Research Article

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Surface Properties and Reactivity of Phosphate-based Glasses by Inverse Gas Chromatography and Dynamic Vapour Sorption

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Abstract: The chemical durability of phosphate-based glasses (PGs) in an aqueous environment is crucial in determining their dissolution properties and their ultimate performance *in vivo*. In this study, inverse gas chromatography (IGC) and dynamic vapour sorption (DVS) were used to investigate the short-term aqueous interactions of PG particles doped with SiO_2 and TiO_2 ($50\text{P}_2\text{O}_5\text{-}40\text{CaO-xSiO}_2\text{-(10-x)TiO}_2$, where $x=7, 5, 3$, and 0 mol%). IGC was used to evaluate the solubility parameter and surface energy of PGs. A good correlation between the polar parts of the solubility parameter and surface energy with glass transition temperature (T_g) and dissolution rates was demonstrated. DVS was applied to monitor the sorption characteristics of the PG particles. An increase in silica content resulted in greater vapour sorption and mass change. Nuclear magnetic resonance spectroscopy data of the PGs post exposure to vapour demonstrated that increased SiO_2 content disrupted the glass network and formed protonated phosphate species. Fourier transform infrared spectroscopy verified the presence of non-reacted water molecules in the PGs depending on SiO_2 content. Moreover, there was a good correlation between the values measured through IGC and DVS, demonstrating the ability of both techniques in predicting the dissolution properties of PGs as consequence of alterations in their chemistry.

Keywords: Phosphate-based glasses, Solubility, DVS (dynamic vapour sorption), IGC (inverse gas chromatography)

1 Introduction

Phosphate-based glasses (PGs) have been studied for a wide range of potential biomedical applications since their degradation and ion release rates can be controlled through their chemistry [1]. These glasses have been investigated for bone regeneration [2], repairing damaged nerves [3, 4], angiogenesis and cell differentiation [5], antibacterial and wound healing [6–8] as well as for helping engineer human craniofacial muscle [9]. PG dissolution occurs by an initial ionic exchange process between the glass and aqueous solution to form a hydrated layer on the glass surface, which is followed by the breakage of P-O-P bonds due to the presence of water molecules and H^+ resulting in the degradation of the glass network [10, 11]. The dissolution rate depends on the chemical durability, which is dictated by a number of factors including bulk composition, surface and textural properties (e.g., specific surface area and porosity) [12–14]. Determination of dissolution rate in glasses often occurs via submersion in an aqueous solution, e.g., deionized water (DIW) [15], cell culture medium [16], or simulated body fluid (SBF) [17] for predetermined time points at which the glasses are removed and weighed to measure the rate of weight loss.

The main network former of PGs is P_2O_5 consisting of a phosphate tetrahedron as the building unit. Since phosphorous has a valence of 5^+ its tetrahedron unit has three single oxygen bonds and one double bonded oxygen [18]. Thus, understanding the effect network modifiers on glass composition is of great importance as this will affect the glass bonding and thus influence the chemical durability and degradation properties. Glass transition temperature (T_g) is a parameter used to indicate chemical durability in which higher T_g values suggest an increase in glass cross-linking density as well as higher volumetric density leading to a more durable glass. In general, incorporation of cationic oxides (e.g., CaO , CuO , MgO , SrO_2 , TiO_2 and Fe_2O_3) into PGs increases the glass durability as well as T_g due to their cross-linking effect [2, 10, 19–23]. These in turn

