Influence of phase separation on the devitrification of 45S5 bioglass

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Abstract

The devitrification of 45S5 variety of bioactive glasses (BGs) in relation to phase separation is studied with scanning electron microscopy (SEM), X-ray powder diffraction (XRD), Fourier transform infrared (FT-IR) spectroscopy, differential scanning calorimetry (DSC) and positron annihilation lifetime (PAL) spectroscopy techniques. It is shown that the type of phase separation (such as spinodal vs. droplet-like) has a pronounced effect on the activation energy of viscous flow and crystallization, the onset temperature of crystallization and the void size distribution at the nanoscale. Generally, the Johnson-Mehl-Avrami (JMA) relation does not describe crystallization kinetics in bulk 45S5 BG. However, for powder samples (< 300 μm) the difference in crystallization kinetics, which is surface driven for the two kinds of glasses, becomes much smaller, and can be described with JMA relation under some circumstances.

Keywords

Bioactive glass; phase separation; crystallization

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1. Introduction

Manufacturing methods and post-fabrication treatment of the well-known 45S5 ‘Bioglass’ ($45\text{SiO}_2 - 24.5\text{Na}_2\text{O} - 24.5\text{CaO} - 6\text{P}_2\text{O}_5$ by wt.%) are shown to have a significant impact on its biological response [1-3]. Many studies have been devoted to understand the effect of devitrification of this bioactive glass (BG) on its physical properties as well as biological performance such as its ability to promote bone growth and regeneration [1-7]. The BG-derived glass-ceramics (crystalline or semi-crystalline) or bioscaffolds prepared by the sintering of their powder exhibit suitable mechanical properties along with broader engineering possibilities [5-8]. At the same time, compared to BG the glass-ceramics show different solubility in body fluid and possibly the protein adsorption profile (protein amount and conformation can depend on surface morphology) – a key factor influencing cells attachment [9]. A common argument is that the phosphorous distribution changes upon crystallization of a glass, causing phosphorous dissolution profile to change, which ultimately affects the distribution of binding sites for proteins and the time to form the hydroxycarbonate apatite (HCA) layer needed for tissue integration [10].

Despite the obvious progress in the applications of 45S5 BG and corresponding ceramics, the fact that this composition belongs to the immiscibility domain of corresponding phase diagram [11] is usually underestimated. For this reason, the final 45S5 glass/ceramic product can be phase-separated at the nanoscale and can have unique properties depending on the quenching rate or post-fabrication treatment (annealing, etc.). The origin of such phase separation pertains to a positive enthalpy of mixing, which drives a glass-forming liquid to separate spontaneously into two compositionally distinct phases. It is a process concurrent to the maximization of entropy, which usually results in a homogeneous mixing of the constituents in glass [12]. Liquid-

liquid immiscibility can lead to droplet-like or spinodal-type phase separation in the glassy state [12,13]. Droplet phase separation is characterized by a sharp boundary between the composition of droplets and rest of the matrix, whereas in spinodal decomposition the phase separated system consists of two interpenetrating networks of diffuse compositional boundary between the two immiscible phases [12,13]. In the latter case the compositions of two phases evolve simultaneously as the degree of phase separation increases and the boundary between phases becomes more distinct. The most famous example of a spinodally phase-separated glass is Corning's extensively investigated sodium borosilicate Vycor glass [13], which consists of two interpenetrating networks one rich and the other depleted in silica.

In principle, the phase separation characteristics of 45S5 BG should be similar to that of Vycor glass. However, little is known about the influence of nanoscale phase-separation on the performance of scaffolds made of 45S5 BG and/or corresponding glass-ceramics. For instance, the existence of spinodal (or droplet-like) phase could result in different (in comparison to the uniform 45S5 glass) final products of crystallization process, efficiency of HCA layer formation, as well as ionic dissolution/leaching rate. The latter plays an especially important role for bone regeneration, since the critical concentrations of soluble silicon and calcium ions are needed to activate several families of genes (those encoding the nuclear transcription factors and potent growth factors, like IGF-II along with IGF binding proteins and proteases that cleave IGF-II from their binding proteins), which result in a modulation of cell cycle response of osteoblasts to BGs [14]. The interconnected nature of the spinodal phase allows formation of the interconnected pore structure in 45S5 BG/ceramics using different post-fabrication treatments (selective leaching [15], for example). The interconnected pore structure is very important for scaffold performance: the interconnected macropores (at least 100 μm in dimensions) are needed

