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Characterization of silica-based and borate-based, titanium-containing bioactive glasses for coating metallic implants

Omar Rodriguez [a,b], Declan J. Curran [a,b], Marcello Papini [a], Lana M. Placek [c], Anthony W. Wren [c], Emil H. Schemitsch [b], Paul Zalzal [d], Mark R. Towler [a,b,e,*]

[a] Department of Mechanical & Industrial Engineering, Ryerson University, Toronto M5B 2K3 Ontario, Canada
[b] St. Michael's Hospital, Toronto M5B 1W8 Ontario, Canada
[c] Inamori School of Engineering, Alfred University, Alfred, NY 14802, USA
[d] Oakville Trafalgar Memorial Hospital, Oakville L6J 3L7 Ontario, Canada
[e] Department of Biomedical Engineering, University of Malaya, Kuala Lumpur, Malaysia

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ABSTRACT

Bioactive glasses have found applications in diverse fields, including orthopedics and dentistry, where they have been utilized for the fixation of bone and teeth and as scaffolds for drug delivery. The present work outlines the characterization of two novel titanium-containing glass series, one silica-based and one borate-based. For the silica-based series, titanium is added at the expense of silicon dioxide whereas for the borate-based series, it is added at the expense of boron oxide as confirmed by Energy Dispersive Spectroscopy. Amorphous structures are obtained for silica-based glass at 15 mol% TiO_2 and for borate-based glasses at 0 mol% and 5 mol%, with low crystal peak intensities exhibited within the remaining glasses. MAS-NMR proves the role of P_2O_5 as a network modifier for both glass series by evidencing only Q^0 structures (and Q^1 structures for the silica-based glasses with crystal structures), whereas FTIR proves that Ti acted as a network modifier in the glass as there was an absence of peaks assignable to titanium bonding. This implies that the two glass series will degrade *in-situ* and release ions at the site of implantation. Additionally, thermal data sourced from these glasses indicate processing windows which make them suitable for enameling onto implants, with the borate-based series exhibiting greater processing windows over the silica-based series, hence making the borate glasses more suitable for coating metallic implants compared to their silica-based counterparts.

1. Introduction

In the field of prosthetics, two technologies for attaching the residual limb and the prosthetic implant are widely utilized: socket attachment and direct skeletal (or bone-anchored) attachment [1]. Socket attachment is the most common method [2], with designs already established for the different applications, *e.g.* below, through or above-knee amputations [3–6]. In general, socket attachment consists of wrapping the prosthetic limb around the residual limb, where the prosthesis serves as the socket for the residual limb, with quadrilateral and ischial containment sockets being the most noteworthy technologies [7]. Compared to socket attachment, direct skeletal attachment (DSA) is a relatively new technology, where an implant is attached directly to the patient's bone at the residual limb. Upon healing, the implant in DSA serves as the attachment mechanism between the prosthesis and the body [1]. In achieving osseointegration, the implant is permanently connected to the bone, resulting in high force and moment interaction between the prosthesis and the body [8]. DSA technology offers the advantage over socket technology *via* a reduction in skin-related complications and residual limb constraints within the socket, which is due to the limited direct contact between the prosthetic implant and the skin [9].

Titanium is regularly used in prosthetics due to its ability to create a permanent bond to bone, *via* osseointegration [10,11], a condition achieved when there is no relative motion between the implant and the bone with which it is in direct contact [12]. It is this characteristic that has also made DSA devices more favorable than socket attachment for prosthetics. Nonetheless, there are concerns regarding DSA that include potential infection, skin irritation and breakdown, implant failure and risk of a broken bone in the residual limb [13–17]. Addressing these concerns will aid in shifting the current paradigm from socket attachment towards DSA.

It is important to understand the overall mechanics of the DSA system, as loads that may negatively affect the residual limb bone may occur in this situation [17]. This places the patients at risk of requiring additional treatment if the bone weakens or fractures due to incomplete osseointegration or due to detrimental bone remodeling induced by

* Corresponding author at: Department of Mechanical and Industrial Engineering, Faculty of Engineering and Architectural Science, 350 Victoria Street, Toronto, Ontario, Canada M5B 2K3.
E-mail address: mtowler@ryerson.ca (M.R. Towler).

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stress shielding [18]. Different approaches have been taken towards improving the patient's experience with regards to DSA, including modifying the implant surface by chemical etching with hydrochloric and sulfuric acid, sandblasting, titanium plasma-spraying, hydroxylapatite (HA) plasma-spraying, coating the implant with a titanium dioxide (TiO_2) layer through anodic oxidation, and with bioactive glass [9,19–21]. Among these methods, HA coating has been used for over 20 years, exploiting its ability to promote bone ingrowth [22–24]; yet there are concerns with HA use as it has no mechanism to retard bacterial or biofilm colonization at the implant site. Coatings have also been produced based on chlorhexidine and silicone with ammonia couplings [25,26], but these have little clinical applicability due to erosion of the compounds as they migrate to the surface. Of these approaches, bioactive glasses have showed encouraging results [19].