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have been shown to decrease the degradation rates, control ionic release through dissolution and subsequently enhance biological responses in the context of osteoblastic cell proliferation as well as antibacterial [8] and potential angiogenic properties [2, 10]. In contrast, the effect of SiO_2 incorporation into PGs is not yet fully understood. For example, it has been shown that an increase in silica content in PGs ($50\text{P}_2\text{O}_5\text{-}30\text{CaO}\text{-(}15-x\text{)NaO}_2\text{-}5\text{Fe}_2\text{O}_3\text{-}x\text{SiO}_2$, where $x = 0, 1, 3$, and 5 mol%) increases both their T_g and the degradation rates [24, 25]. In contrast, previous work has also shown that, substituting Fe_2O_3 with SiO_2 in the glass composition ($50\text{P}_2\text{O}_5\text{-}40\text{CaO}\text{-}x\text{Fe}_2\text{O}_3\text{-(}10\text{-}x\text{)SiO}_2$, where $x = 0, 5$ and 10 mol%), decreased T_g and volumetric density of PGs and consequently their chemical durability which led to a higher dissolution rate in DIW and phosphate buffered saline (PBS) [26]. Similar findings were reported by substituting TiO_2 with SiO_2 in the glass compositional range ($50\text{P}_2\text{O}_5\text{-}40\text{CaO}\text{-}x\text{SiO}_2\text{-(}10-x\text{)TiO}_2$, where $x = 10, 7, 5, 3$, and 0 mol%) which led to a less stable glass structure and higher degradation rate [20]. It was shown that SiO_2 incorporation into PGs decreases the glass chemical durability by disrupting the glass network, and decreases the formation of strong P-O-Ti bonds, which have a direct effect on T_g [27, 28].

Network modifying oxides not only control the bulk properties, but also the surface properties of PGs [29]. Surface energy and the hydrophilic/hydrophobic nature of glasses are traditionally measured *via* contact angle measurements [30–32], which may not be sensitive enough to measure changes in surface properties due to slight changes in glass chemistry [19, 20]. For example, while the substitution of TiO_2 with SiO_2 in PGs led to a decrease in T_g and density, and an increase in glass dissolution, no significant difference was reported between the contact angle measured polar surface energy of the glasses with small incremental increases in SiO_2 content [20]. It was shown that only glasses with highest silica content (up to 10 mol% SiO_2) and no TiO_2 exhibited the highest polar surface energy, which was attributed to the formation of Si-OH groups [20]. To this end, there is a need to better understand and evaluate the capability of other techniques to overcome the limitations of conventional methods of evaluating the surface properties of PGs.

Therefore the objective of this study was to explore the potential of inverse gas chromatography (IGC) as a technique to investigate the surface properties of PGs. IGC is a technique that has been mainly used to characterize the solubility parameters, surface and bulk properties of polymers, pharmaceuticals, minerals and nanomaterials [33]. In the context of bioceramics, it has been suggested that IGC can be used as a rapid and accurate technique to suc-

cessfully measure and compare the surface energies of various particles and porous, textured morphologies [34]. For example, IGC was utilized to measure the surface energies of rough and porous biosurfaces by comparing synthetic and naturally derived hydroxyapatite samples [35]. It was suggested that biological apatite, derived from bovine trabecular bone, has higher surface heterogeneity with high surface energy domains due to the presence of impurities and surface defects. It was proposed that this apatite is more suitable for protein adhesion and cell attachment when compared to synthetic apatite [35]. Therefore, it was hypothesized that IGC could be used as a technique to characterize the surface and bulk properties of bioactive and soluble glass particles. To investigate this, the solubility parameter and surface energy of PGs of four different formulations in the compositional range of ($50\text{P}_2\text{O}_5\text{-}40\text{CaO}\text{-}x\text{SiO}_2\text{-(}10-x\text{)TiO}_2$, where $x = 7, 5, 3$, and 0 mol%) were determined via IGC to evaluate the effect of SiO_2 and TiO_2 incorporation into PGs on their chemical durability, solubility and surface properties. The surface property parameters were correlated with T_g as an indicator of chemical durability as dictated by glass composition [20] and dissolution rates in DIW [20] as well as sorption parameters, used to define their immediate aqueous interaction and determined by dynamic vapour sorption (DVS). DVS, which is a gravimetric technique that measures vapour sorption under controlled variable relative humidity (RH) values, has recently been used to characterize the aqueous interactions of soluble and bioactive glasses [36–38]. Therefore, the aim of this work was to provide an insight into using the complementary IGC and DVS techniques in predicting the surface properties and reactivity of PGs.