for new tissue ingrowth and blood vessel formation, while the nanopores determine degradability of bioscaffold in vivo [16,17]. The presence of nanopores may also influence cell attachment [18,19]. Thus, in addition to various known methods of engineering nano/macro porous glasses or ceramics [20], spinodal phase decomposition is shown to be a useful factor to introduce interconnected nanopore structure in the scaffolds made of 45S5 glass/ceramics [21]. Nevertheless, the physical properties of 45S5 glass phase-separated at the nanoscale, as well as the influence of spinodal phase separation on the pore distribution, crystallization kinetics and glass-ceramics formation have not been studied well.

So, in the present work, we have studied the classic melt-quenched 45S5 glass composition with signatures of droplet-like or spinodal phase-separation at the nanoscale, as well as corresponding ceramics prepared by the devitrification of these parent glasses. Thermodynamic properties of the obtained glasses/ceramics have been investigated by conventional differential scanning calorimetry (DSC). The X-ray photoelectron spectroscopy (XPS), VIS-IR spectroscopy, X-ray diffraction (XRD) analysis in combination with scanning electron microscopy (SEM) are used to characterize electronic and structural features of these important biomaterials. The pore structure of melt-quenched 45S5 glass (both droplet-like and spinodally phase separated) and ceramics is studied with positron annihilation lifetime (PAL) spectroscopy, which is proven to be a very efficient probe for both open and closed pores at sub-nanoscale [22].

2. Materials and methods

The 45S5 glass ($45\text{SiO}_2 - 24.5\text{Na}_2\text{O} - 24.5\text{CaO} - 6\text{P}_2\text{O}_5$ by wt.%) was synthesized using melt-quenching and casting in stainless steel molds. High purity (99.99 % or better) carbonates

(Alfa Aesar) CaCO_3 , Na_2CO_3 , silicon dioxide SiO_2 and calcium phosphate tribasic $\text{Ca}_5\text{OH}(\text{PO}_4)_3$ powders were used as raw precursors, and melted in a Pt crucible. To induce spinodal phase decomposition the melt was quenched from 1550 °C into preheated molds. For comparison we have used a commercial 45S5 Bioglass, which had pronounced droplet-like phase separation (Fig. 1). The two types of phase-separation viz. spinodal and drop-like arise from the difference in the melt temperature just prior to casting, and the quench rate during solidification. Our 45S5 glasses were transformed into glass-ceramics by heating in two steps – annealing of the material at 650-670 °C for 3 hours to induce nucleation, followed by another heat treatment at ~730-750 °C for 6 hours to facilitate their growth [23]. The powder of a given sample was obtained by ball milling (~1 hour) of bulk pieces followed by sieving through a collection of 5 sieves (500µm, 300µm, 150µm, 75µm, 32µm) to separate particles by size.

The composition of the prepared glasses was checked with XPS. No significant difference was found between the droplet-like and spinodally phase separated glasses (Table 1). The XPS spectra were recorded in a normal emission mode on sample surfaces freshly fractured inside the ultra-high vacuum of the Scienta ESCA-300 spectrometer using monochromatic Al K_α X-rays (1486.6 eV). The XPS data consisted of survey scans over the entire binding energy (BE) range and selected scans over the core-level photoelectron peaks of interest. The surface charging from photoelectron emission was neutralized using a low energy (< 10 eV) electron flood gun. The experimental positions of core levels for all of the investigated samples were adjusted by referencing to the 1s core level peak of adventitious carbon at 284.6 eV [24]. Data analysis of the XPS spectra was conducted using the standard CASA-XPS software package.