The use of bioactive materials has proliferated since the development of Hench's 45S5 Bioglass® in the 1960s [27] due to its favorable interaction with living tissue. Bioglass was the first synthetic to chemically adhere to both hard and soft tissue [27]. While Hench acknowledged that Bioglass® is unsuitable as a coating [28], he developed criteria for an optimal bone replacement material [29], which included that "the material should resorb at the same rate that bone is regenerated, with byproducts that are beneficial and easily excreted by the body so that bone will restore to a healthy state". *In-situ* degradation of these materials makes them desirable for clinical applications owing to the release of beneficial ions to the surrounding tissues promoting antibacterial behavior, bone formation and growth, tissue healing, etc. [30–32]. Bioactive glasses have been employed for coating metals [33–35], yet some of these proposed compositions contain aluminum [33,35], which has been associated with defective bone mineralization alongside concerns over its neurotoxicity [36]. Other compositions have been deficient in zinc [34,35], an antibacterial component [32,37,38] to aid in the healing process, also known to inhibit the growth of caries-related bacterial such as *Streptococcus mutans* [39]. Although virtually all materials facilitate biofilm formation which may lead to bacterial infection, bacteria attach less readily to glass [40], providing a rationale for a glass-based solution. As bioactive glasses influence genetic expression, differentiation and cell proliferation by the release of ions [31,41–43], engineering control of the biological response *via* dissolution products creates an opportunity for innovation. The proposed compositions in this work are expected to provide superior performance as they are expected to inhibit bacterial growth due to the addition of zinc, while the absence of aluminum minimizes the possibility of the coating causing toxicity in surrounding tissues. Furthermore, incorporating titanium in the glass compositions is expected enhance osseointegration [10–12].

This study outlines the characterization of two novel bioactive glass series, a silica-based glass series and a borate-based glass series that contain increasing amounts of titanium oxide (TiO_2). Titanium is employed to exploit its osseointegrative capability at the interface of the metallic implant and the bone. TiO_2 will be added in increments of 5 mol% up to 20 mol%. Characterization techniques included energy dispersive spectroscopy (EDS), X-ray diffraction (XRD) differential scanning calorimetry (DSC), Fourier transform infrared (FTIR) spectroscopy, particle size analysis (PSA) and magic-angle spinning-nuclear magnetic resonance (MAS-NMR).

2. Materials and methods

2.1. Glass preparation

Silica-based and borate-based glasses were formulated for this study. The glass compositions, as well as the nomenclature, are reported in Table 1. TiO_2 was added at the expense of SiO_2 for the SRT series and at the expense of B_2O_3 for the BRT series. The glasses were prepared by weighing out appropriate amounts of analytical grade reagents (Fisher Scientific, Ottawa, ON, Canada & Sigma-Aldrich, Oakville, ON, Canada), firing (1400–1500 °C for 1 h for the silica-based glasses, 1200 °C for 1 h for borate-based glasses) in silica crucibles, and shock quenching in water. The resulting frit was then ball-milled, and sieved to retrieve glass particulates ≤20 μm.

Table 1
Glass formulations (mol%).

	Silica-based glass					Borate-based glasses				
Reagent	SRT0	SRT1	SRT2	SRT3	SRT4	BRT0	BRT1	BRT2	BRT3	BRT4
TiO_2	0	5	10	15	20	0	5	10	15	20
SiO_2	52	47	42	37	32	0				
B_2O_3	0					52	47	42	37	32
CaO	12					12				
P_2O_5	6					6				
Na_2O	14					14				
ZnO	16					16				

2.2. Network connectivity (NC)

Network connectivity (NC) provides information on the ability for a glass to degrade and interact with the surrounding tissues [44]. Network connectivity for the proposed formulations was calculated using Eq. (1).

$$NC = \frac{BO - NBO}{NBS} \quad (1)$$

where *BO* is the number of bridging oxygens, *NBO* the number of non-bridging oxygens and *NBS* the total number of bridging species. As network formers, 2 BO are contributed to the glass network per SiO_2 and B_2O_3 in each Q^2 unit; as network modifiers, 2 NBO are contributed per Ca^{2+} and 1 NBO per Na^+. As for P_2O_5, recent work by Hill [45–47] provided insight on the role of phosphates in the glass network, demonstrating its role as an orthophosphate Q^0 (glass modifier) in a SiO_2–P_2O_5–CaO–Na_2O series. Supported by this work, P_2O_5 may only be considered as a glass modifier, with 3 NBO per PO_4^{3-}, and supporting data will be gathered through ^{31}P MAS-NMR. As for ZnO and TiO_2, these reagents behave as network intermediates; therefore, in considering ZnO as a glass former 1 BO is added, and 2 BO are added for TiO_2. Considering these reagents as modifiers, 2 NBO are contributed per Zn^{2+} and per TiO_6^{2-}.

2.3. X-ray diffraction (XRD)

X-ray diffraction (XRD) was performed to confirm that an amorphous state was achieved for all fired materials. Samples were analyzed over the range of $20° \le 2\theta \le 80°$, with a step size of 0.05° using a PANalytical X-ray diffractometer (PANalytical, QC, Canada). CuKα (1.54 Å) anode was employed, with a generator voltage of 30 kV and a tube current of 10 mA. Crystalline phases were identified using the International Centre for Diffraction Data (ICDD) standard diffraction patterns.

2.4. Particle size analysis (PSA)

After grinding and sieving of the glass, particle size analysis (PSA) was undertaken to retrieve the average particle size of the glass powder. Particle size analysis was achieved using a BeckmanCoulter Multisizer 4 particle size analyzer (BeckmanCoulter, Fullerton, CA, USA). Three powder samples per glass were evaluated in the range of 2 μm–60 μm. Results were analyzed by Multisizer 4 software, with means and standard deviations based on counting statistics of 30,000 particles per measurement.