INORGANIC CEMENT-BASED SYSTEMS AS BIOMATERIALS

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Abstract

Inorganic cement-based biomaterials are found within the group’s phosphates, silicates and aluminates. In this paper a comparison of the property profile of calcium phosphates (CP), calcium aluminate (CA) and calcium silicate (CS) based materials based is presented with focus on biocompatibility and mechanical properties.

Biocements are often based on various calcium phosphate salts – often in combination with Ca-sulphates. These salts can be made to cure \textit{in vivo} and are attractive as replacements for the natural calcium phosphates of mineralised tissues. However, these products have low compression strength values - in the interval 10-40 MPa - and are questioned as load bearing implants.

Materials based on Ca-aluminates and Ca-silicate with chemistry similar to that of Ca-phosphates contribute to some additional features of interest with regard to dental and orthopaedic applications. These features are related to the amount of water involved in the curing process, the early and high mechanical strength obtained, and the biocompatibility profile including \textit{in situ} reactions with phosphates ions of the body fluid. Compressive strength of cements based on Ca-silicate and Ca-aluminate is in the range 80-200 MPa depending on the water to cement ratio.

1. INTRODUCTION

Three different cement systems – Calcium phosphates (CP), Calcium aluminates (CA) and Calcium silicates (CS) are discussed in some details in this paper. Ceramic biomaterials are often based on phosphate-containing solubable glasses, and various calcium phosphate salts [1-3]. These salts can be made to cure \textit{in vivo} and are attractive as replacements for the natural calcium phosphates of mineralised tissues. The Ca-phosphate products are gaining ground in orthopaedics as resorbable bone substitutes. Materials based on CA and CS with chemistry similar to that of Ca-phosphates contribute to some additional features of interest with regard to dental and orthopaedic applications. The inherent difference in water uptake between CP and CA/CS-systems gives benefits as:

- Higher mechanical strength.
- Possibility to add fillers, e.g. for improved radio opacity.
- Tuneable handling properties, e.g. rheology.

The examination in this paper is mainly restricted to bioactivity aspects and mechanical property profile of the systems.
2. MATERIALS AND METHODS

The materials used were Ca-aluminate and Ca-silicate materials synthesised by Doxa AB. Ca-aluminate materials are based on the phase CaO\textsubscript{x}Al\textsubscript{2}O\textsubscript{3} or 12CaO\textsubscript{x}7Al\textsubscript{2}O\textsubscript{3}, and the Ca-silicate material on 3CaO\textsubscript{x}SiO\textsubscript{2}.

Additive used in the Ca-aluminate material was zirconia (among others for radio opacity). The main additive in the Ca-silicate was calcium chloride (as accelerator). Preparation of the final powder compositions includes mixing the constituents using silicon nitride balls in a polyethylene container with iso-propanol. The alcohol was evaporated and polymeric residues were removed. The reaction liquid is water. The powder mix was sterilized by electron beam radiation. The aqueous solutions were steam sterilized.

Reference material in the studies was a commercial Ca-phosphate based material.

2.1 Evaluation methods and sample preparation

2.1.1 Microstructural evaluation including bioactivity.

The \textit{in vitro} bioactivity tests were conducted according to the outline in the ISO-standard ISO/WD 23317. Discs were made and allowed to set in 100 % RH at 37 °C before they were transferred into phosphate buffer saline (PBS) and stored at 37 °C for 1h, 24 h, 7 days and 30 days, respectively. After the storage, all samples were gently rinsed with water and dried. The surface and bulk composition was analysed for the presence of apatite, using thin-film X-ray diffraction (TF-XRD) and SEM combined with EDX. The microstructure was studied with transmission electron microscopy (TEM, Jeol 2010 F) with a scanning module (STEM). TEM samples were prepared using focused ion beam microscopy (FIB). “H-bar lift-out” technique was used enabling a very high site-specific accuracy [4,5]. The setting and working time was determined using the Gillmore needle method and the extrusion time through 11 gauge needles, respectively.

2.1.2 Mechanical properties.

The materials were evaluated with regard to compressive strength (ISO 9917), biaxial flexural strength (ASTM F-394, flexural strength testing of ceramic materials) and Young’s modulus (slope of compressive strength-strain curve) as function of time when stored in phosphate buffer solution at body temperature. The mechanical properties were determined after 1h, 24 h, 7 days and 16 weeks. The compressive strength was measured on cylindrical samples with 4.7 mm diameter and more than 7 mm in height. The flexural strength was measured on discs with 5 mm diameter and thickness around 0.7 mm. The number of samples at each test was eight.