2 Materials and methods

2.1 PG production

Four different compositions of the melt-quench derived PGs ($50\text{P}_2\text{O}_5\text{-}40\text{CaO}\text{-}x\text{SiO}_2\text{-(}10-x\text{)TiO}_2$, where $x = 7, 5, 3$, and 0 mol%) were produced, as previously reported ²⁰. Briefly, P_2O_5 , CaHPO_4 , SiO_2 (Alfa Aesar, Canada), and TiO_2 (Sigma-Aldrich, Canada) precursors were dry blended at 350°C for 20 min. The precursors were then melted in a platinum crucible at the range of $1350\text{-}1500^\circ\text{C}$ for 3.5h, cast in a pre-heated cylindrically shaped graphite mould (10 mm in diameter), and annealed at the range of $450\text{-}550^\circ\text{C}$ for 2h to remove residual stresses [20]. Melt-derived glass rods were pulverized by mortar and pestle. Afterwards, particles were sieved in the range of 38

and 45 μm with the specific surface area of $0.124 \pm 0.001 \text{ m}^2/\text{g}$ (for Si_7Ti_3 , $n=3$), which was measured by a Micromeritics TriStar 3000 (Micromeritics Instrument Corporation, USA) using the Brunauer–Emmet–Teller nitrogen adsorption method [39]. These sieved particles underwent analysis through IGC, DVS, scanning electron microscopy, Fourier transform infrared spectroscopy, nuclear magnetic resonance and x-ray diffraction, as described below. T_g , dissolution and ion release data were taken from a previously reported study [20].

2.2 IGC

Inverse gas chromatography experiments were conducted in a Surface Energy Analyser, SEA (Surface Measurement Systems Ltd, UK), in which the solubility parameter [40] and surface energy [41, 42] of the various glass compositions were investigated. Approximately 1 g of PG particles ($n=2$) was loaded into a glass column and all measurements were performed at $37 \pm 1^\circ\text{C}$. Helium was used as a carrier gas with the flow rate of 5 mL/min. Different types of probe molecules, hexane, heptane, octane, ethanol, 1-butanol, 1-propanol, dichloromethane (DCM), toluene and acetonitrile (Sigma-Aldrich, Canada) were injected to calculate the dispersive, H-bond and polar part of the solubility parameter analyzed using the SMS-iGC advanced software (SMS Ltd, UK). The retention volume of each probe molecule was measured to calculate the Flory-Huggins interaction parameter. Then, by varying the probe molecule, the solubility parameter (δ), a measure of the square root of the cohesive energy density, was determined from the calculated Flory-Huggins interaction parameter (SMS-iGC Advanced Software performed all calculations) [43, 44]. By choosing different types of probe molecule (non-polar, polar and H-bond), different components of the solubility parameter were also calculated. Additionally, the SEA was utilized to examine surface energy of PG particles ($n=3$) at 50% surface coverage. The retention volumes were calculated from the retention times from the peak maximum to determine the surface energies. The Schultz method was applied for the dispersive components, and the Della Volpe scale for the specific (polar) components.

2.3 Vapour sorption

The interaction of the various PG particles with vapour sorption was analyzed using a DVS Intrinsic (SMS Ltd., UK) by measuring mass changes ($\pm 0.1 \mu\text{g}$) under controlled temperature and humidity. Approximately 50 mg of PG

particles was placed in an aluminum pan and inserted into a chamber with a constant temperature of $37 \pm 0.05^\circ\text{C}$. Two methods of analysis were carried out: 1) the RH was increased stepwise at 5% RH up to 90% RH then back down to 0% RH while the relative mass change was measured when equilibrium ($dm/dt < 0.002\% \text{ min}^{-1}$) was reached or after maximum of 4 h; 2) the PG particles were immediately exposed to 90% RH for 24 h, which was then reduced back down to 0% RH for another 24 h. For both methods, the PG particles were dried at 0% RH and 37°C for 1 h prior to RH increase.