Positron annihilation lifetime (PAL) spectra were recorded with the fast coincidence system (ORTEC) of 230 ps resolution (FWHM of a single Gaussian, determined by measuring

^{60}Co isotope) at the temperature, $T = 22\text{ }^{\circ}\text{C}$ and relative humidity, $RH = 35\%$. Each PAL spectrum was measured with a channel width of 6.15 ps (total number of channels 8000) and contained $3 \cdot 10^6$ coincidences in total. Isotope ^{22}Na (activity $\sim 50\text{ kBq}$) was used as source of positrons (prepared from aqueous solution of $^{22}\text{NaCl}$, wrapped with Kapton[®] foil of 12 μm thickness and sealed), which was sandwiched between two identical samples. All the PAL spectra of the investigated samples (dried at $120\text{ }^{\circ}\text{C}$ for 4 hours in vacuum before the measurements) were decomposed into four discrete exponentials $s(t) = \sum (I_i / \tau_i) \exp(-t / \tau_i)$ with average positron lifetime τ_i and intensity I_i of i positron decay component ($i = 4$) using standard LT 9.0 program [25]. The additional peaks into the envelope of fitted curve were added only if they significantly improved goodness of the fit. The uncertainties in the determination of lifetimes (τ_i) and corresponding intensities (I_i) were $\pm 0.005\text{--}0.5\text{ ns}$ (increasing with increasing τ_i) and $\pm 0.2\text{--}1\%$, respectively.

FT-IR measurements on samples polished to high optical quality were performed in a reflection mode (nearly normal incident angle), using Varian 7000e spectrometer.

Rigaku “MiniFlex II” diffractometer was used for X-ray powder diffraction (XRD) studies. The XRD patterns were recorded within $15\text{--}60^{\circ}$ angular range, 0.02° scan step and 1 s integration time.

DSC data were acquired for bulk and powder samples using NETZSCH 404/3F microcalorimeter pre-calibrated with a set of standard elements. DSC curves were recorded in a nitrogen atmosphere with 2, 5, 10, 15 and 20 K/min heating rates. Three independent DSC measurements were performed in each case to confirm the reproducibility of the obtained results. Raw DSC data were processed using NETZSCH PC software package.

3. Results and discussion

Spinodally phase-separated 45S5 glass appears slightly purple in the reflected light in comparison to the glass with droplet-like phase separation (Fig. 1a). This color originates from the scattering of light caused by the co-existence of two interconnected phases with close refractive indexes [26]; UV-VIS spectroscopy testified that no characteristic color lines were present in UV-VIS absorption spectra. High-resolution SEM images in Fig. 1b,c show the difference in the structure of the colorless and purple tinged glasses at the nanoscale. Two interconnected phases can be clearly seen in Fig. 1c, which is characteristic of spinodal type phase decomposition, whereas fingerprints of droplet-like phase separation with sharp compositional boundaries are visible on the surface of colorless samples (Fig. 1b). In the latter case, the droplets are too big ($\sim 1 \mu\text{m}$) to cause color as a result of scattering. However, in both cases the matrix of the investigated glasses consists of two immiscible amorphous phases: one is supposed to be silica-rich and the other has to contain more sodium/calcium ions and phosphorus [21].

FT-IR reflection spectra of the two types of 45S5 glasses recorded in the region of fundamental vibrations absorption show only subtle differences (Fig. 2), which is not surprising owing to the integral nature of the measured spectra (averaged through a relatively large macroscopic surface area). As compared to fused silica, where the bending vibrations of SiO_4 tetrahedral units at $\sim 800 \text{ cm}^{-1}$, asymmetric stretch modes at $\sim 1123 \text{ cm}^{-1}$ and $\sim 1220 \text{ cm}^{-1}$ are observed (Fig. 2) [27-29], the 45S5 glass has these optical modes shifted towards lower frequencies ($\sim 700 \text{ cm}^{-1}$ for bending and $\sim 1050\text{-}1100 \text{ cm}^{-1}$ for asymmetric stretching vibrations, respectively [28, 30]), which is typical for any other alkali and alkaline earth containing glasses [31]. Also, new bands at ~ 900 and $\sim 850 \text{ cm}^{-1}$ emerge, which are associated with the stretching

vibrations of SiO_4 tetrahedra having one or two non-bridging oxygens (NBO) in the nearest surrounding of Si atoms (so-called Q_3 and Q_2 groups) [28,30]. The band at $\sim 600 \text{ cm}^{-1}$ is usually attributed to phosphate complexes, having P-O bending vibrations in this range [32].

