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Synthesis and *in vitro* studies of phosphosilicate glasses doped with cerium and zinc oxides

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Introduction

Since 1969, when the concept of bioactive materials was introduced (1), the field of bioactive ceramics has expanded to include a variety of compositions and several different glasses, and glass-ceramics have been found to bond to living bone (2). Hench et al (1) first demonstrated bonding to bone for glass composed of: SiO_2, 45; Na_2O, 24.5; CaO, 24.5 and P_2O_5, 6 wt%, called Bioglass 45S5; subsequently various kinds of bioactive ceramics have been developed to improve and/or add new important properties for clinical applications.

We report the results of *in vitro* (SBF, 3) studies of glasses based on the Bioglass, formula and doped by the addition of CeO_2 (1.5-13.5 wt%) and ZnO (5-20 wt%). Zn-doped glasses with increased P_2O_5 content (11.2-18.6 wt%) were also studied. The choice of zinc relates to its role as a regulator of biomineralization processes (4). The choice of cerium relates to its low toxicity associated with bacteriostatic properties (5), which promotes its use in several drugs (6). The glasses were characterized by ICP, scanning electron microscopy/ energy dispersive spectroscopy and X-ray diffractometry techniques and the glass structures were determined by a combined experimental/computational (molecular dynamics) approach.

Materials and Methods

The batches were prepared by mixing the reagents Na_2CO_3, $CaCO_3$, $Na_3PO_4 \cdot 12H_2O$, SiO_2 and $ZnCO_3$ or CeO_2. The glass preparation and characterization were performed as reported elsewhere (7). Classical MD simulations were performed with the DL_POLY program (8) using Cerius2 (Accelrys Inc.) as a graphical interface.

Results and Discussion

The addition of small oxide quantities (1.5 wt% for CeO_2 and 5-10 wt% for ZnO) did not significantly alter the ability of the *in vitro* apatite formation on the glass surface. After 15 days, a mixed-metal (Ca-Zn) or (Ca-Ce) phosphate-based layer was identified. High metal contents improved the chemical durability of the glass, the bioactivity was strongly inhibited and there were no hints of apatite formation observed even after prolonged soaking in SBF. In the case of Ce-doped glasses, this behavior was due to the degree of the covalent character of the Ce-O bond, which makes its hydrolytic dissociation difficult. Therefore, in this case apatite formation was prevented both by the improved glass durability and by the ability of cerium to interact with phosphate giving rise to an amorphous insoluble phase ($Ce_2O_3 \cdot CePO_4$). Cerium concentration was always extremely low and the ion was immobilized in a solid phase. In the case of Zn-glasses the formation of an insoluble phase was observed in a minor entity with respect to the Ce-glasses (for example, $CaZn_2(PO_4)_2$, white zone in Fig. 1); this could be interesting in view of considering these glasses as a metal supplier. The increment of chemical durability in the Zn-glasses can be rationalized by a thorough analysis of the glass structure determined by MD simulations. The zinc ions acted as a network former in the glass compositions studied. A gradual increment in the polymerization degree of the network was observed as a function of zinc concentration, which resulted in a global reinforcement of the glass network. The obstruction of the percolation channels observed at a high zinc content prevented Ca^{2+} and PO_4^{3-} glass constituent release; and therefore, inhibited apatite formation.

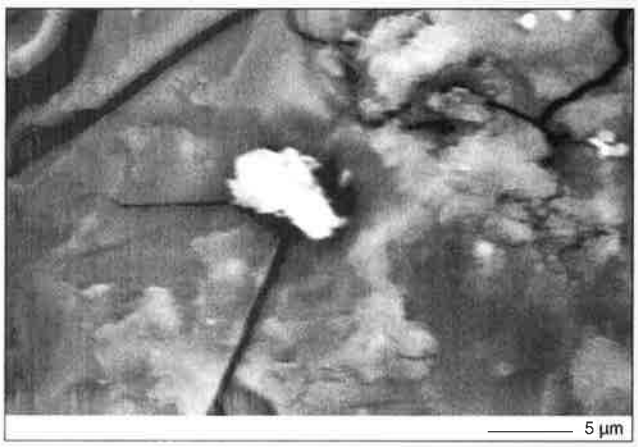

Figure 1 - SEM micrograph of glass doped with 10 wt% of ZnO after 2 weeks of soaking in SBF.

The SiO_2, 39.4; Na_2O, 22.6; CaO, 22.6; P_2O_5, 10.4; ZnO, 5.0 wt% glass composition seems to demonstrate an optimal ratio of Zn/P to improve the glass strength and simultaneously yield a Ca/P ratio able to preserve rapid apatite formation.

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References

1. Hench LL, Splinter RJ, Allen WC, Greenlee TK Jr. Bonding mechanisms at the interface of ceramic prosthetic materials. J Biomed Mater Res 1972; 2: 117.
2. Hench LL. Bioceramics: from concept to clinic. J Am Ceram Soc 1991; 74: 1487 and ref. therein.
3. Kim H-M, Miyaji F, Kokubo T. Bioactivity of Na_2O-CaO-SiO_2 Glasses. J Am Ceram Soc 1995; 78: 2405 and ref. therein.
4. Kokubo T, Kushitani H, Sakka S, Kitsugi T, Yamamuro T. Solutions able to reproduce *in vivo* surface-structure changes in bioactive glass-ceramic A-W. J Biomed Mater Res 1990; 24: 721.
5. Ladefoged K, Jarnum S. Calcium, phosphorus, magnesium, zinc, and nitrogen balance in patients with severe short bowel syndrome. Met Ions Biol Sys ed H Sigel 1983; 15.
6. Burkes S, McCleskey CS. The bacteriostatic activity of cerium, lanthanum and thallium. J Bacteriol 1947; 54: 417.
7. Lusvardi G, Malavasi G, Menabue L, Menziani MC. Synthesis, characterization and molecular dynamics simulation of Na_2O-CaO-SiO_2-ZnO glasses. J Phys Chem B 2002; 106: 9753.
8. Fox CL Jr, Modak SM, Stanford JW, Fox PL. Metal sulfonamides as antibacterial agents in topical therapy. J Plast Reconstr Surg 1979; 13: 89 and ref. therein.