2.4 Scanning electron microscopy (SEM)

An Inspect F50 Field Emission Scanning Electron Microscope (FEI Corporation, USA) was used to analyse the morphological characteristics of the PG particles before and after exposure to vapour sorption with an applied voltage of 10 kV.

2.5 X-ray diffraction (XRD)

Glass particles were analyzed with a Bruker D8 Discover X-ray diffractometer (Bruker AXSS Inc., USA) equipped with a $\text{CuK}\alpha$ ($\lambda = 0.15406 \text{ nm}$) target set to a power level of 40 mV and 40 mA before and after DVS analysis. Using an area detector, 3 frames of 23° were collected from $10 - 80 2\theta$ ($^\circ$).

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

A Spectrum 400 (PerkinElmer, Waltham, MA) in the attenuated total reflection (ATR) mode was used. Spectra were generated with 4 cm^{-1} resolution in the $4000\text{--}650 \text{ cm}^{-1}$ wavenumber range with 64 scans for each sample.

2.7 Nuclear magnetic resonance (NMR)

^{31}P magic angle spinning nuclear magnetic resonance (MAS NMR) spectra were obtained at a radiofrequency of 161.8 MHz on a Varian VNMRs400 spectrometer. Samples were placed in 4 mm rotors. At $180\text{--}360^\circ$ a pulse was applied and 256 scans were accumulated with decoupling of ^1H during acquisition to observe protonated phosphate groups.

Table 1: Solubility parameter and surface energy as determined through IGC. Dispersive part of the solubility parameter (δ_{dis}) as measured by hexane, heptane and octane, polar part of the solubility parameter (δ_{polar}) as measured by toluene, DCM and acetonitrile, H-bond of the solubility parameter (δ_H) part as measured by ethanol, propanol and butanol, and the total solubility parameter (δ_{total}). Dispersive part of the surface energy ($SE_{dis}(IGC)$), and Polar part of the surface energy ($SE_{polar}(IGC)$).

Sample	δ_{dis} [(MPa) ^{0.5}]	δ_{polar} [(MPa) ^{0.5}]	δ_H [(MPa) ^{0.5}]	δ_{total} [(MPa) ^{0.5}]	SE_{dis} [mN/m]	SE_{polar} [mN/m]
Si0Ti10	28.21±1.21	13.11±0.26	14.85±0.61	34.49±0.66	32.12±0.17	3.88±0.27
Si3Ti7	25.04±1.67	17.20±0.90*	43.99±4.15*	53.49±4.01*	31.03±2.14	4.65±0.32*
Si5Ti5	23.69±1.43	17.31±0.75*	43.41±1.53*	52.42±1.31*	33.26±0.79	5.13±0.45*
Si7Ti3	29.91±0.95	19.05±0.56*	45.50±4.75*	57.75±3.86*	34.47±0.25	5.37±0.21*

* Statistically significant compared to the Si0Ti10 ($p < 0.05$).

2.8 Statistical analysis

Statistical significance of the solubility parameters between sample means was determined using a Student's t-test at a significance level of $p < 0.05$.

3 Results

3.1 Surface and solubility properties as measured through IGC

The solubility parameters (δ) and surface energy (SE) of the various PG compositions were evaluated using IGC to characterize their reactivity (Table 1).

