenting vibrational transitions of the polymer. The peak of free silanol Si–OH groups is observed at 3850 cm^{-1} and at the peaks 3740–3675–3646 cm^{-1}, where the first is attributed to the precipitated silanol groups that can be reached, then the signal disappears, while the other peaks indicate the range of surface or terminal free silanol groups,

The FT-IR spectrum of the hybrid copolymer also shows a medium and broad peak at 3411 cm^{-1}, indicating the presence of OH from the alcoholic solvent in the gel polymer, which was not removed. The spectrum also shows a weak peak at 2918 cm^{-1}, attributed to C–H from CH_2–CH_2–Si. The peaks of the Si–H group at 2329 and 2359 cm^{-1} are also easily identified as there is no interference from other bands in this part of the spectrum. A rather sharp peak is observed at 1708 cm^{-1}, attributed to the carbonyl group. This peak appears because of the multiplicity of carbonyl groups in the polymer as it contains two monomers (one organic and one inorganic). The important spectral region is 1000–1100 cm^{-1}, which includes the appearance of an expansion peak at 1063 cm^{-1} of the Si–OCH_3 group and a peak at 3850–3740 cm^{-1}, attributed to the silanol groups. The presence of these peaks indicates that the polymer is successfully prepared. The other peaks observed at 669 and 464 cm^{-1} correspond to the bending vibrations of one of the two groups Si–C or Si–O, respectively.

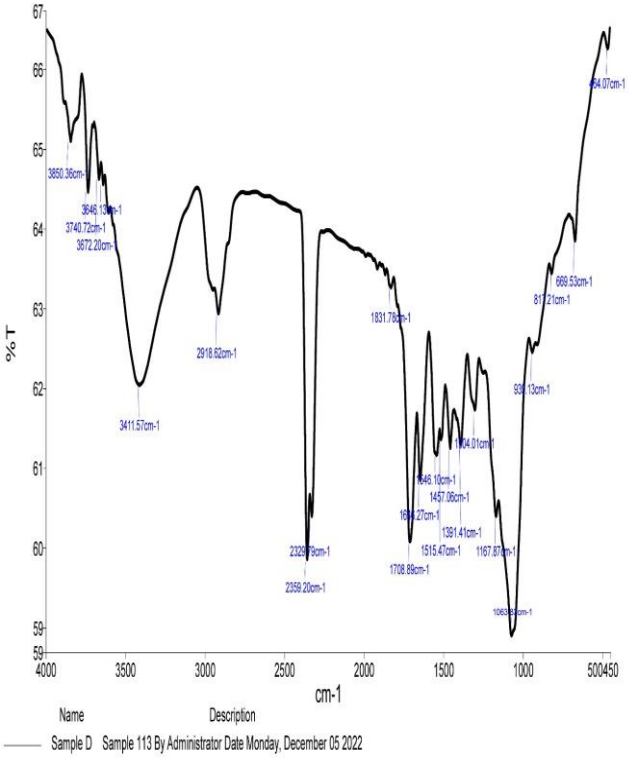

Figure 4. FT-IR spectrum of bioactive copolymer EMA-co-TMSPMA.

Then, the FT-IR spectrum of bioactive hybrid polymer (random) EMA-*co*-TMSPMA-*co*-HPMA is verified to understand its chemical composition. The composition of EMA-*co*-TMSPMA-*co*-HPMA is similar to the previous polymer except that it contains HPMA as a hydrophilic monomer. Further, $CaCl_2$ solution was added to release the calcium ion (Ca^{2+}). The FT-IR spectrum of EMA-*co*-TMSPMA-*co*-HPMA (random) is similar to that of the gel polymer, which indicates that they have similar structures, as the samples of the gel and solid hybrid polymers with hydrophilic and hydrophobic bioactivities under study indicate the presence of similar peaks in both polymers [18,19]. More importantly, it is the decay of the OH group and its appearance as a weak and broad peak at 3413 cm^{-1} to indicate the diminishing concentrations of the alcohol solvent in the solid polymer, which was eliminated due to the different preparation conditions of temperature and time. The spectrum of the bioactive hybrid polymer exhibits peaks at 3849, 3734, 3674, and 3618, cm^{-1} (Figure 5). The two main peaks at 3734 and 3849 cm^{-1} correspond to the precipitated and terminal silanol groups, respectively.

