Polymerization of ε-Caprolactone Initiated through Powders of Biological and Nonbiological Glasses

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ABSTRACT: Eight biomedical glasses and three commercial glasses, as finely divided powders, were tested as initiators for the ring-opening polymerization of ε-caprolactone in bulk and in vacuo at 185°C. All the glass powders were able to initiate the polymerization, along with Pyrex, which was totally inert toward the monomer as the inner surface of a phial. The obtained polymers were examined with Fourier infrared transform spectroscopy and atomic force microscopy. The molecular weights were measured by viscometry in $CHCl_3$. The presence of a fraction of the polymer firmly linked to the glass was quantitatively checked by the determination of the weight loss from the residues of the extraction with $CHCl_3$ after calcination in a kiln at 945°C. The molecular weights and weight losses per unit surface were elaborated mathematically so that a possible correlation between these properties and the atomic compositions of the glasses could be better investigated. Two possible initiation mechanisms, induced by the hydroxyls present on the glass surface, were proposed: one for free poly(ε-caprolactone) and one for poly(ε-caprolactone) linked to the glass. © 2002 Wiley Periodicals, Inc. J Appl Polym Sci 87: 1579–1586, 2003

Key words: biomaterials; dental polymers; initiators; polyesters; ring-opening polymerization

INTRODUCTION

In the field of biomaterials, the formation of a hydroxyapatite (HA) layer on biological glasses is attributed to hydroxyl groups present on the surfaces of intermediate silica gels formed for ion-exchange processes. This kind of process is, therefore, possible for all materials (organic and inorganic) that can have on their surfaces hydroxyls of the same nature.

Composites and blends between a bioactive either ceramic or glassy material and a bioresorbable polymer have been proposed for use in orthopedics and dentistry.[1–3] By reacting ε-caprolactone (CL) and poly(ethylene glycol) (PEG) in the presence of HA without a catalyst[4] to obtain a composite of HA (powdered or microgranular) and a poly(ε-caprolactone)-*block*-poly(oxyethylene)-*block*-poly(ε-caprolactone) (PCL–POE–PCL) copolymer for applications in dentistry,[4,5] we have ascertained that HA is able to initiate even the polymerization of CL independently of PEG under the same reaction conditions. This property of HA has led to a more general chemical problem, whether hydroxyls on any surface can also initiate polymerization processes. Recently, the same ability has also been shown by slightly hydrated alumina.[6]

These results have led us to check whether or not CL can be polymerized into poly(ε-caprolactone) (PCL) at different molecular weights by other bioactive inorganic materials, such as biological glasses, which are the subject of this article.

EXPERIMENTAL

Materials and methods

The first eight glasses listed in Table I were prepared by the thorough and intimate mixing of the proper starting powders (all reagent-grade chemicals) and by the fine milling of them in a jar mill with ZrO_2 balls as grinders. The powdered reagents were melted via heating in Pt crucibles at a suitable temperature (1250–1550°C, depending on the composition), for almost 30 min, in a laboratory kiln. Blocks of glass were produced either by the melt being poured into graphite containers in which it was allowed to cool or by the melt being shock-quenched directly into water.

The six glasses identified as biological are bioactive and/or bioresorbable glasses. In particular, glass A

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TABLE I
Composition of the Glasses as Molar Percentages

Glass	Biological						Ionomeric		Industrial		
	AP40	RKKP	A	ION/1	RK	AKRA15	D	γ	Cristallo	Bohemia	Pyrex
SiO_2	46.21	46.07	46.12	10.96	46.52	44.09	42.6	38.37	83.56	75.94	75.94
Al_2O_3	—	—	—	3.99	—	1.15	16.27	16.98	—	—	1.07
P_2O_5	4.95	5.24	2.63	21.93	3.91	2.49	—	6.29	—	—	—
CaO	35.68	35.34	26.90	57.16	30.43	25.51	14.32	6.29	—	11.62	0.32
Na_2O	4.65	4.61	24.32	—	16.52	23.29	—	—	0.70	—	4.29
K_2O	0.13	0.13	—	1.57	2.61	—	—	6.29	6.43	12.44	—
MgO	4.36	4.39	—	3.21	—	—	—	—	—	—	—
CaF_2	4.01	3.98	—	1.17	—	—	26.81	25.78	—	—	—
PbO	—	—	—	—	—	—	—	—	9.31	—	—
B_2O_3	—	—	—	—	—	—	—	—	—	—	12.94
Ta_2O_5	—	0.14	—	—	—	0.13	—	—	—	—	—
La_2O_3	—	0.10	—	—	—	0.09	—	—	—	—	—
NiO	—	—	—	—	—	0.78	—	—	—	—	—
Fe_2O_3	—	—	—	—	—	2.22	—	—	—	—	—
Cr_2O_3	—	—	—	—	—	0.23	—	—	—	—	—

