Effect of silica and titania doping on calcium phosphate-based glass properties for bone tissue engineering

Maziar Shah Mohammadi[1], Naser Muja[1], Christoph Stähli[1], Martin N Bureau[2,1], Showan N Nazhat[1]
[1] Department of Mining and Materials Engineering, McGill University, Montreal, QC, H3A 2B2, Canada
[2] Industrial Materials Institute, National Research Council Canada, QC, J4B 6Y4, Canada

Statement of Purpose: Bone defects are worldwide healthcare problems. Tissue engineering provides a biological substitute to damaged or diseased tissues (Rose FRAJ *et al*. Biochem Biophys Res Commun 2002;292:1). Phosphate-based glasses have been investigated for tissue engineering applications due to their complete degradation which can be predicted and controlled through their chemistry (Gao H *et al*. J Controlled Release 2004; 96:21). Besides acting as a source of calcium and phosphate ions, doping the glass compositions with modifying oxides would release favourable ionic species that may be beneficial for tissue regeneration. Silicon substituted calcium phosphates, such as hydroxyapatite or tricalcium phosphate, have been shown to have better biological properties than pure calcium phosphates (Pietak AM *et al*. Biomaterials 2007;28:4023). Titania can stabilize the phosphate network and has been proven to improve cell attachment and viability (Abou Neel EA *et al*. Acta Biomaterialia 2008;4:523). Therefore, this research aims to develop novel phosphate-based glasses doped with both silica and titania in order to tailor the properties of phosphate based glasses for potential application in bone tissue engineering.

Methods: P_2O_5, $CaHPO_4$, SiO_2 and TiO_2 precursors were used to produce melt derived phosphate-based glasses (PG). The compositions investigated were $P_{50}Ca_{40}Si_{(10-x)}Ti_x$ where x = 0, 3, 5, 7 and 10 mol%. The glass transition temperature (T_g), obtained from differential thermal analysis, was correlated to the density of each composition. The dissolution and effect on pH in deionised distilled water were investigated over 28 days. Inductively coupled plasma (ICP) technique was used to quantify the release of phosphorous, calcium, silicon and titanium ions upon degradation. Ion release rates were correlated with glass weight loss. Contact Angle (OCA, future digital scientific (FDS)) was carried out with ultrapure water and diiodomethane to investigate the effect of glass composition on their surface properties. OWRK (Owens, Wendt, Rable and Kaelble) method was used to calculate the polar, dispersive and total surface energy of each glass composition. Live/dead assay with MC3T3-E1 preosteoblasts was conducted using confocal laser scanning microscopy (Zeiss LSM5 Exciter) after staining the cells with calcein-AM and ethidium bromide homodimer-1 in order to determine the cell viability after 1, 4 and 7 days.

Results: By increasing the TiO_2 content in the glass composition, the density and T_g increased confirming a cross-linking effect of titania in the phosphate network. Solubility analysis showed a rapid dissolution rate in the glass containing 10% SiO_2 and 0% TiO_2 (Si10Ti0); however, by substituting SiO_2 with TiO_2 the weight loss decreased significantly. Si has been hypothesised to disrupt the phosphate network leading to a higher degradation rate (Patel A *et al*. J Mater Sci:Mater Med 2006;17:937). On the other hand, TiO_2 can increase the glass stability by forming P-O-Ti bonds (Brow PK *et al*. Phys Chem. Glasses 1977;38:300) that are more stable towards hydrolysis than P-O-P bonds.

Table 1. Weight loss ($mg.mm^{-2}.h^{-1}$) and ions release ($ppm.h^{-1}$) rates for different PG formulations

Code	Weight loss	P^{5-}	Ca^{2+}	Si^{4+}	Ti^{4+}
Si10Ti0	3×10^{-3}	17.47	9.3	1.78	-
Si7Ti3	1×10^{-4}	0.71	0.38	0.04	0.036
Si5Ti5	4×10^{-5}	0.3	0.16	0.013	0.025
Si3Ti7	3×10^{-5}	0.13	0.08	0.0015	0.016
Si0Ti10	8×10^{-6}	0.04	0.02	-	0.007

The weight loss and ion release rates are presented in Table 1. Ion release was in line with weight loss. The pH of the medium decreased in high SiO_2 content due to the prompt release of phosphate species, and increased towards the initial pH value by increasing the TiO_2 content. A reduction in contact angle was observed for the glasses containing more silica when tested with water; showing more hydrophilicity. A higher surface energy was also observed at higher silica content. By doping the PG with titania, the water contact angle increased, and the surface energy decreased. MC3T3 preosteoblasts showed a better response on titania containing PG. Cells were viable at day 1 and 4 on all the glass compositions. However, dead cells were observed on Si10Ti0 at day 7 which significantly decreased by incorporating 3% TiO_2. The greatest cell viability obtained at 5, 7 and 10% TiO_2. Confocal images at day 7 are shown in Fig. 1 as an example.

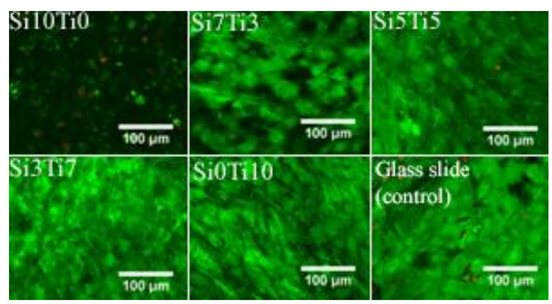

Fig. 1. MC3T3 preosteoblasts at day 7 in culture on PGs

Conclusions: With silica and titania doping, the structure, solubility, ion release as well as the surface energy and wettability of PG could be controlled. Doping the PG with titania improved cell attachment and viability. However, the role of silica presence in these glasses on cellular osteogenic differentiation requires further investigation. Therefore, doping the phosphate-based glasses with both silica and titania is a potential way to tailor the glass properties for tissue engineering applications.

Acknowledgements: This work was supported by NSERC and McGill Engineering Doctoral Award, and Hatch Faculty Fellowship.