The dispersive component of the solubility parameter did not indicate a specific trend, and only the Si5Ti5 PG composition was statistically different when compared with Si0Ti10 and Si7Ti3 compositions ($p < 0.05$). In contrast, the polar and H-bond components of the solubility parameter of the silica containing PG particles were statistically significant ($P < 0.05$) when compared to that of the Si0Ti10 PG particles. Additionally, the dispersive component of the surface energy did not show any statistically significant difference ($P > 0.05$). However, the polar part of the surface energy of the silica containing glasses was significantly different ($P < 0.05$) when compared to that of Si0Ti10 PG. Figure 1 correlates the polar part of the solubility parameter and polar surface energy with T_g (Figure 1a&1b) and dissolution rate (Figure 1c&1d) of the PG particles [20].

3.2 Vapour sorption

3.2.1 Exposing PG particles to different relative humidity percentages

DVS was used to gravimetrically measure the sorption and desorption of water vapour of the PG particles after exposure to different RH values. Figure 2(a) shows one full cycle of sorption and desorption isotherms of the four PG compositions with different amounts of silica (0, 3, 5 and 7 mol%) exposed to the variable RH values in the range of 0-90% RH with a 5% step size of increase/decrease. The sorption phase of all compositions indicated two different regions; first, an initial small increase in mass up to approximately 65% RH; secondly, a dramatic increase in mass up to 90%. This sudden inflection point increase was determined as the specific % RH value in which the mass change increased by more than 70% compared to the previous RH % and can be explained by deliquescence phenomena [45, 46]. However, it should be noted that the calculated isotherms do not show a true isotherm since the mass change from 75 to 90% RH (except for Si0Ti10) did not reach equilibrium after 4 h. The total water content adsorbed up to 60% RH for Si0Ti10, Si3Ti7, Si5Ti5 and Si7Ti3 were 0.016, 0.018, 0.053 and 0.119 mg of water, respectively. The Si7Ti3 particles exhibited the highest total sorption at 90% RH (17.42% mass change). Figure 2(b) shows a linear relationship between the inflection point with T_g and glass dissolution rate [20]. Along with T_g , an increase in silica content decreased the inflection point, while it increased the PG dissolution rate. A linear regression ($R^2 = 0.9879$) between inflection point and T_g of PGs with different silica contents demonstrated the ability of DVS to provide complementary information on glass durability.

Figure 1: (a) Correlation between the polar part of the surface energy as measured by IGC and glass transition temperature (T_g) [20]. (b) Correlation between the polar part of the solubility parameter as measured by IGC and glass transition temperature (T_g) [20]. (c) Correlation between the glass dissolution rate [20] and the polar part of the surface energy as measured by IGC. (d) Correlation between the glass dissolution rate [20] and the polar part of the solubility parameter measured by IGC (Error bars: Standard deviation: SD, $n = 3$).

3.2.2 Sorption kinetics at 90% RH

PG particles were directly exposed to 90% RH for 24 h in order to investigate the effect of silica content on glass sorption kinetics (Figure 2c). The sorption phase of all four compositions at 90% RH was characterized by a linear increase in mass up to 24 h. It can be observed that PG particles with the highest silica content (Si7Ti3) showed the highest rate and percentage increase in mass. Desorption for 24 h at 0% RH was characterized by a rapid decrease in mass and reached equilibrium after approximately 0.5, 1, 2 and 5 h for Si0Ti10, Si3Ti7, Si5Ti5 and Si7Ti3, respectively. Figure 2(d) show a linear relationship between glass dissolution rate with the rate of sorption up to 24 h of exposure to 90% RH and the percentage of mass change at 24 h and 48 h. There was an increase in the sorption rate and the mass changes and dissolution rates with an increase in silica content. Additionally, phosphorous ion release rate [20] of the various PG compositions was corre-

lated with mass change% at 24 h and the inflection points (as measured through DVS) to demonstrate higher silica content is the glass composition leads to the higher phosphorous ion release rate (Figure S1).

The polar parts of both the solubility parameter and surface energy (as measured through IGC) were correlated with the inflection points (as measured through DVS) of the various PG compositions to verify the ability of both techniques in predicting the dissolution properties of PGs (Figure 3).