has the same chemical composition as Hench's 45S5 Bioglass[1] but is produced at ISTEC Laboratories with a different thermal cycle; Bioglass is a bioactive glass now far beyond the clinical testing phase,[7] whereas AP40 and RKKP are still being tested in vitro[8] and more recently on rats.[9] The two glasses identified as ionomeric were expressly produced for a saline ionomeric crosslinking of poly(carboxylic acid) chains,[10] induced by the freeing of polycharged cations in an appropriate manner (e.g., the ionic flow rate and Z potential) and by positive ions on the surface. The freed divalent and trivalent cations (particularly Ca^{2+} and more efficiently Al^{3+}) produce a three-dimen-

sional, ionically crosslinked molecular network with poly(carboxylic acid) chains;[11] the cations remaining bound to the surfaces of the glass grains produce ionic bonds, having both chemical and mechanical characteristics, with many ionomeric chains, which are able to include even these grains in the whole polymeric structure obtained. The last three glasses—Cristallo, Bohemia, and Pyrex—came from broken consumer goods industrially produced, traded in the market, and consequently identified as industrial. They were used for comparison, all the others being biomedical, so that our information would be complete. All the glasses were shattered, milled into granules of the
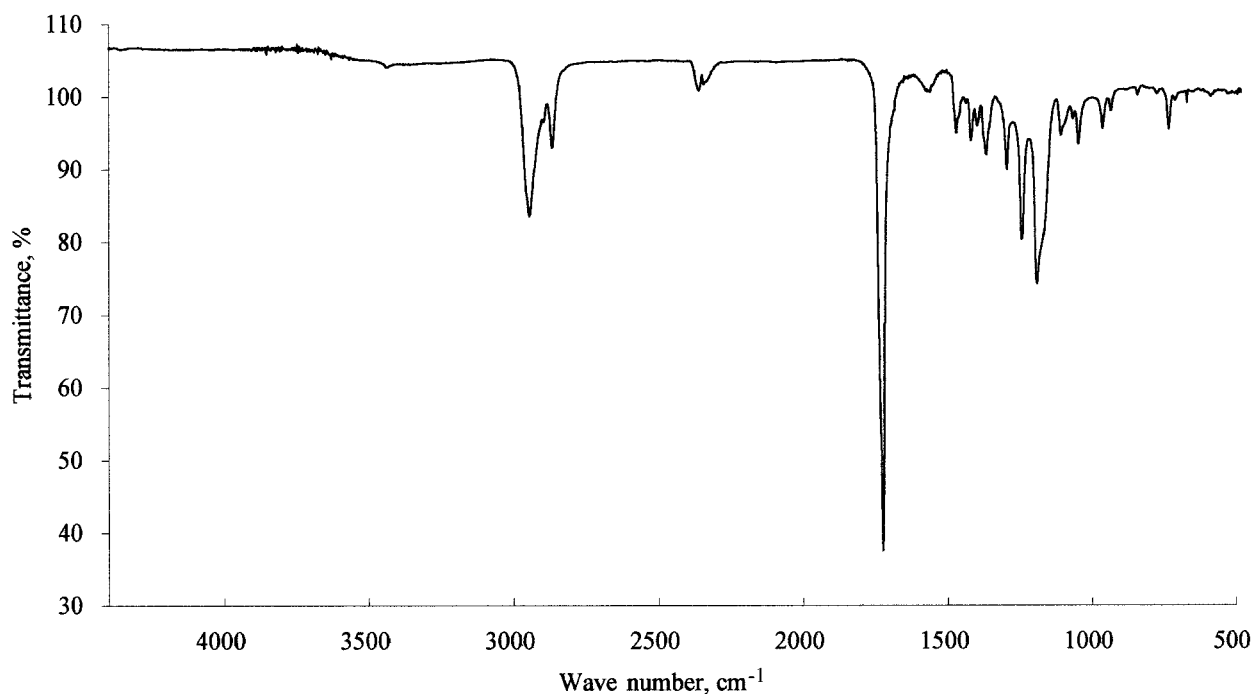

Figure 1 FTIR spectrum (KBr disk) of the fraction of the composite between glass A and PCL soluble in $CHCl_3$.

