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Doping of a high calcium oxide metaphosphate glass with titanium dioxide

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ABSTRACT

This study investigates the effect of doping a high calcium oxide containing metaphosphate glass series $(CaO)_{40}(Na_2O)_{10}(P_2O_5)_{50}$ with TiO_2 (1, 3, and 5 mol%). TiO_2 incorporation increased the density and glass transition temperature while reduced the degradation rate (5 mol% in particular) by twofold compared with $(CaO)_{30}$ system reported previously. This has been confirmed by ion release and the minimal pH changes. TiP_2O_7, $NaCa(PO_3)_3$ and CaP_2O_6 phases were detected for all TiO_2-containing ceramics. XPS showed that the surface is composed of Ca, P, and Ti. Ti was recognized mainly as TiO_2, but its total amount was lower than theoretical values. ^{31}P magic angle spinning (MAS) NMR showed a downfield shift of the ^{31}P lineshape with increasing TiO_2, interpreted as an effect of the titanium cation rather than an increase in the phosphate network connectivity. FTIR showed that incorporation of TiO_2 increased the strength of the phosphate chains, and the O/P ratio while introducing more Q^1 units into the structure at the expense of the Q^2 units. There were no differences, however, in surface topography roughness and free energies between these glasses. These results suggested that TiO_2 and CaO were acting synergistically in producing glasses with controllable bulk and structural properties.

1. Introduction

Bioactive and bioresorbable biomaterials that can stimulate specific and controlled cell responses at the molecular level are now of major interest as scaffolds for tissue engineering [1]. Phosphate glasses based on the ternary P_2O_5–CaO–Na_2O system have the potential to be used as scaffold materials. They are degradable and the degradation rate is strongly dependant on composition, and accordingly a wide range of materials with different degradation rates can be obtained by tailoring the glass chemistry [2–4]. Furthermore, their degradation products can be eliminated by the normal physiological mechanisms of the body [5].

Several attempts have been made in order to harmonize the degradation behavior with the end application. For example, substituting Na_2O with CaO yielded glass systems that were less degradable, since Ca^{2+} ions have much stronger field strengths than Na^+ and a chelating structure could be formed with ionic bonding between two adjacent phosphate tetrahedra [6,7]. The degradation can also be reduced by an increase of the cross-linkage or the introduction of highly insoluble ions, which makes the glass structure less susceptible to solution attack [8]. Reducing the degradation in turn has led to better biocompatibility [9], for instance, an enhanced bone cell growth together with an up regulation of antigen expression has been observed [10]; in addition, a minimal inflammatory response was also induced by the extracts of low soluble glasses [11,12].

Titanium dioxide (TiO_2) has been used previously for the production of bioactive and biocompatible phosphate-based glasses. TiO_2 acts as a nucleating agent, and although it is miscible in the molten glass, it induces phase separation during cooling of the melt. It was observed that the addition of 0.5 mol% TiO_2 enhanced the bioactivity which started to decrease upon further increase of the TiO_2 content [13].

In our previous study, it has been shown that the addition of TiO_2 into $(CaO)_{30}(Na_2O)_{20}(P_2O_5)_{50}$ phosphate glasses improved the cellular

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response by adjusting the glass degradation [14]. Therefore, it was assumed that TiO_2-containing glasses that maintain the TiO_2 at 1, 3, and 5 mol% and increasing the CaO content (to 40 mol%) could further improve the cellular response by introducing further control of their degradation. Metaphosphate glasses with high calcium content have already been shown to be better for cellular proliferation than those with low calcium content [9]. Hence, the aims of this study were; (a) to prepare glasses of the general formula $(CaO)_{40}(Na_2O)_{10-x}(P_2O_5)_{50}(TiO_2)_x$, where $x = 0$, 1, 3 and 5, (b) analyze the thermal and structural properties of these glasses using differential scanning calorimetry (DSC), differential thermal analysis (DTA), X-ray powder diffraction (XRD), X-ray photoelectron spectroscopy (XPS), nuclear magnetic resonance, and FTIR spectroscopy (c) conduct *in vitro* studies on glass degradation, ion release, and pH changes of the degrading medium and (d) to correlate these results to surface properties; roughness, wettability and surface free energy of the glasses.

2. Experimental

2.1. Manufacture of the glasses

Glass rods of 15 mm diameter were prepared using NaH_2PO_4, $CaCO_3$, P_2O_5 and TiO_2 (all chemicals were >98% purity,) as precursors by the conventional melt quenching process at the corresponding temperatures and time given in Table 1. Each rod was then sectioned into approximately 1 mm thick discs using a diamond saw with methanol as a coolant/lubricant. These discs were then subjected to a series of grinding and polishing steps using waterproof silicon carbide papers; P# 120 for 30 s at 300 RPM to flatten the surface, then P# 500, 1000, 2400, respectively, for 1 min at 500 RPM to smooth the surfaces, and finally P# 4000 for 2 min to get a smooth mirror-finish surface on a Struers Rotopol-11. These discs were used for density, degradation and surface free energy measurements. However, powdered samples, prepared by grinding pieces of glasses in an agate mill, were used thermal, NMR, and FTIR studies. Crystalline powdered samples were used for XRD.