The remaining peaks in the IR spectrum of the bioactive organic–inorganic hybrid polymer (solid) (EMA-*co*-TMSPMA-*co*-HPMA) are similar to those in the spectrum of the gel polymer with a spectrum change in the vibrational transitions. The remaining Si–OCH_3 group in the polymer exhibits a sharp peak at 1042 cm^{-1}, and this polymer also indicates that the polymer has been successfully prepared. The wide range of IR peaks allowed the clarification of relevant minor differences between the two observed polymers.

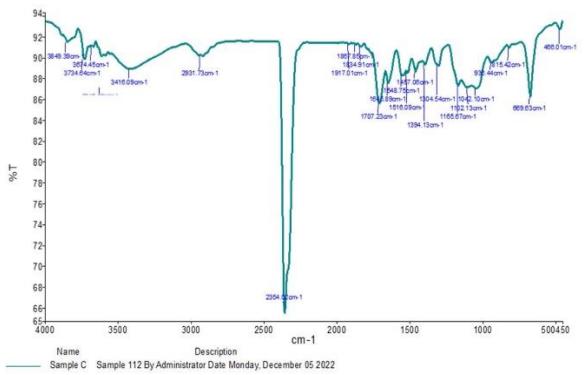

Figure 5. FT-IR spectrum of bioactive copolymer EMA-co-TMSPMA-co-HPMA.

X-ray analysis data of the biologically active organic–inorganic hybrid polymer (EMA-*co*-TMSPMA-*co*-HPMA) were verified. While the nature of the prepared polymer is gelatinous initially, it hardens eventually when left for two weeks to form bioactive glass. Figure 6 shows a broad peak at 18.32°, indicating the presence of the binary system (CaO–SiO_2). It is possible to identify the apatite phase from the two peaks that lie between 45 and 25°, particularly at 31.00° and 43.20°, with low crystallinity, the binary system and the apatite phase contained in the biologically active hybrid polymer based on methacrylate monomers with the ability to form apatite.

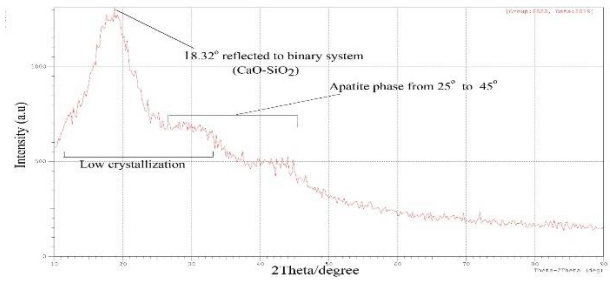

Figure 6. X-ray diffraction analysis of hybrid copolymer EMA-co-TMSPM-co-HPMA.

Thermal analysis of the random hybrid copolymer (EMA-*co*-TMSPMA-*co*-HPMA) was conducted. The preparation and thermal stability determination of the copolymer were confirmed using thermogravimetric analysis (TGA) and derivative thermogravimetric (DTG) analysis to investigate the reliable quantitative and qualitative evaluation of the TGA curve Which is almost impossible without obtaining a thermogravimetric analysis derivative that gives the height of the DTG peak at any mass-loss temperature, namely, the initial temperature T_i and the final temperature T_f and the maximum temperature T_{max} of the rate of mass loss, according to a thermal equilibrium capable of recording the TGA and DTG curves simultaneously at the same time [20].

Thermal analysis was performed at a temperature ranging from +25°C to +810°C at a heating rate of 20 °C/min in air. The weight of the sample used in the analysis was 5.7794 mg. As shown in Figure 7, there are six steps for polymer decomposition.

The decrease in the weight percentage of the hybrid polymer is owing to the elimination of moisture from the polymer. The solvent, especially the entrapped solvent, contributes the largest share to the decrease in weight percentage. The formation of the hybrid polymer structure that contains bonds –O–Si– and –C–Si– showed superior thermal oxidation resistance owing to the attachment of the polymer to the char layer because it contains silicon bonds, in which the rearrangement of silicon environments occurs to the redistribution reactions that occur. It involves the exchange of –O–Si– and –C–Si– bonds during the final stages of pyrolysis at which time heat transfer or flame has been resisted into the polymer hybrid structure, reaching complete decomposition at a temperature of 478.83°C.