TABLE II
SSAs, or Whole Surface Developed per Unity of Weight, of the Glass Particles; (*M*) Values of the Fractions Soluble in CHCl₃; WL Percentages by the Residues of the Extraction with CHCl₃ After Calcination in The Kiln at 945°C and Their USWL

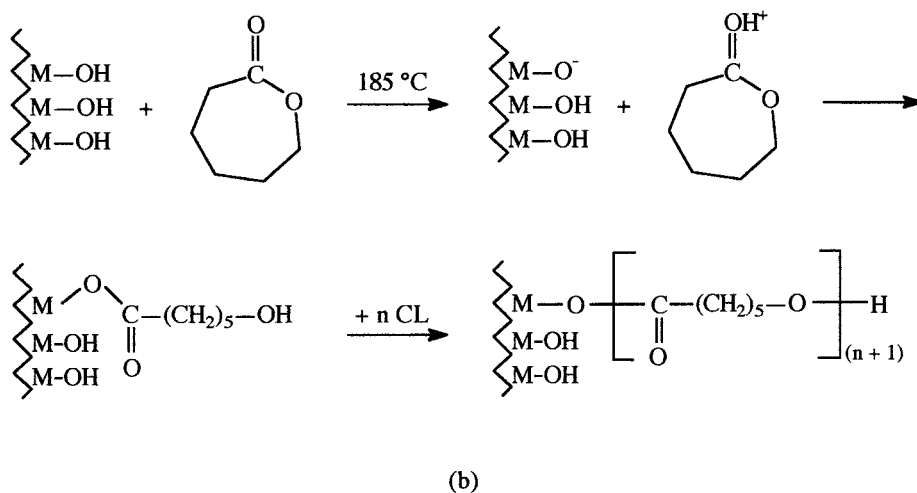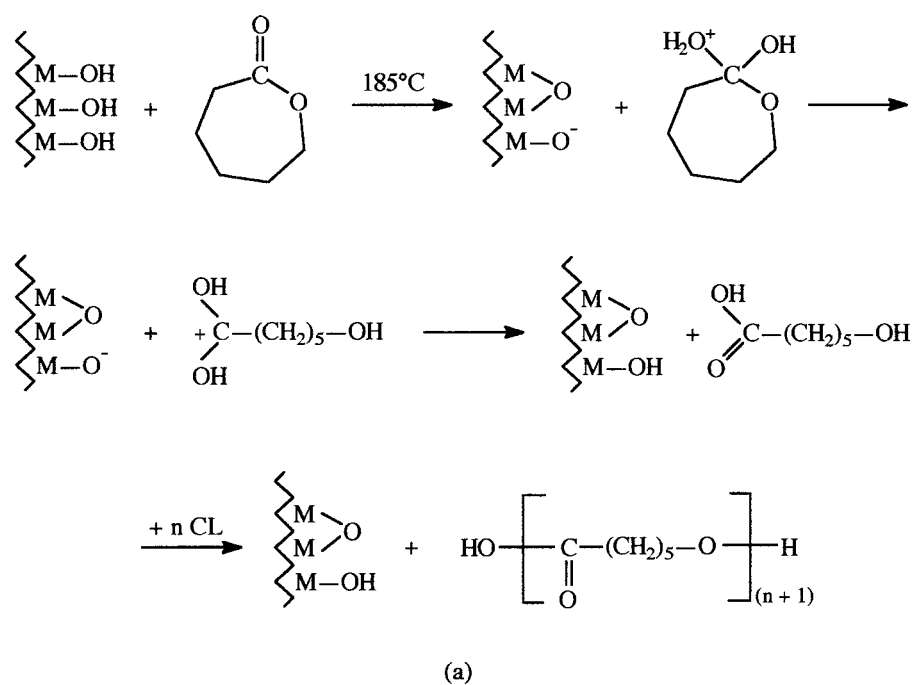| Glass	Biological						Ionomeric		Industrial		
	AP40	RKKP	A	ION/1	RK	AKRA15	D	γ	Cristallo	Bohemia	Pyrex
SSA (m²/g)	0.46	0.47	0.60	0.51	0.62	1.35	1.57	1.11	0.47	0.66	0.92
M (Dal)	17000	20000	2500	18000	6000	2000	10500	10000	6000	10000	8000
WL (%)	1.26	0.70	5.86	—	1.38	0.23	4.70	0.86	0.91	—	0.79
USWL (% m²)	2.7391	1.4894	9.7666	—	2.2258	0.1704	2.9936	0.7748	1.9362	—	0.8587

(a)

(b)

Figure 2 Possible mechanisms of polymerization initiation, by hydroxyls on the glass surface, for the synthesis of (a) free PCL and (b) PCL linked to the glass surface. The symbol M indicates any suitable electropositive atom on the glass surface.

