Effect of sodium on bioactive sol-gel-derived borate glasses

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A B S T R A C T

Bioactive, sol-gel derived borate glasses (SGBGs) can rapidly convert to hydroxy-carbonated apatite (HCA) in simulated body fluid (SBF). The processing conditions and compositional changes in four-component glasses have previously been investigated, yet the effect of certain elements, such as sodium, on the processing and bioactivity has not been explored. Therefore, in this study, a borate substituted Bioglass® "45S5" of the formulation $(46.1)B_2O_3-(26.9)CaO-(24.4)Na_2O-(2.6)P_2O_5$; mol %, was created as the baseline glass and the amount of sodium was incrementally decreased three times, while maintaining the ratio of the other elements, until a sodium-free, three-component composition was generated $(61.0)B_2O_3-(35.6)CaO-(3.4)P_2O_5$; mol%. Decreasing sodium content altered the gelation behaviour, textural properties, and greatly influenced reactivity as measured through gravimetric changes when exposed to water vapour. Furthermore, ion release profiles corresponded with the different glass compositions, however, interestingly, sodium content had very little effect on rate of conversion to HCA in SBF, which was observed to be within 2 h, according to x-ray diffraction, attenuated total reflectance-Fourier-transform infrared spectroscopy, and scanning electron microscopy. This study aims to serve as a basis to develop more simplified SGBG systems for tissue engineering applications.

1. Introduction

The ability for glasses to form a surface, bone mineral-like, hydroxycarbonated apatite (HCA) layer after submersion in physiological fluids ("bioactivity") was first discovered in silicate systems [1, 2]. During this process [3], the glass releases ions which play a key role in HCA conversion that can lead to the direct integration with native bone tissue. The release of these ions has also been recently implicated in soft tissue engineering applications [4] since they can stimulate the body's natural healing processes, thereby expanding the classical definition of bioactivity for glasses [3, 5]. Compared to silicate-based glasses, bioactive borate glasses have lower chemical durability, which can allow for a more rapid and complete conversion to HCA [6–11]. During this process, these glasses exhibit the "volume reduction" model where the HCA is deposited directly on the surface of the glass and continues towards the core until none of the original glass remains [7]. The more rapid ion release and ability to fully convert has also made bioactive borate glasses prime candidates for soft tissue engineering applications, such as wound healing [12–15].

Regardless of composition, most bioactive glasses are traditionally generated through the melt-quench process, which involves the high temperature melting of oxides followed by their rapid cooling ("quenching") to preserve the amorphous structure. With the advent of the sol-gel process; a robust, low temperature, aqueous based processing approach, it has been possible to create bioactive glasses with orders of magnitude higher specific surface area values [16]. This process typically uses a mixture of metal alkoxide precursors to form a colloidal

suspension of particles in a liquid (the "sol"), which then undergo hydrolysis and condensation reactions to form a "gel"; essentially the glass network [17]. This gel then undergoes drying and heat treatment (calcination) to eliminate excess precursor organic materials and to densify the glass structure while still maintaining high specific surface areas and porosities.

From a biomedical application prospective, sol-gel derived glasses offer distinct advantages when compared to their melt-quench derived equivalents. For example, the increased surface area and porosity values allow for more rapid ion release rates and thus increased conversion rates to HCA [18, 19] and expanded the bioactive silicate-glass compositional range up to 90 mol% SiO_2 compared to the melt-quench derived limit of ~60 mol% SiO_2 [16]. Furthermore, it is possible to achieve higher homogeneity due to the precursor materials and the processing temperatures are lower. Thus, fluxes such as sodium, which was originally added to bioactive glass compositions to make melting and homogenization easier, maintain a physiological balance of sodium at the glass-HCA interface and modify the local pH in the implant vicinity [5], are not necessary in the sol-gel process [19]. Since then, numerous ternary sol-gel glasses excluding sodium have been created [20].

Nonetheless, Chen et al. recently created the first sol-gel derived Bioglass® "45S5" $[(46.1)SiO_2-(26.9)CaO-(24.4)Na_2O-(2.6)P_2O_5$ (mol %)] with sodium in order to increase the mechanical properties while creating a more biodegradable crystalline phase [21]. The addition of sodium as a network modifier and creates more non-bridging oxygens, thus lowering the chemical durability and increasing the

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biodegradability. After calcination, the resultant glasses were semi-crystalline, which commonly occurs with other sol-gel derived "45S5" glasses [22–26]. This is mainly due to the requirement of reaching high enough calcination temperatures to eliminate the precursor nitrates. A 45S5-like composition [(49.2)SiO_2-(25.8)CaO-(23.3)Na_2O-(1.7)P_2O_5 (mol%)] has also been reported to partially crystallize after calcination [27]. Despite this, amorphous versions of this glass composition have been reported in literature through adjustments in precursor materials, processing routes, and most importantly, calcination temperatures [28–30].

Although, sol-gel derived glasses with borate as the main component have been far less studied [31–34], the first reported composition, (80)B_2O_3-(20)Na_2O (mol%), incorporated sodium [35]. These glasses, however, were not made with the intent of biomedical applications. Borate has also been added to bioactive, sol-gel silicate- [36, 37] and phosphate-glasses [38, 39] as a modifier to help improve the mechanical and bioactivity properties. Furthermore, we have previously reported on a wide compositional range of highly bioactive sol-gel derived borate glasses (SGBGs, 36–61 mol% B_2O_3) [40] based on variations of a borate substituted, "45S5" composition whose melt-quench derived composition has been previously studied [7, 41]. These glasses demonstrated specific surface areas and porosities at least two orders of magnitude greater than the melt-quench equivalent leading to a 25-fold increase in HCA conversion rate. Recently, we have also shown that similar sodium-containing SGBG compositions, can be produced using a variety sol-gel precursors and processing parameters while still maintaining their high bioactivity; converting to HCA within 2 h according to x-ray diffraction [42]. However, while it is known that sodium is not needed for bioactive silicate sol-gel glasses, there has yet to be a systematic study reporting on the effect of sodium content on the properties of SGBGs. Therefore, this study examined the effect of incrementally decreasing the sodium content on the processing, structural, reactivity, and bioactivity properties of these glasses.