In principle, viscosity of the phase separated silicate glass should be higher than the viscosity of homogeneous glass of the same composition, because the separated silica-rich matrix has high viscosity and dominates flow behavior. Indeed, the activation energy of viscous flow for the phase separated glasses, calculated using Ozawa plot [33] for glass transition temperature determined at various heating rates, is found to be dependent on the degree and type of phase separation. Thus, the value of the activation energy of viscous flow for spinodally phase separated glass was found to be $\sim 100 \text{ kJ/mol}$ lower than the one for droplet-like phase separated 45S5 glass. We can speculate then that in the case of droplet-like phase separation more alkaline ions are removed from the glass matrix into the droplets, leading to higher viscosity of the residual silica-rich phase.

The 45S5 glass transforms into a glass-ceramic by heating the material at $>700^\circ\text{C}$ for more than 0.5 h, resulting in several possible crystalline phases viz. $\text{Na}_2\text{Ca}_2\text{Si}_3\text{O}_9$, $\text{Na}_2\text{CaSi}_2\text{O}_6$ – combeite [34,35] and $\text{Na}_2\text{Ca}_4(\text{PO}_4)_2\text{SiO}_4$ - silicorhenanite [6,36]. XRD data of as-prepared glasses and fully crystallized samples (after DSC scans) are shown in Fig. 3. Predominant crystalline phase identified in both ceramics prepared from droplet-like and spinodally phase-separated parent glasses is combeite $\text{Na}_2\text{CaSi}_2\text{O}_6$. For a spinodally phase-separated glass the additional reflections in Fig. 3b are caused by crystalline Si, which was added to the powder for calibration purposes.

From comparison of typical DSC scans for the investigated samples (Figs. 4 and 5) it can be ascertained that crystallization kinetics differs for glasses with different types of phase

separation and it also depends on whether the sample is in bulk or powder form. In particular, the activation energy of crystallization calculated according to the Ozawa method [33] is found to be higher for the bulk glass with droplet-like phase separation (compare curves for bulk samples in Figs. 6,7). This can be explained by the fact that crystallization of this glass starts at ~30 K lower temperatures than that of the spinodally phase separated sample, where the viscosity of supercooled liquid is generally higher. The higher viscosity means more constraints for structural rearrangements needed for crystallization to occur. In the case of glass with spinodal type of phase separation, crystallization starts at higher temperatures where the viscosity of the supercooled liquid is lower (Fig. 6,7) and structural rearrangements are easier. So, we may conclude that big droplets of Na/Ca/P-rich phase provide more nuclei for crystallization, initiating the process at lower temperatures.

Decrease in the particle size of powder samples causes significant broadening of the crystallization peak and its shift towards lower temperatures (Fig. 4,5). The activation energy for crystallization becomes much higher than for the bulk samples and almost equal in magnitude for the droplet-like and spinodally phase-separated glasses when the particle size is less than 150 μm (Fig. 6,7). The onset temperature of crystallization also becomes almost the same for both types of the material and simultaneously shifts by ~30-50 K towards lower values in comparison to bulk crystallization (Fig. 6,7). Therefore, we conclude that extended surface area of powdered samples provides a high enough concentration of nucleation sites that the entire crystallization is governed by the processes on the surface. A typical SEM picture of polycrystal formed at the surface of 45S5 BG is shown in Fig. 8. The value of the crystallization activation energy for powdered samples of <300 μm sizes (~350-390 kJ/mol) agrees well with activation energy

values ~ 350 kJ/mol obtained earlier for 45S5 powder prepared by tape casting technique (particle sizes < 10 μm) [37].