TABLE III
Composition of the Glasses as Atomic Percentages and Coefficients from WMLR of M and USWL Values
(Constrained to 0 at the Origin)

Glass	Biological						Ionomeric		Industrial			Coefficients from WMLR	
	AP40	RKKP	A	ION/1	RK	AKRA15	D	γ	Cristallo	Bohemia	Pyrex	CM	C%
Na^+	9.30	9.22	48.64	—	33.04	46.58	—	—	1.40	—	8.58	−227	0.34
K^+	0.26	0.26	—	3.14	5.22	—	—	12.58	12.86	24.88	—	−433	−0.55
Mg^{2+}	4.36	4.39	—	3.21	—	—	—	—	—	—	—	356	0.08
Ca^{2+}	39.69	39.32	26.90	58.33	30.43	26.29[a]	41.13	32.07	—	11.62	0.32	−75	−1.22
Pb^{2+}	—	—	—	—	—	—	—	—	9.31	—	—	−1300	−2.37
X^{3+}[b]	—	0.20	—	7.98	—	7.38	32.54	33.96	—	—	28.02	−425	−1.07
Si^{4+}	46.21	46.07	46.12	10.96	46.52	44.09	42.60	38.37	83.56	75.94	75.94	288	0.37
P^{5+}	9.9	10.48	5.26	43.86	7.82	4.98	—	12.58	—	—	—	508	1.69
Ta^{5+}	—	0.28	—	—	—	0.26	—	—	—	—	—	9760	1.00
F^-	8.04	7.96	—	2.34	—	—	53.62	51.56	—	—	—	286	1.35
O^{2-}	161.99	163.81	156.61	205.48	162.15	161.93	148.33	171.71	183.56	175.94	198.52	—	—
Total charge	332.02	335.58	313.22	413.30	324.30	323.86	350.28	394.98	367.12	351.88	397.04	$R^2 = 0.995$	$R^2 = 0.987$
R	2.8870	2.8723	3.0480	3.3036	2.9840	2.8554	1.9740	2.0223	2.1968	2.3168	1.9096	—	—
Y	2.2260	2.2553	1.9038	1.3929	2.0320	2.2892	4.0519	3.9555	3.6065	3.3663	4.1808	—	—

R = ratio between oxygen and network-making atoms; Y = nonbridging oxygen atoms = $2Z - 2R$ (Z = mean coordination number of network-making atoms = 4).
[a]Together with Ni^{2+} content.
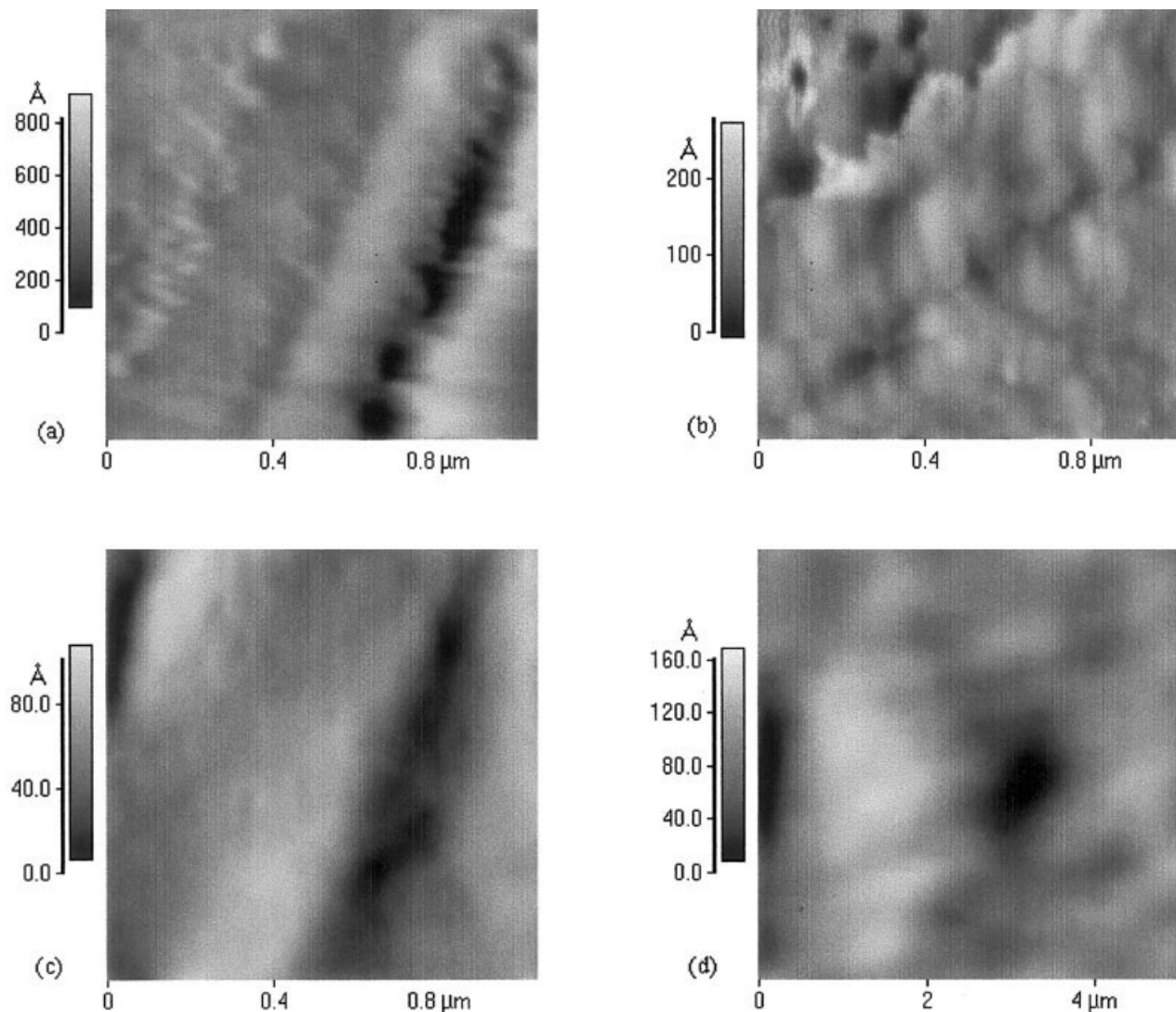[b]Sum of all trivalent cations (B^{3+}, Al^{3+}, La^{3+}, Cr^{3+}, and Fe^{3+}).