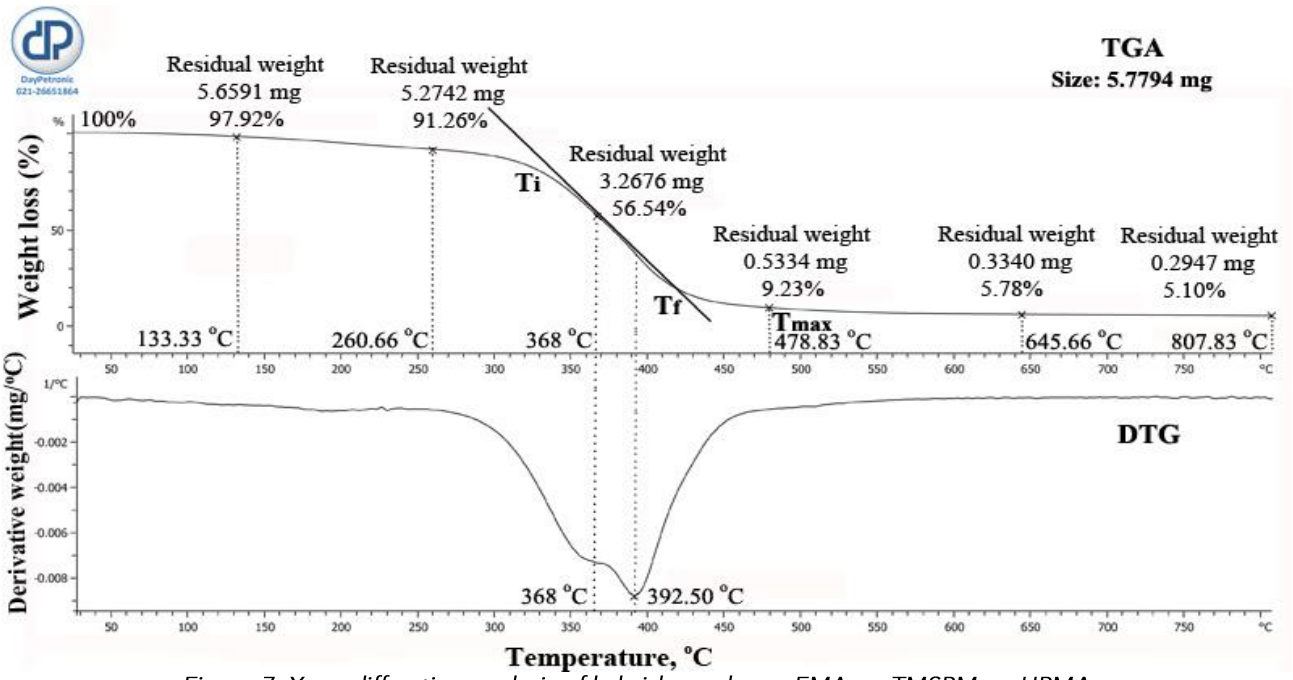

Figure 7. X-ray diffraction analysis of hybrid copolymer EMA-co-TMSPM-co-HPMA.

The TGA results coincided with the DTG results of the hybrid polymer, which is very useful for determining the characteristics of the hybrid polymer. The characterization can be done by comparing the degrees of complete decomposition of the polymer, especially the melting point, in the two results. where it was observed in the same Figure 7 the presence of two successive endotherm peaks Their bottom bottoms are at a temperature of 368 °C and 392.50 °C, and they are compatible with the TGA analysis that includes the largest mass loss and thus the decomposition of the hybrid polymer, which begins after 260.66 °C, which is the starting temperature of the largest decomposition of Ti, which continues to the temperature of 478.83 °C, which is the temperature decomposition completes T_f. The result of this decomposition appears at 478.83°C, which is the maximum temperature T_{max}, in which it was found that the hybrid polymer has lost 90.77% of the weight used in the analysis, which is an equivalent of 5.2460 mg of the weight of the sample. Therefore, the DTG spectrum can be used to determine the melting point of the sample, and the large peak in the spectrum corresponds to the weight lost during the pyrolysis of the sample.