The crystallization kinetics as studied with DSC are usually analyzed with Johnson-Mehl-Avrami (JMA) nucleation-growth model [38,39]. However, the JMA equation for non-isothermal conditions is valid only if a certain number of criteria are satisfied: the entire nucleation process takes place during the early stages of the transformation, and becomes negligible afterward; the overall crystallization rate is defined only by the temperature and does not depend on the previous thermal history [40,41]. Fundamental kinetic equations for non-isothermal crystal growth from preexisting nuclei have been developed by Ozawa [33] and a simple method of kinetic analysis of DSC data for these processes has been proposed [38,39]:

$$\frac{d\alpha}{dt} = Af(\alpha)e^{\left(-\frac{E_a}{RT}\right)} \quad (1)$$

where α is fraction of crystallized volume

$$\alpha = \frac{1}{\Delta H_c} \int_0^T \phi dT \quad . \quad (2)$$

Here ϕ is the specific heat flow measured with DSC (W/g) and ΔH_c is the total enthalpy change associated with the crystallization process; the pre-exponential factor A and activation energy E_a are kinetic parameters that should not depend on the temperature T and α ; and

$$f(\alpha) = m(1-\alpha)[- \ln(1-\alpha)]^{1-1/m} \quad (3)$$

is an algebraic expression of the JMA model [38,39].

It has been demonstrated that the JMA exponent m is a characteristic parameter linked to crystal forming morphology. In particular, $m \sim 1$ means predominant surface crystallization [42], while $m \sim 3$ corresponds to three-dimensional bulk crystallization [43]. If one applies JMA

model straight to the investigated 45S5 glasses, then $m \approx 1$ is typically obtained for powdered samples with $<300 \mu\text{m}$ particle sizes and $m \approx 3-4$ for the bulk samples. However, the validity of JMA equation for the investigated glasses should be demonstrated first. A simple test for the applicability of JMA model is proposed by Malek [38]. It is based on the analysis of probe functions:

$$y(\alpha) = \phi e^{\left(\frac{-E_a}{RT}\right)} \quad (4)$$

$$z(\alpha) = \phi T^2 \quad (5)$$

For JMA equation to be valid the maximum of the $z(\alpha)$ function should occur around $\alpha=0.63\pm0.02$ value. As seen from Fig. 9, the maximum for $z(\alpha)$ function is around $\alpha=0.55-0.56$ for bulk (and powder with particle sizes $> 300 \mu\text{m}$) samples of both spinodally and droplet-like phase-separated samples. So, we may conclude that the JMA equation is not applicable to describe the crystallization kinetics of bulk 45S5 BG, which is consistent with previous studies [44]. The same is true for powdered samples with particle sizes $< 300 \mu\text{m}$ of droplet-like phase separated glass, which also demonstrate significant deviation from $\alpha=0.63$ value expected for the validity of the JMA model (Fig. 9b); the α values are significantly higher than predicted. However, in the case of spinodally phase-separated glass (Fig. 9a), the JMA model can be applied for the analysis of crystallization kinetics of powder samples with small particle sizes ($< 300 \mu\text{m}$). So, the mean value of m (about 1) obtained for small particles ($< 300 \mu\text{m}$) of spinodally phase-separated glass is consistent with surface initiated crystallization mechanism proposed by Clupper and Hench [37] for tape cast 45S5 glass (particle size less than $10 \mu\text{m}$). Therefore, we may conclude that for small particle sizes (when the crystallization is mostly surface-driven) and

spinodal-like phase separation, the crystallization kinetics can still be approximated with the JMA model.

The evolution of nanopores during phase separation and crystallization is studied with PAL spectroscopy. The main potential of the PAL spectroscopy method lies in its ability to characterize the local free volumes (including both open and closed pores) in materials on a sub-nanometer scale [22,45]. The PAL method is particularly effective when positronium (Ps) is formed (*ortho*-Ps and *para*-Ps), because the energetic and geometric characteristics of this electron-positron bound state (hydrogen-like atom) are well determined, which allow quantification of free volume dimensions [46]. Thus, it is possible to estimate the average hole size from the *ortho*-Ps lifetime in a given material [47,48]. Assuming approximately spherical shape of the free volume, the *ortho*-Ps lifetime (τ_o) can be related to the average radius of holes (R) by a semi-empirical Tao-Eldrup equation [47,48]:

$$\tau_o = \left[2 \left(1 - \frac{R}{R + \Delta R} + \frac{1}{2\pi} \sin \left(\frac{2\pi R}{R + \Delta R} \right) \right) + 0.007 \right]^{-1}, \quad (6)$$

where ΔR is an empirically determined parameter (in the classical case $\Delta R \approx 0.1656$ nm), describing effective thickness of the electron layer responsible for the pick-off annihilation of *ortho*-Ps in the hole [47,48].