Figure 3 AFM images, made in the noncontact mode, of the two biological glasses and the residues remaining after the extraction of the glass–PCL composites with CHCl₃: (a) glass ION/1, (b) the residue on the surface of ION/1, (c) glass A, and (d) the residue on the surface of A. The surface areas were 1 μm $\times$ 1 μm.

proper dimensions, and accurately sieved so that particles would be obtained with a mean diameter of 40 $\pm$ 15 μm. The obtained powders were freed from excessively fine fractions by being vibrated in distilled water for about 2 h. Because the nature of the interactions possibly involved depends on the surface, not on the volume, the specific surface areas (SSAs) of the glass particles were measured by the Brunauer-Emmet-Teller (BET) method.[17] With the term *SSA*, we indicate the whole surface (m²) developed per unity of weight (g).

Polymerization procedure

The CL ring-opening polymerization was carried out according to the procedure previously followed for HA and alumina.[4,6] The reaction mixtures were prepared by the introduction, under an atmosphere of N₂, of known volumes of CL (Janssen Chimica, Saunderton, United Kingdom) into Pyrex phials containing preweighed amounts of the finely ground glass powders. The glass-to-monomer weight ratio was always 3:10. The phials were connected to a vacuum line, evacuated, sealed off, and placed in an oven (at 185°C) in which they were fastened to a rotating bar so that the reaction mixtures remained homogeneous. After 10–11 days, each phial was opened, and the solid product was characterized with different techniques.

Product characterization

Each product obtained was repeatedly extracted with CHCl₃ and a suspension decanted in an Imhoff graduated cone until there was a total absence of the polymer in the liquid phase. The soluble fractions were
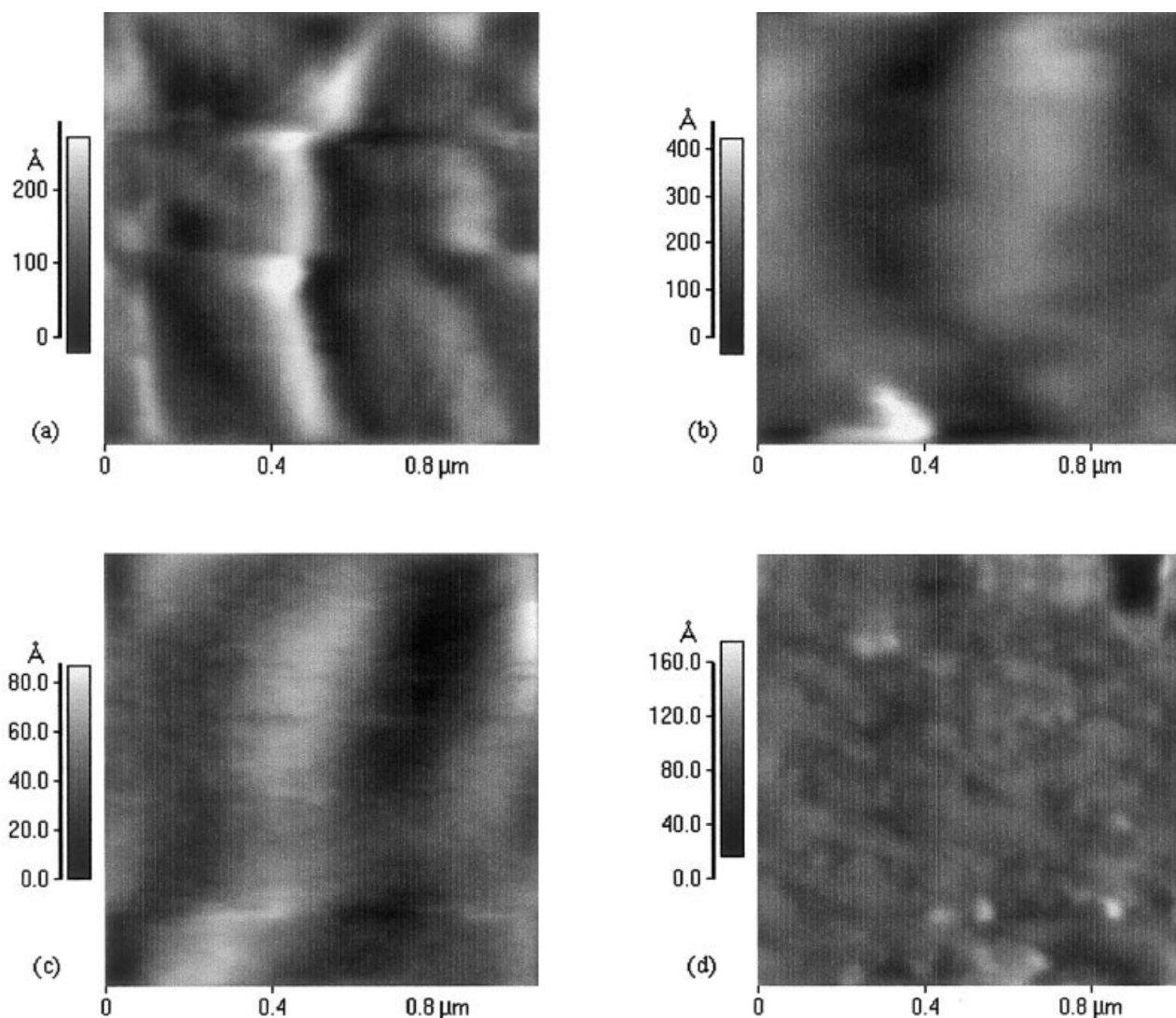
Figure 4 AFM images, made in the noncontact mode, of the two ionomeric glasses and the residues remaining after the extraction of the glass–PCL composites with CHCl$_3$: (a) glass γ, (b) the residue on the surface of γ, (c) glass D, and (d) the residue on the surface of D. The surface areas were 1 μm $\times$ 1 μm.