Conclusions

The hybrid bioactive ceramic copolymer showed high temperature biodegradability with biorubber behavior when in the gel form. The formation of an apatite layer on the hybrids was confirmed within 2 weeks by FT-IR and X-ray diffraction data, but there are still many fields that need improvement. These polymer hybrid biomaterials are provided to maintain the adhesion strength of this polymer with normal bone tissue and to maintain the high mechanical strength of the hybrid polymer

References

[1] Jones JR. Review of bioactive glass: From Hench to hybrids. Acta Biomaterialia 9;2013: 4457–4486.

[2] Hench LL. The story of Bioglass. J Mater Sci, Mater Med., 17; 2006:967–978.

[3] Hench LL, Splinter RJ, Allen WC, Greenlee TK. Bonding mechanisms at the interface of ceramic prosthetic materials. J Biomed Mater Res Symp., 334; 1971:117–141.

[4] Kokubo T. Bioactive glass-ceramics – properties and applications. Biomaterials 12; 1991:155–163.

[5] LeGeros RZ. Properties of osteoconductive biomaterials: calcium phosphates. Clin Orthop Relat Res 395; 2002:81–98.

[6] Pereira MM, Jones JR, Hench LL. Bioactive glass and hybrid scaffolds prepared by sol-gel method for bone tissue engineering. Adv Appl Ceram 134(1); 2005: 35-42.

[7] Pereira MM, Jones JR, Orefice RL, Hench LL. Preparation of bioactive glass-polyvinyl alcohol hybrid foams by the sol-gel method. J Mater Sci Mater Med 16(11); 2005: 1045-1050.

[8] Chung JJ, Jones JR, Georgiou TK. Toward Hybrid Materials: Group Transfer Polymerization of 3-(Trimethoxysilyl)propyl Methacrylate. Macromol. Rapid Commun 36; 2015: 1806−1809.

[9] Wei Y, Jin DL. A new class of organic-inorganic hybrid dental materials. Abstr Pap Am Chem S 214; 1997: 145-Poly.

[10] Paul PP, Timmons SF, Machowski WJ., Organic-inorganic hybrid dental restorative composites. Abstr Pap Am Chem S 214; 1997:146-Poly.

[11] Mousa WF, Kobayashi M, Shinzato S, Kamimura M, Neo M, Yoshihara S, Nakamura T. Biological and mechanical properties of PMMA-based bioactive bone cements. Biomaterials 21(21); 2000: 2137-2146.

[12] Hennig W, Blencke BA, Bromer H, Deutscher KK, Gross A, Ege W. Investigations with bioactivated polymethylmethacrylates. J Biomed Mater Res 13(1); 1979: 89-99.

[13] Heikkila JT, Aho AJ, Kangasniemi I, YliUrpo A. Polymethyl- methacrylate composites: Disturbed bone formation at the surface of bioactive glass and hydroxyapatite. Biomaterials 17(18); 1996: 1755-1760.

[14] Ohtsuki C, Miyazaki T, Tanihara M. Development of bioactive organic-inorganic hybrid for bone substitutes. Mat Sci Eng C-Bio S 22(1); 2002: 27-34.

[15] Ohtsuki C, Miyazaki T, Kamitakahara M, Tanihara M. Design of novel bioactive materials through organic modification of calcium silicate. J Eur Ceram Soc 27(2-3); 2007: 1527-1533.

[16] Chung JJ, Yoo J, Sum BST, Li S, Lee S, Kim TH, Li Z, Stevens MM, Georgiou TK, Jung Y, Jones J R. 3D Printed Porous Methacrylate/Silica Hybrid Scaffold for Bone Substitution. Adv. Healthcare Mater. 10; 2021: 1-13.

[17] Chung JJ, Fujita Y, Li S, Stevens MM, Kasuga T, Georgiou TK, Jones JR. Biodegradable inorganic-organic hybrids of methacrylate star polymers for bone regeneration. Acta Biomaterialia 54; 2017: 411–418.

[18] Macon ALB, Page SJ, Chung JJ, Amdursky N, Stevens MM, Weaver JVM, Hanna JV, Jones JR. A structural and physical study of sol–gel methacrylate–silica hybrids: intermolecular spacing dictates the mechanical properties. Phys. Chem. Chem. Phys. 17; 2015: 29124-29133.

[19] Kister O, Roessner F. Synthesis and characterization of mesoporous and amorphous silica modified with silica-organo-sulfogroups. J Porous Mater 19; 2012:119–131

[20] Erdey L, Paulik F, Paulik J. Differential thermogravimetry. Nature 174; 1954: 885-886.