Typical PAL spectra for 45S5 glasses and glass-ceramics are shown in Fig. 10, giving the best-fit parameters as listed in Table 2. Four discrete exponentially decaying components can be distinguished in these spectra (Fig. 10), using iterative curve fitting procedure of the LT program [25]. The first component (τ_1, I_1) includes free annihilation, *para*-Ps decay and is related also to the positrons' bulk lifetime (τ_b) in the sample. The second component (τ_2, I_2) is usually caused by positrons that are trapped before annihilation in the free volume devoid of significant electron

density in the glass structure, where formation of Ps is impossible for any other reason (geometric, energetic, inhibition of Ps formation, etc.) [49]. However, this component may convolute with greater bulk lifetime component of another phase, if it is present in the material.

The remaining two components (τ_3, I_3), (τ_4, I_4) can be directly associated with *ortho*-Ps formation (Table 2). These lifetimes can be related to corresponding pores via Tao-Eldrup relation (Eq. (6)) assuming *ortho*-Ps is in the ground (often denoted as “1s”) state, which is usually satisfied at low temperatures and for relatively small pores. As seen from Table 2, the as-prepared 45S5 glasses both spinodally and droplet-like phase-separated contain almost the same amount of voids $R_3 \sim 1.7 \text{ \AA}$ in radius (estimated from τ_3 and I_3 values). However, spinodally phase-separated glass contains more voids of larger radius $R_4 \sim 3.6 \text{ \AA}$ (Table 2) in comparison to the droplet-like phase-separated material (estimated by τ_4 and I_4 values). These void sizes normally are associated with fine pores within the oxide building blocks (individual coordination polyhedra) of the silica network and their interconnection [22,50]. After droplet-like phase separation or ceramization process the voids agglomerate together, forming voids of larger dimensions ($R_3 \sim 3.2\text{-}3.3 \text{ \AA}$ and $R_4 \sim 4.2\text{-}4.4 \text{ \AA}$ in radii, see Table 2), which most probably reside within the boundaries between the devitrified crystallites and residual glassy phase, or different glassy phases. At the same time structure densifies at a finer scale, as indicated by the increase of I_l intensity after ceramization of both types of 45S5 phase-separated parent glasses (Table 2). This behavior can be understood if one takes into account the fact that bulk lifetime of positrons is generally lower in crystalline material (formed crystallites) than in the corresponding glass [49].

On the basis of the studies performed thus far, we may predict that spinodal type nanostructure would produce a biomedically superior glass/ceramics than the glass comprising of

droplet type nanostructure. We note that within the broad classification of spinodal or droplet type nanostructures, we can have significant variations of the distribution of two phases, which may also impact the cell response. In other words, the conditions of glass fabrication may need to be further optimized for improving the cell response, but the basic premise of superior performance of the spinodal nanostructure will remain. This advantage of spinodal nanostructure may apply to other silicate compositions as well, which are derived from standard 45S5 composition for instance.