2.2. Bulk glass characterization

2.2.1. Density measurements

Density measurements were conducted on triplicate samples using Archimedes' Principle, on an analytical balance with an attached density kit with ethanol as the immersion liquid for these measurements.

2.2.2. Thermal characterization

Thermal characterization was carried out using both Pyris Diamond DSC and Setaram Differential Thermal Analyzer as previously described (18) to determine glass transition (T_g) crystallization (T_c), and melting temperatures (T_m) at a heating rate of 20 °C min^{-1}.

2.2.3. Degradation studies

The surface area of the glass discs were calculated from the dimensions obtained with Mitutoyo Digimatic Vernier Callipers. Three glass discs from each composition were used for this experiment. They were placed in glass bottles containing 25 ml of high purity water (18.2 MΩ cm resistivity) obtained from PURELAB UHQ-PS with the pH adjusted to 7 ± 0.2 using few drops of NH_4OH. At various time points (0.25, 1, 5, 12, 19, and 26 days), the solutions were removed for ion release analysis. Simultaneously, the discs were taken out of their respective containers, blot dried with tissue and weighed to assess the weight loss. The discs were then placed in a fresh solution of high purity water and placed back into the incubator at 37 °C. Applying a weight loss method [3,4] to these data, a plot of cumulative degradation (% weight loss per unit area) as a function of time was produced.

2.2.4. pH measurements

At every time point pH measurements were taken after transferring the glass discs to a fresh solution (high purity water, pH 7 ± 0.2). The measurements were collected using a Hanna Instruments pH 211 Microprocessor pH meter with attached glass combination pH electrode. This electrode was calibrated using pH colorkey buffer solutions.

2.2.5. Ion release measurements

Ion release studies were simultaneously conducted, and the medium was analyzed for cation (Ca^{2+} and Na^+) and anion (PO_4^{3-}, $P_2O_7^{4-}$, $P_3O_9^{3-}$, and $P_3O_{10}^{5-}$) release by ion chromatography. Inductively coupled plasma mass spectrometry (ICP-MS) was used to determine the amount of Ti^{4+} ions released from all glass compositions at the previously mentioned time points. The instrument was calibrated using the ICP multi-element standard V diluted in ultrapure water to a range of 1–800 ppb, and the Ti^{4+} concentration in the ultrapure water was set as 0 ppb.

2.3. Structural characterization

2.3.1. X-ray powder diffraction

For X-ray powder diffraction (XRD) analysis, the powdered samples were annealed in a ceramic pot from room temperature to the corresponding crystallization temperature, obtained from the differential thermal analyzer, at a heating rate of 20 °C min^{-1} using Lenton Furnace. The temperature was maintained at this temperature for three hours to ensure proper crystallization, and finally it was reduced to room temperature at the same rate used for heating. The data was collected on Brüker D8 Advance Diffractometer in flat plate geometry, using Ni filtered Cu Kα radiation and a Brüker Lynx Eye detector. Data was collected from 10° to 100° 2θ with a step size of 0.02° and a count time of 0.1 s. The phases were identified using the Crystallographica Search-Match (CSM) software and the International Center for Diffraction Data (ICDD) database (vols. 1–42).

2.3.2. X-ray photoelectron spectroscopy

The surface chemical composition of the glass samples with increasing titanium content was measured using X-ray photoelectron spectroscopy (XPS) (Thermo Escalab 220iXL). Measurements

Table 1
Glass codes, melting regime used, the calculated density (ρ) in g cm^{-3}, and glass transition temperature (T_g) in °C.

Glass code	Glass composition (mol%)					Processing temperature		Properties	
	Notation	Calcium oxide	Sodium oxide	Phosphorus pentoxide	Titanium dioxide	Melting temperature (°C)/time (h)	Annealing temperature (°C)/time (h)	ρ (g cm^{-3})	T_g (°C)
$(CaO)_{40}(Na_2O)_{10}(P_2O_5)_{50}$	CNP	40	10	50	0	1100/1	350/1	2.62 ± 0.00	459 ± 2
$(CaO)_{40}(Na_2O)_9(P_2O_5)_{50}(TiO_2)_1$	CNPT1	40	9	50	1	1300/1	420/1	2.64 ± 0.01	479 ± 2
$(CaO)_{40}(Na_2O)_7(P_2O_5)_{50}(TiO_2)_3$	CNPT3	40	7	50	3	1300/3	420/1	2.65 ± 0.00	506 ± 1
$(CaO)_{40}(Na_2O)_5(P_2O_5)_{50}(TiO_2)_5$	CNPT5	40	5	50	5	1300/3	420/1	2.67 ± 0.00	518 ± 0.4