cast onto KBr disks and examined with Fourier infrared transform (FTIR) spectroscopy with a PerkinElmer 1600 apparatus. The molecular weights of the polymers so identified were measured with viscometry in CHCl$_3$. A possible presence of the polymer somehow linked to the glasses was checked by the determination, with an aliquot of each insoluble fraction, of the weight loss (WL) after calcination via heating in a kiln at 945°C in a porcelain crucible.

The insoluble fractions were also examined with atomic force microscopy (AFM). The observations were carried out with an Autoprobe CP system (Park Scientific Instruments, Sunnyvale, CA) operating in the noncontact mode to minimize perturbations of the surface by the tip. Images of square areas of 1 μm $\times$ 1 μm (256 pixels $\times$ 256 pixels) were acquired with gold-coated, all-silicon cantilevers (2-μm-thick silicon Ultralevers, Park Scientific Instru-

ments, Geneva, Switzerland) with integrated high-aspect-ratio conical tips with a spring constant of 10–20 N m^{-1}. The background slope of the images was removed by the performance of the data acquisition in the alternating current track image mode, which matched the average gray scale of each line. The background curvature was removed by a flattening routine in image processing software from Park Scientific Instruments (Sunnyvale, CA). The best third-order polynomial fit to the average height profile was subtracted from each line of the entire image to take account of possible distortions due to lateral displacements of the sample surface below the AFM tip. A filter process was applied to prevent the noise. Noise could result from several sources. First, a 60-Hz electrical noise could be picked up by the instruments during the scans. Second, room light could contribute 120-Hz noise (a second har-

TABLE IV
RMS σ (nm) for the Glasses ION/1, A, γ, and D and for the Corresponding Residues of the Extraction with $CHCl_3$

Material	ION/1		A		γ		D	
	Glass	Residue	Glass	Residue	Glass	Residue	Glass	Residue
RMS σ	12.7	3.79	2.02	1.46	5.20	6.86	1.57	1.33

monic of 60 Hz). Third, random environmental vibrations could be transmitted to the instruments. Moreover, 1/f noise appeared in the images, especially in the fast scan direction where 1/f noise is a type of noise whose power spectra $P(f)$ as a function of the frequency f behaves like: $P(f) = 1/f^a$, where the exponent a is very close to 1 (this is where the term "1/f noise" comes from). The surface profiles so obtained were compared with those of the glasses.

RESULTS AND DISCUSSION

The polymerization of CL occurred with all the glasses listed in Table I. After 10–11 days of heating at 185°C, the viscosity in all the phials greatly increased; with cooling at room temperature, their contents appeared as solid masses. The products were recovered and repeatedly extracted with $CHCl_3$, as described in the Experimental section.