3.3 Morphological and chemical analysis pre and post vapour sorption

The sieved PG particles were characterized in terms of morphology and structure before and after exposure to vapour sorption (water molecules) through SEM, FTIR, XRD and NMR. Figure 4 shows the SEM micrographs of the PG par-

Figure 2: (a) One full vapour sorption and desorption isotherm cycle of the different PG compositions exposed to increasing and decreasing RH% where the RH was changed by successive steps of 5% over a range of 0 to 90%. (b) Correlation between the inflection point and glass dissolution rate [20] and glass transition temperature (T_g) [20]. (c) Vapour sorption and desorption curves of the different PG compositions directly exposed to 90% for a 24 h period and subsequently to 0% RH for a further 24 h. (d) Correlation between glass dissolution rate [20] and rates of weight increase, as well as mass change at 24 h (end of sorption phase) and 48 h (end of desorption phase).

Figure 3: Correlation between solubility parameter (SP) and polar part of the surface energy as measured by IGC (SE(IGC)-Polar) with the inflection point as determined from DVS isotherms.

ticles before and after vapour sorption (24 h at 90% RH), respectively. Figures 4a-4c show the glass particles with particle sizes in the range of 38-45 μm . The surface appearance in the glass particles post exposure to 90% RH was monitored (Figures 4d-4f). Figure 4i&4j show the XRD patterns of the PG particles before and after vapour sorption (24h, 90% RH), respectively. The broad humps before and after exposure to vapour (90% RH up to 24) verified that the amorphous nature of the materials was maintained [47].

Figure 5a&5b show the ATR-FTIR spectra of the PG particles with different compositions before and after exposure to vapour sorption (24 h at 90% RH), respectively. All as-made PG particles showed the various phosphate peaks associated with PGs. In all spectra six phosphate peaks of stretching modes of vibration can be observed including the PO_2 asymmetric stretch at 1250 cm^{-1} , two P-O^- stretching mode bonds at 1000 and 1100 cm^{-1} , an asymmetric

Figure 4: SEM micrographs of the different PG particle compositions before (a, b, c and d for SiO₂Ti₁₀, Si₃Ti₇, Si₅Ti₅, and Si₇Ti₃, respectively) and after vapour sorption (e, f, g and h for SiO₂Ti₁₀, Si₃Ti₇, Si₅Ti₅, and Si₇Ti₃, respectively). (Insets showing higher magnifications). XRD patterns of the different PG particles pre (i) and post (j) vapour sorption after 24 h at 90% RH followed by 24 h at 0% RH.

stretching mode peak at 900 cm^{-1} and double symmetric stretching mode peaks in the range of $700\text{--}800\text{ cm}^{-1}$ attributed to (P-O-P) bond [48–50]. ATR-FTIR showed that there is a small shift of asymmetric (P-O-P) peak to the higher wavelength with increasing Si⁴⁺ [49]. Further, PG particles with higher amount of silica (7 mol% Si) shows sharper peak due to the stretching of ionic P-O⁻ bond at 1000 cm^{-1} [51]. Figure 5b shows ATR-FTIR spectra of PG particles after exposure to vapour sorption. The appearance of a broad peak in the range of $3000\text{ to }3800\text{ cm}^{-1}$ and presence of another peak at 1660 cm^{-1} can be attributed to the sorption of water molecules (OH-group) during conditioning at 90% RH [51], which was more pronounced with increased silica content led to more pronounced OH-group peaks.

³¹P MAS NMR spectroscopy was used to investigate the structure of the PG particles. Figure 5 shows the NMR

spectra of the different PGs compositions before and after vapour sorption (24 h at 90% RH). In Figure 5c&5d, a main peak at a chemical shift of -27 ppm shows Q² phosphate species (two bridging oxygen atoms in the phosphate tetrahedron) [52, 53]. This Q² phosphate structure is expected for a metaphosphate composition due to the 50 mol% P₂O₅ content [54]. Post exposure to vapour, structural changes can be observed for Si₅Ti₅ and Si₇Ti₃, where two new peaks were observed at chemical shifts of approximately -1 ppm (attributed to Q⁰(1H)) and -11 ppm (attributed to Q¹(1H)) [55, 56] (Figure 5d). The presence of these new chemical shifts after exposure to vapour sorption can be explained by water molecule interactions with PGs particles and the formation of protonated phosphate species due to the hydrolysis of the phosphate unit or from the hydration of existing chain endings [37].