4. Conclusions

It is shown that type of phase separation (spinodal vs. droplet-like) has a pronounced effect on the devitrification characteristics of 45S5 BG. In particular, it appears that activation energy of viscous flow for a spinodally phase separated 45S5 glass is lower than that for the droplet-like phase separated glass. Crystallization starts at lower temperatures and the activation energy of crystallization is higher for droplet-like phase separated glass, whereas the spinodally phase separated glass crystallizes at higher temperatures and, therefore, has a lower activation energy of crystallization. The JMA equation is found to be not applicable to the crystallization kinetics analysis for both types of bulk 45S5 BGs. However, for small particle sizes ($< 300 \mu\text{m}$), where crystallization processes are mostly surface driven, JMA equation still works under certain conditions, viz. for spinodally phase separated 45S5 glass powder with small particle size. The nature of phase separation also affects the pore distribution at the nanoscale as shown by PAL spectroscopy. As-prepared 45S5 glasses both spinodally and droplet-like phase-separated contain almost the same amount of fine voids $R_3 \sim 1.7 \text{ \AA}$ in radius, whereas spinodally phase-separated

glass contains more voids of larger dimensions $R_v \sim 3.6 \text{ \AA}$. After ceramization these voids show the tendency to agglomeration in both types of materials.

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Figure captions

Fig. 1. As-prepared 45S5 glasses phase separated to a different degree (a); SEM picture of fresh fractures of droplet-like (b) and spinodally (c) phase separated 45S5 glasses.

Fig. 2. FT-IR spectra of droplet-like and spinodally phase separated 45S5 glasses. Spectrum of fused silica is shown for comparison.

Fig. 3. XRD spectra of spinodally and droplet-like phase separated 45S5 glasses (a) and obtained ceramics (b).

Fig. 4. Typical DSC heating curves for spinodally (a, b) and droplet-like (c, d) phase separated 45S5 glasses measured for the bulk (a, c) and $<32\ \mu\text{m}$ powder (b, d) samples.

Fig. 5. DSC heating curves for spinodally (a) and droplet-like (b) phase separated 45S5 glasses measured for different particle size at 5 K/min heating rate.

Fig. 6. Ozawa plots [33] for the estimation of the crystallization activation energy for spinodally phase-separated glass of different particle size.

Fig. 7. Ozawa plots [33] for the estimation of the crystallization activation energy for droplet-like phase-separated glass of different particle size.

Fig. 8. Typical polycrystal formed at the surface of 45S5 sample.

Fig. 9. $Z(\alpha)$ functions for spinodally (a) and droplet-like (b) phase separated 45S5 glasses. Open symbols correspond to bulk samples, full symbols stand for $<32\ \mu\text{m}$ powder.

Fig. 10. PAL spectra obtained for spinodally (a) and droplet-like (b) phase-separated 45S5 glasses and ceramics with example of fit components for glass samples.

Table 1. Composition of the investigated spinodally and droplet-like phase separated 45S5 glasses and derived ceramics, determined from XPS data.

Sample	Composition, at. %				
	O	Si	Ca	Na	P
Theoretical	55.2	16.3	9.5	17.2	1.8
Spinodally phase-separated glass	50.1	18.9	8.8	20.5	1.6
Ceramics out of spinodally phase-separated glass	49.4	19.3	9.4	19.9	1.9
Droplet-like phase-separated glass	49.8	17.9	9.0	21.3	1.9
Ceramics out of droplet-like phase-separated glass	50.7	19.0	8.8	19.4	2.1

Table 2. Fitting results of PAL measurements in phase separated 45S5 bioglass and derived ceramics: τ_i in ns, I_i in %, R_i in Å.

	Component fit								Voids	
Sample	τ_1	I_1	τ_2	I_2	τ_3	I_3	τ_4	I_4	R_3	R_4
	(± 0.005)	(± 1)	(± 0.005)	(± 1)	(± 0.01)	(± 0.4)	(± 0.05)	(± 0.2)		
Spinodally phase separated										
glass	0.180	50	0.420	44	1.026	4.7	2.859	1.0	1.73	3.58
ceramics	0.180	55	0.420	41	1.467	2.8	3.762	0.6	2.33	4.16
Droplet-like phase separated										
glass	0.180	47	0.420	47	1.035	4.7	3.444	0.3	1.73	3.97
ceramics	0.180	52	0.420	45	1.383	2.9	4.240	0.3	2.22	4.43

Fig. 1.

Fig. 2.

Fig. 3.

Fig. 4.

Fig. 5.

Fig. 6.

Fig. 7.

Fig. 8.

Fig. 9.

(a)

(b)

Fig. 10.

Graphical Abstract