Figure 1 shows the FTIR spectrum of the soluble fraction of the polymer synthesized on glass A and cast from $CHCl_3$ onto KBr. All the absorption peaks typical of PCL are present: a doublet at about 2950 and 2870 cm^{-1}, attributable to ν_{as} and ν_s of methylene groups; the main aliphatic polyester absorption at 1724 cm^{-1}; and a series of dense peaks below 1500 cm^{-1}, typical of PCL.[4,6] The spectra of the other soluble fractions are substantially identical. These results demonstrate that all these glass powders can initiate the polymerization of CL. Also, the Pyrex, which was totally inert toward CL as the inner surface of a phial, was able to polymerize, in the form of a finely divided powder, the same monomer.

The data reported in Table II show that the average viscometric molecular weights (M) of the fractions soluble in $CHCl_3$ were independent of the SSAs, or the whole surface (m^2) developed per unity of weight (g), of the glass particles. The WL percentages from the residues of the extraction with $CHCl_3$, after calcination in a kiln at 945°C, as well as the weight loss per unit surface (USWL), showed that only glasses A and D seemed to not have a negligible quantity of organic material firmly linked to their structures.

Figure 2 shows two possible initiation mechanisms induced by the hydroxyls present on the glass surface for the free PCL and for that linked to the glass. We should consider, however, that the ionomeric glasses can bind ionically to the carboxyl groups and that the

mechanism of Figure 2(a) gives PCL with a carboxyl end group. Moreover, the adhesion of albumin, a macromolecule with many charges on its surface, has been observed on many glasses, including some of those listed in Table I.[12]

Table III reports the values of the coefficients related to the composition of the glasses (given as atomic percentages), coming from weighed multiple linear regression (WMLR) and obtained by computer with the program Statistica [Edition 99, StatSoft, Inc., Tulsa, OK].

At this point, an evaluation was performed, intended to establish if the properties measured, which characterized these glasses, depended in some way on their chemical compositions. To this end, the atomic compositions of all the species present were extracted from the molar compositions of the chemical compounds. We assumed a linear trend, as described by the following equation:

$$\text{Property } \xi = \sum_{i=1}^{N} C_{\xi i} X_i \qquad (1)$$

where $C_{\xi i}$ is the coefficient of influence, for which the ith atomic component, of the overall N value of the glass, contributes to the property ξ and X_i is the amount of the ith atomic component. The codes CM and $C\%$ used in Table III correspond to those $C_{\xi i}$ values that refer to M and USWL of Table II, respectively. Both of these produced a very reliable WMLR, with $R^2 > 0.98$, whereas all the others gave far lower R^2 values, thereby compromising not only the linear trend hypothesis for them but even the existence of a correlation, however scarce.

Concerning the role of oxygen (the principal or unique anionic partner), no significant differences appeared when the computation was performed with or without the amounts in bridging and nonbridging being shared. However, this could derive from the fact that the ratio of bridging oxygen atoms to nonbridging oxygen atoms depends closely on the ratio of the network former and nonformer cationic species; in practice, in the development of a set of linear equations, the influence of all cationic species reflects on those of bridging and nonbridging oxygen atoms, thereby being considered twice. Furthermore, although every cation for its specificity is able to widely

modulate the property, oxygen atoms (to which all the cations are bonded) can produce only a mean value that is substantially indistinct, not differing very much between bridging and nonbridging atoms.

The positive values of such coefficients contribute to increased values of M and USWL in Table II; negative values act in the opposite way. A strong contribution to enhancing the molecular weight in the bulk (a high value of CM) seems to be given by Ta^{5+}, a transition element, which could stabilize the growing ends by a somewhat different mechanism than that shown in Figure 2(a). It is known that tantalum organometallic complexes catalyze the living ring-opening polymerization of norbornene[13,14] and cyclopentadiene;[14] nevertheless, the great differences in the chemical structures of such tantalum catalysts and monomers, in comparison with those studied in this article, do not allow us to make hypotheses about the mechanism. A significant negative effect seems to be given by Pb^{2+}, which has a highly polarizable lone electron pair. All other ions seem to make quite low contributions. P^{5+}, Ta^{5+}, and F^- play active roles concerning the amount of linked PCL, as expressed by the coefficient $C\%$, whereas Pb^{2+}, Ca^{2+}, and trivalent ions act as antagonists. No correlation appears between the two properties, which are substantially influenced by different atomic species.

The noncontact AFM images of four glasses (ION/1, A, γ, and D), together with the corresponding residues of the extraction with $CHCl_3$, with surface areas of 1 μm $\times$ 1 μm, are shown in Figures 3 and 4. The data in Table IV show that both the glasses and the residues had low root-mean-square values of roughness (RMS σ), except for ION/1. The differences between the values of the glasses and those of the residues are consistent with the residue calcination data (see Table II) for glasses A and D, for which the observed decreases in roughness of about 30 and 15% could be due to the polymer coating. Conversely, the strong decrease in roughness for the ION/1 surface, as well as the roughness increase for γ, cannot be explained as an effect of the coating. Indeed, the data in Table II show no polymer coating on ION/1 and a negligible coating on γ, if any. Moreover, a roughness increase for the surface due to a polymer coating is very difficult to explain with arguments only derived from morphological analysis.[15,16] However, because the roughness of a material is somehow related to its tribology and mechanical properties, any variation in the roughness due to a polymer coating may be interesting for the use of these glasses as biomaterials in dentistry.