Figure 5: (a and b) ATR-FTIR spectra of the different PG particles pre and post (24h at 90%RH and followed by 24h at 0% RH) exposure to vapour sorption. (c and d) ³¹P MAS NMR spectra before and after exposure to vapour sorption.

4 Discussion

Finding new approaches to evaluate the dissolution characteristics of PGs is of great interest in determining their potential biological and therapeutic properties, *in vivo*. The most applied methods to correlate solubility and surface properties of PGs are through conventional methods such as long-term immersion in DIW, weight loss and ion release rate determination, and contact angle measurements, all of which may lack reliability, objectivity and accuracy [19, 20]. Additionally, T_g has been used as an indicator of glass cross-linking density and chemical durability which has generally been shown to inversely correlate with glass dissolution rate [27, 28].

In this study, IGC was used to investigate the effect of substituting TiO₂ with SiO₂ on the solubility parameter and surface energy of a PG compositional range (50P₂O₅-40CaO-xSiO₂-(10-x)TiO₂, where x = 7, 5, 3, and 0 mol%). Previously, it was shown that the substitution of TiO₂ with SiO₂ in PGs led to a decrease in glass density and T_g and thus an increase in glass dissolution and ionic release rates [20]. From a biological response perspective, it was shown that, when compared to glasses with 0 and 3%

SiO₂ content, the ionic dissolution products from PGs with 5 and 7 mol% SiO₂ led to an increase in alkaline phosphatase activity of MC 3T3-E1 pre-osteoblast cells, *in vitro* [20]. Consequently, the solubility and degradation characteristics of these PGs can be modified by their doping with different amount of silica and titania for a particular cellular response. It has also been demonstrated that the addition of SiO₂ to PGs leads to the disruption of the phosphate glass network and an increase in degradation and ion release rates [24]. In addition to the disruption of the glass network, silica incorporation into PGs also leads to the formation of surface Si-OH bonds, which contributes to their polar surface parameters [24]. However, regardless of this PG network modifying effect of SiO₂ on T_g and dissolution rates, contact angle measurements showed no significant effect on the glass surface energies [20]. This lack of sensitivity reflected similar findings on the effect of other dopants on the surface properties of PG, such as Fe₂O₃ [19] and CuO [37], when evaluated through contact angle measurements.

According to IGC measurements, it was found that the dispersive (non-polar) properties of the PG particles were not affected by the incorporation of TiO₂ or SiO₂, whereas

substituting TiO_2 with SiO_2 increased the polar and H-bond parts therefore increasing polarity. It is known that the polar nature of PGs originates from P-O-P bond [19], and the addition of TiO_2 into the glass network results in reduced polar characteristics [27] due to the formation of the less hydrolysable P-O-Ti bonds. The substitution of TiO_2 with SiO_2 in the glass structure results in more hydroxyl groups (Si-OH) at the surface of the PG particles leading to an increase in polar properties [20, 57]. This alteration in the polar properties of PGs was detected via IGC, which was more sensitive comparing to contact angle measurements, which did not fully distinguish between the small changes in glass polar properties [20]. Furthermore, the correlation between solubility parameter or surface energy and T_g of the PG particles suggested the potential of IGC in predicting the bulk properties of PGs along with their surface properties. This result also suggested that IGC can be a more sensitive technique than contact angle measurement, which enables a more precise calculation of the different components of solubility and surface energy.

