Physical properties and in vitro bioactivity of biphasic calcium silicate bone cements

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Statement of Purpose: When bone tissue is damaged or fails, a variety of biomaterials are used to achieve a direct chemical bond between bone and bone-repair materials. Several materials such as glass-ionomer cement, bioactive glass cement, calcium phosphate-based cement that satisfy this requirement, have attracted investigation as a suitable bone repair material. Self-setting cements can be handled by the surgeon in paste form and injected into bone defects. They then set to form a mineral matrix at the contact of which healing bone tissue can form.

Silicon may play an important role in the early stage calcification [1]. The silicate ions might provide favorable sites for nucleation of the apatite on the Si-containing biomaterials when immersed in simulated body fluid. The aim of this study is to develop a biphasic calcium silicate cement using sol-gel methods. This cement consisted of calcium silicate powder as a solid phase and phosphate solution as a liquid phase. The major techniques used for characterizing the samples included scanning electron microscopy (SEM), diametral tensile strength (DTS), and X-ray diffractometry (XRD). Setting time of bone cements was also measured.

Methods: Tetraethyl orthosilicate (TEOS) and calcium nitrate were used as precursors for SiO_2 and CaO, respectively, and nitric acid as a catalyst, in addition to ethanol as the solvent. SiO_2/CaO molar ratio was in the range of 7:3 to 3:7. The general procedure of a sol-gel route, such as hydrolysis and aging, was adopted. After solvent vaporization of the above-mentioned mixture solution in an oven at 120^{o}C, the as-dried gel was heated in air to 900^{o}C for holding 2 h, and then cooled to room temperature to produce various biphasic calcium silicate powders.

To prepare the cement, the liquid phase for setting reaction was the $(NH_4)_2HPO_4$ - $NH_4H_2PO_4$ solution. The cement samples were prepared using a liquid-to-powder (L/P) ratio of 0.5- 0.7 mL/g dependent on the kind of the cement. After mixing, the samples were placed into a cylindrical stainless steel mould, and stored in an incubator at 100% relative humidity and 37^{o}C for hydration. The setting time of the cements was tested according to the international standard ISO 9917-1 for water-based cements. An physiologic solution with an ionic composition similar to that of human blood plasma, Hanks' solution, was used as immersion solution to evaluate the bioactivity of cement samples. The diametral tensile testing of cement samples was conducted on an EZ-Test machine. One-way analysis of variance (ANOVA) was used to evaluate the significant differences between the means in the DTS or setting time data. The results were considered statistically significant at $p < 0.05$. The surface of samples was coated with gold and observed under a SEM. Phase analysis was performed using an XRD.

Results: The resulting XRD patterns show that, when containing the highest amount of SiO_2 in the powders, $CaSiO_3$ was a dominant phase. With the amount of CaO greater than SiO_2, the diffraction peaks of β-Ca_2SiO_4 became stronger. After mixing with ammonium phosphate solution, the products of the hydration process were apatite with broad peaks at $2\theta = 32\text{-}34^o$ in combination with calcium silicate hydrates (C–S–H) gel appearing at $2\theta = 29.3^o$. SEM indicated the formation of entangled platelike crystals and pores. The five cement samples hardened within 9 min. With increasing calcium content, the setting time of the cement shortened, reaching 3 min. As for DTS, the variations in the strength of various cements were found to also depend on the calcium contents. The cement samples with the greatest SiO_2 amount had a value of 1.9 MPa. On the contrary, the greatest calcium amounts of cement samples became 0.9 MPa. It is worth noting that he highest DTS value is 2.8 MPa that belongs to the cement of SiO_2/CaO = 1. One-way ANOVA analysis showed that there were statistically significant differences ($p < 0.05$).

After immersion in Hanks' solution for as little as 1 h, the cement samples with equimolar SiO_2/CaO ratio induced the precipitation of apatite spherulites, where the amount of this precipitate increased with immersion time, as supported by XRD. In the case of conventional CPCs, the apatite formation took place after several days in a physiologic solution, whereas for CSCs it took only 1 h. Although the detailed mechanism of fast apatite precipitation for CSCs was not yet fully understood, two dependent processes were thought to proceed synergistically when the cements are immersed in Hanks' solution. Functional groups, such as Si–OH, on the surface of SiO_2–CaO-based bioactive glasses and ceramics have been shown to act as nucleation centers for apatite precipitation [2]. The elution of calcium possibly originating from the less-ordered hydration products could greatly assist apatite growth by promoting local Ca supersaturation, thereby increasing the ionic activity product of the apatite in the surrounding fluid, which accelerated the nucleation rate of apatite. It is noticeable that Hanks' solution did not adversely affect the DTS values of the five different CSCs, even after 90 days of immersion, indicating that there was no in vitro degradation of bond strength.

Conclusions: A novel CSCs could self-harden to form apatite and C–S–H gel within 9 min. The cement samples having an equimolar ratio of SiO_2/CaO had the highest DTS value of 2.8 MPa. The cements may promote the precipitation of a "bone-like" apatite layer on the cement surfaces when exposed to a physiologic solution. All cements can retain their strength, even after immersion in a physiologic solution for 90 days. The biphasic CSCs appeared to be a potential candidate as a bone repair material.

References:

1. Carlisle EM. Science 1970;167**:**279-280.
2. Kokubo T. Biomaterials 2006;27:2907-2915.