CONCLUSIONS

The results reported in this article are still preliminary. However, both the ability of such glass powders to initiate the polymerization of CL, and the presence of a polymer coating, linked to the surface of glass A appear very interesting. Indeed, glass A has a chemical composition (shown in Table I) identical to that of Bioglass, a bioactive glass already used as a biomaterial in dentistry.[7] Although the quantity of the linked polymer experimentally found is minimal, it could enhance the compatibility between the organic and inorganic components of composites as a PCL coating on ceramics in PCL–POE–PCL/HA composites.[4]

References

1. Hench, L. L. J Am Ceram Soc 1991, 74, 1487.
2. Verheyen, C. C. P. M.; de Wijn, J. R.; van Blitterswijk, C. A.; de Groot, K.; Rozing, P. M. J Biomed Mater Res 1993, 27, 433.
3. Devin, J. E.; Attawia, M. A.; Laurencin, C. T. J Biomater Sci Polym Ed 1996, 7, 661.
4. Cerrai, P.; Guerra, G. D.; Tricoli, M.; Krajewski, A.; Guicciardi, S.; Ravaglioli, A.; Maltinti, S.; Masetti, G. J Mater Sci Mater Med 1999, 10, 283.
5. Cerrai, P.; Guerra, G. D.; Tricoli, M.; Krajewski, A.; Ravaglioli, A.; Martinetti, R.; Dolcini, L.; Fini, M.; Scarano, A.; Piattelli, A. J Mater Sci Mater Med 1999, 10, 677.
6. Cerrai, P.; Guerra, G. D.; Palla, M.; Tricoli, M.; Krajewski, A.; Ravaglioli, A.; Guicciardi, S.; Maltinti, S.; D'Acunto, M.; Narducci, P. Macromol Mater Eng 2001, 286, 546.
7. Froum, S. J.; Weinberg, M. A.; Tarnow, D. J Periodontol 1998, 69, 698.
8. Tinti, A.; Taddei, P.; Azzoni, C. B.; Di Martino, D.; Krajewski, A.; Mazzocchi, M.; Ravaglioli, A. In Drug Delivery Systems, Proceedings of the 6th Periodical International Meeting and Seminar on Ceramics, Cells and Tissues, Faenza, Italy, 2000; Ravaglioli, A.; Krajewski, A., Eds.; IRTEC-CNR: Faenza, Italy, 2000; p 60.
9. Azzoni, C. B.; Carretta, P.; Mognaschi, E; Di Martino, D.; Tinti, A.; Taddei, P.; Krajewski, A.; Mazzocchi, M.; Ravaglioli, A. In Biomimetic Engineering, a New Role for Ceramics, Abstracts of the 7th Periodical International Meeting and Seminar on Ceramics, Cells and Tissues, Faenza, Italy, June 13–15, 2001; IRTEC-CNR: Faenza, Italy, 2001; p 51.
10. Mazzocchi, M.; Foresti, G.; Krajewski, A.; Ravaglioli, A. In Ceramic–Polymer Composites, Proceedings of the 4th Periodical International Meeting and Seminar on Ceramics, Cells and Tissues, Faenza, Italy, 1998; Ravaglioli, A.; Krajewski, A., Eds.; IRTEC-CNR: Faenza, Italy, 1998; p 221.
11. Habert, A. C.; Huang, R. Y. M.; Burns, C. M. J Appl Polym Sci 1979, 24, 489.
12. Krajewski, A.; Malavolti, R.; Piancastelli, A. Biomaterials 1996, 17, 53.
13. Wallace, K. C.; Schrock, R. R. Macromolecules 1987, 20, 448.
14. Rietveld, M. H. P.; Teunissen, W.; Hagen, H.; van de Water, L.; Grove, D. M.; van der Schaaf, P. A.; Mülenbach, A.; Kooijman, H.; Smeets, W. J. J.; Veldman, N.; Spek, A. L.; van Koten, G. Organometallics 1997, 16, 1674.
15. Stone, V. W.; Jonas, A. M.; Nysten, B.; Legras, R. Physical Review B 1999, 60, 5883.
16. Magonov, S.; Whangbo, M.-H. Surface Analysis with STM and AFM: Experimental and Theoretical Aspects of Image Analysis; VCH: Weinheim, 1996; Chapter 13, p 277.
17. Brunauer, S.; Emmet, P. H.; Teller, E. J Amer Chem Soc 1938, 60, 309–319.