DVS has been used to predict the reactivity and solubility of PGs by gravimetrically measuring their immediate aqueous interactions [37]. In this study, DVS was applied to determine the sorption isotherms of the SiO_2 and TiO_2 doped PG particles, when exposed to a relative humidity range between 0 to 90% at 5% intervals and when directly exposed to 90% RH for up to 24 h, which was used to approximate the aqueous environment. In the first approach, all compositions indicated two different regions of sorption, an initial small increase in mass up to approximately 65% RH and a second dramatic increase in mass up to 90%. The % RH value at this dramatic increase in mass termed as the inflection point and can be explained by deliquescence phenomena [45, 46]. A good linear correlation between the inflection point with T_g and dissolution rate of PGs with different silica contents indicated the ability of DVS to provide complementary information on glass durability. Furthermore, a good correlation between the rate and extent of mass change with T_g and glass dissolution rates when the glasses were directly exposed to 90% RH, verified the ability of DVS to measure glass reactivity. It is expected that by replacing of titania with silica, the PG network disruption leads to a less chemically durable glass, which is more reactive with water vapour molecules [20] as aided by the formation of surface Si-OH bonds [58]. Moreover, there was a good correlation between the polar parts of both the solubility parameter and surface energy (as measured through IGC) and inflection points (as measured through DVS), showing the potential ability of both tech-

niques in predicting the dissolution properties of PGs as consequence of alterations in their chemistry.

Morphological characterization of the PGs post exposure to vapour sorption, indicated their surface interaction with water molecules, which led to the formation of a layer on their surface. The surface transformation has been observed in previous work where phosphate- and silicate-based glasses were exposed to vapour sorption using DVS [37, 38]. NMR showed that with increasing SiO_2 content, there was a chemical shift to the more negative frequencies and a slight decrease in the peak width [20], which can be attributed to the presence of more linear chain segments of P-O-P bonds and is responsible for the polar nature of PGs [10, 24]. Additionally, after vapour sorption, the presence of new chemical shifts can be attributed to the interaction of water with phosphate network [37]. The PGs retained a fraction of non-reacted water molecule, as supported by the ATR-FTIR absorption band at 1630 cm^{-1} [59, 60], which increased with silica content. In PGs with higher silica content (Si5Ti5 and Si7Ti3), a fraction of water caused the hydrolysis of the phosphate units as supported by NMR peaks at -1 and -11 ppm [55, 56]. It can be concluded, that only non-reacted water molecules are trapped into the glass network when substituting TiO_2 with only up to 3 mol% SiO_2 . Increasing silica content to 5 and 7 mol% results in the presence of both non-reacted and reacted water molecules, which is in the form of hydrolyzed phosphate units. The greater presence of hydrolyzed phosphate units in Ti5Si5 and Ti3Si7 is likely to increase the glass dissolution and ionic release rates [20] (as demonstrated in Figure S1). Along with PO_4^{3-} it is known that the dissolution of phosphate glasses leads to release of a range of polyphosphates [61], including $\text{P}_2\text{O}_7^{4-}$, which is responsible for the upregulation in alkaline phosphatase in osteoblastic cells, including those found in MC3T3-E1 cells [20].

5 Conclusions

IGC and DVS were used to analyse the surface and short-term aqueous interactions of PG particles doped with either TiO_2 and SiO_2 . Good correlation between solubility parameter and surface energy with dissolution rates in DIW demonstrated that IGC is a precise technique in accurately determining surface properties of PG particles when compared with conventional methods such as contact angle measurement. Furthermore, DVS analysis correlated with T_g and dissolution in DIW. PGs with higher silica content showed an increase in the rate and extent of mass

change. These results demonstrate that IGC and DVS can be complementary techniques in evaluating the physico-chemical properties of PG particles and be used to correlate their potential biological responses.

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Appendix

Figure S1: Correlation between phosphorous ion release rates and (a) mass change at 24 h (end of sorption phase), as well as (b) with the inflection point as determined from DVS isotherms.