2. Experimental

2.1. Materials and methods

Table 1 gives an overview of the SGBG compositions investigated in this study. The baseline composition was a previously examined [40, 42] borate substituted Bioglass® (Na24) [(46.1)B_2O_3-(26.9)CaO-(24.4)Na_2O-(2.6)P_2O_5; mol%], and the amount of sodium was incrementally decreased by ≈8 mol%, while maintaining the ratios of the remaining components, until a three component, sodium-free SGBG composition (Na0) [(61.0)B_2O_3-(35.6)CaO-(3.4)P_2O_5; mol%] was generated.

The glasses were fabricated based on a previously described method [40]. Briefly, boric acid (≥ 99.5%) and anhydrous ethanol (Sigma Aldrich, Canada) were mixed and magnetically stirred in a watch glass-covered Teflon beaker at 40 ± 3 °C to aid dissolution. Once the solution became clear, triethyl phosphate (> 99.8%; Fisher Scientific, Canada), calcium methoxyethoxide (20% in methoxyethanol; Gelest, USA), and sodium methoxide (25 wt% in methanol; Fisher Scientific, Canada) were added in a drop wise manner at 30 min intervals. Once the final addition was complete, the sol was mixed for an additional 30 min or until gelation occurred, followed by transferring into sealed polypropylene vials, and aged at 37 °C for 10 days. The gels were then

Table 1
SGBG Compositions and Codes (mol%).

ID	B_2O_3	CaO	P_2O_5	Na_2O	% CaO + Na_2O
Na24	46.1	26.9	2.6	24.4	51.3
Na16	51.1	29.8	2.9	16.3	46.1
Na8	56.0	32.7	3.2	8.1	40.8
Na0	61.0	35.6	3.4	0	35.6

transferred to crystallization dishes and dried in air at room temperature (RT) for 1 day, followed by oven drying at 120 °C for 2 days. Finally, a calcination step was undertaken at 400 °C at a rate of 3 °C/min, with a 2 h dwell period, followed by furnace cooling. The calcined glasses were then ground to a particle size fraction of 25–75 μm and stored in a desiccator until analysis.

2.2. Glass particle characterization

The average particle size (D_{avg}) and median diameter (D_{50}) of the glass powders was determined using a Horiba LA-920 (ATS Scientific Inc., Canada). The specific surface area (SSA) was measured with nitrogen gas adsorption and desorption isotherms collected with a Micromeritics TriStar 3000 (Micromeritics Instrument Corporation, USA) gas sorption system (n = 3). SSA values were determined using the Brunauer–Emmett–Teller (BET) method [43] while the average pore width and pore volume were calculated using the Barrett–Joyner–Halenda (BJH) method [44].

2.3. X-ray diffraction (XRD)

XRD diffractograms of the glasses were analyzed using a Bruker D8 Discover X-ray diffractometer (Bruker AXSS Inc., USA) equipped with a CuKα (λ = 0.15406 nm) target set to a power level of 40 mV and 40 mA. Three frames were collected from 10 to 70 2 theta (°), using an area detector, and merged in post processing while phase identification was carried out using X'Pert Highscore Plus (PANalytical, Netherlands).

2.4. Attenuated total reflectance-Fourier transform infrared spectroscopy (ATR-FTIR)

ATR-FTIR spectroscopy was carried out between 4000 and 650 cm^{-1} with a resolution of 4 cm^{-1} using 64 scans per sample using a Spectrum 400 (Perkin-Elmer, USA). The collected spectra were baseline corrected then normalized to the total area surface area under absorption bands using Spectrum software (Perkin-Elmer, USA).

2.5. Scanning electron microscopy (SEM)

SEM was carried out on Pt sputter coated samples. Analysis was performed with an Inspect F50 Field Emission Scanning Electron Microscope (FEI Corporation, U.S.A.) at 5 kV.

2.6. Reactivity

The aqueous interactions of SGBG particles were investigated through dynamic vapour sorption (DVS) using a DVS Intrinsic (Surface Measurement Systems Ltd., U.K.), which measures mass changes (± 0.1 μg) under controlled relative humidity (RH) and temperature. Approximately 5 mg of glass powder were placed in an aluminum pan and inserted into a chamber at 37 ± 0.05 °C which were then directly exposed to 90% RH for 6 h and then to 0% RH for a further 6 h.

2.7. Inductively coupled plasma-optical emission spectrometry (ICP-OES)

The release of boron, calcium, sodium, and phosphorus ions from glass powders (n = 3) at a 1.5 mg/mL ratio in deionized water (DIW), was quantified using an inductively coupled plasma–optical emission spectrophotometer (Thermo Scientific iCAP 6500, USA). Collected aliquots at 0.5, 6, and 24 h were filtered through a 0.2 μm nylon filter then stored in a 15 mL falcon tube followed by dilution with 4% (w/v) nitric acid (Fisher Scientific, Canada). Serially diluted solutions of boron (0.5, 5, 50 ppm), calcium (0.2, 2, 20 ppm), sodium (1, 10, 100) and phosphorous (0.1, 1, 10 ppm) were used as standards. Furthermore, the pH change of the solution due to glass dissolution at the same timepoints was measured (n = 3) with an Accumet XL20 pH meter (Fisher