Bioactivity in silica/poly(γ-glutamic acid) sol-gel hybrids through Ca chelation

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Introduction:

Bioactive glasses are unsuitable as scaffolds for bone regeneration sites under cyclic loading. We propose to soften bioactive glass by combining it with a polymer to form a hybrid. Hybrid materials have the potential for superior toughness and flexibility as the two components interact at the molecular level.[1] Covalent coupling can provide further strength to form Class II hybrids (Fig. 1).[2] Poly(γ-glutamic acid) (γPGA) is a natural polypeptide that has both amine and carboxylic functional groups in the repeating unit which are available for covalent coupling and ionic crosslinking. This calcium chelating polymer was used as both a calcium source and the glass toughening agent, eliminating the need for other calcium sources such as calcium nitrate and calcium chloride.[2, 3] The ionic crosslinking effect on the hybrid mechanical properties can be isolated and examined by comparing hybrids formed with calcium (Ca^{2+}) or sodium ions (Na^{+}). The aim of this work is to examine a novel calcium source for bioactive bone scaffolds: calcium salt poly(γ-glutamic acid).

Materials and Methods:

Hybrids were formed through the sol-gel method with polymers of varying molecular weights (120 - 30 kDa). Calcium salt and sodium salt forms of γPGA were functionalised with 3-glycidoxypropyl trimethoxysilane (GPTMS). Meanwhile tetraethoxysilane (TEOS) was hydrolysed. These two solutions were combined to form Class II hybrids with 40 wt% γPGA. The effect of molecular weight was examined for hybrids with and without ionic crosslinking (calcium salt and sodium salt form respectively of γPGA). Hybrids were characterised by ^{13}C and ^{29}Si NMR spectroscopy (to examine the degree of covalent coupling and silica network connectivity), SIMS, compression testing, weight loss and bioactivity testing using ICP, BCA protein assay, FTIR, SEM and XRD.

Results and Discussion:

γPGA hybrids were successfully formed and were found to be homogeneous over all polymer molecular weights (Fig. 2a). TOF-SIMS showed an even distribution of Ca and Si ions (Fig. 2b). As the calcium salt form of the polymer was used in these hybrids, the calcium map also shows the polymer distribution as the calcium ions were chelated to the polymer. Thus these are true hybrid materials as the organic (polymer) and inorganic (silica) components are integrated at the molecular level. γCaPGA hybrids were found to have superior mechanical properties over the sodium containing hybrids (Fig. 3). The compressive strength and strain to failure was 330 to 540 MPa and 25 - 40 % respectively for γCaPGA hybrids and 100 to 200 MPa and 10 - 15 % for γNaPGA. The compressive strength was greatest at 80 kDa, a mid-range molecular weight, possibly due to finer interweaving of the organic and inorganic components. Thus ionic crosslinking from the divalent calcium ions resulted in a marked improvement in mechanical properties, especially compared to the brittle nature of bioactive glass. The calcium containing hybrids successfully formed hydroxycarbonate apatite (HCA) within one week of immersion in simulated body fluid, which is the first step to bonding to bone. The degradation rate was faster for the hybrids with sodium. Thus calcium was an important component of hybrid materials, not just for bioactivity, but the ionic crosslinking provided increased mechanical properties and immersion behaviour.

References:
[1]Lin, S., et al., J. Mater. Chem. **2009,** 19, 1276-128. [2]Poologasundarampillai, G., et al., J. Mater. Chem., **2010,** 20, 8952-8961. [3]Valliant, EM and Jones, JR, Soft Matter, **2011**, 7, 5083-5095. [4]Valliant, EM et al., Acta Biomateriallia, Submitted.

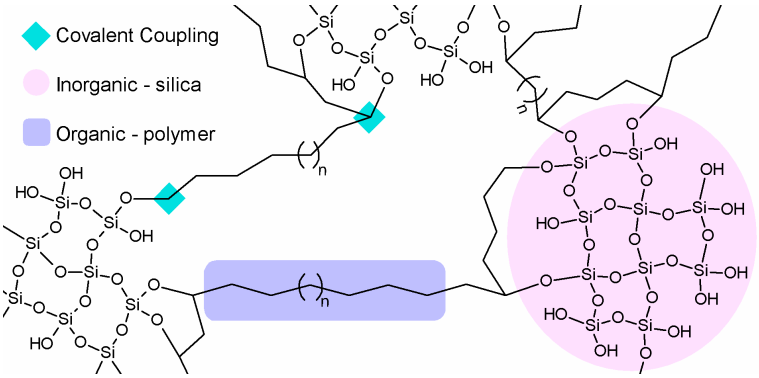

Fig. 1. Schematic of a Class II hybrid with covalent coupling between organic and inorganic components

a) b)

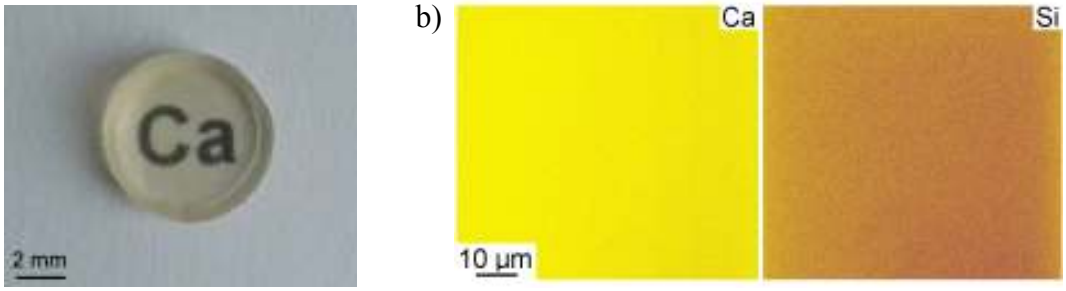

Fig. 2. a) Hybrid of 40 wt% γCaPGA with M_w 120 kDa b) TOF−SIMS imaging of calcium and silicon distribution for the sum of 410 scans

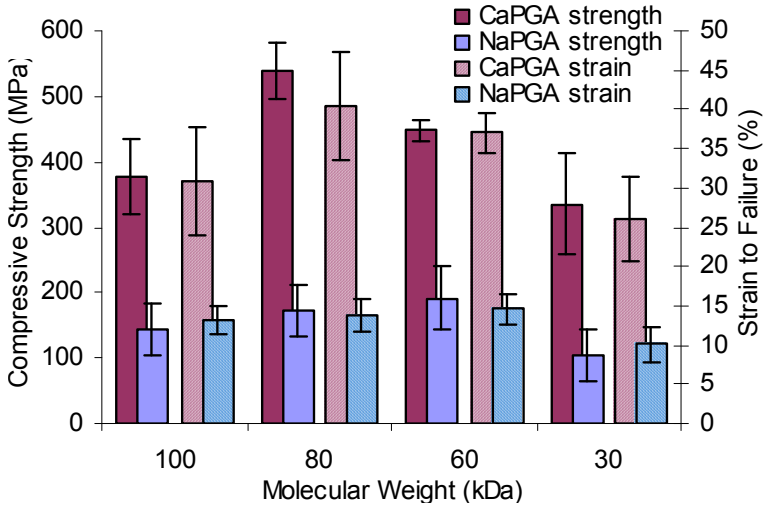

Fig. 3. Compressive strength and strain to failure for γCaPGA and γNaPGA Class II hybrids with molecular weights of 30 - 100 kDa