3. RESULTS

The results are presented under the following headings: reaction mechanisms, handling and the microstructure developed, bioactivity and mechanical property profile.

3.1 Reaction mechanisms, handling and microstructure developed.

The Ca-aluminate and the Ca-silicate reaction mechanisms differ in one respect considerably from those of Ca-phosphate reactions. This has to do with the amount of water involved in the hydration reactions, and this can easily be seen when comparing the chemical formula of the phases formed in the curing reactions. See Table 1. The water content of the final chemical products has a great influence upon the optimisation of the water/cement ratio.
(w/c) with regard to handling properties and the final microstructure, especially the residual porosity, which can be reduced substantially for the systems, where the water consumption is high. Working and setting time of the systems are shown in Table 2. Typical microstructures of one hydrated Ca-aluminate and one Ca-silicate system are shown in Fig. 1. High resolution transmission electron (HRTEM) microscopy reveals nano-size porosity below 5 nm, and hydrates in the size range 20-50 nm., see Fig. 2.

Table 1. The water involved in the hydration of three selected systems.

<table>
<thead>
<tr>
<th>System</th>
<th>Typical phase(s)</th>
<th>Oxide formula</th>
<th>Mol % H₂O</th>
<th>Weight-% in hydrated product</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ca-phosphate</td>
<td>Apatite</td>
<td>10CaO 3P₂O₅ H₂O</td>
<td>7</td>
<td>Approx 5</td>
</tr>
<tr>
<td>Ca-aluminate</td>
<td>Katoite + gibbsite</td>
<td>3CaO Al₂O₃ 6 H₂O + Al₂O₃ 2H₂O</td>
<td>&gt; 60</td>
<td>Approx 25</td>
</tr>
<tr>
<td>Ca-silicate</td>
<td>Tobermorite + amorphous phases</td>
<td>5CaO 6SiO₂ 5H₂O + Ca, Si H₂O</td>
<td>&gt; 30</td>
<td>Approx 20</td>
</tr>
</tbody>
</table>

Table 2. Setting and working time of the systems studied. Time measured from start of mix.

<table>
<thead>
<tr>
<th>System</th>
<th>Working time (min)</th>
<th>Setting time (min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ca-aluminate</td>
<td>Approx. 5</td>
<td>8-12</td>
</tr>
<tr>
<td>Ca-silicate</td>
<td>Approx. 10</td>
<td>15-18</td>
</tr>
<tr>
<td>Ca-phosphate</td>
<td>5</td>
<td>10-12</td>
</tr>
</tbody>
</table>

Figure 1. SEM micrographs of hydrated Ca-silicate (left, white bar = 20 µm) and hydrated Ca-aluminate (right, white bar = 10 µm).
3.2 Mechanical properties.

The mechanical properties tested for the three Ca-based cement systems and the time dependence of the strength developed for the system studied are compiled in Tables 3-4.

Table 3: Mechanical property profile of the Ca-aluminate, Ca-silicate and Ca-phosphate systems studied

<table>
<thead>
<tr>
<th>Property profile after 7 days</th>
<th>Ca-aluminate based material</th>
<th>Ca-silicate based material</th>
<th>Ca-phosphate based material</th>
</tr>
</thead>
<tbody>
<tr>
<td>Compressive strength (MPa)</td>
<td>&gt;100</td>
<td>105</td>
<td>35</td>
</tr>
<tr>
<td>Flexural strength (MPa)</td>
<td>60</td>
<td>40</td>
<td>25</td>
</tr>
<tr>
<td>Young’s modulus (GPa)</td>
<td>15</td>
<td>11</td>
<td>3</td>
</tr>
</tbody>
</table>

Table 4: Time dependence of compressive strength (MPa) in the systems studied.

<table>
<thead>
<tr>
<th>System</th>
<th>Compressive strength, 1h</th>
<th>Compressive strength, 24h</th>
<th>Compressive strength, 7 days</th>
<th>Compressive strength, 16 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ca-aluminate</td>
<td>40</td>
<td>80</td>
<td>&gt;100</td>
<td>&gt;100</td>
</tr>
<tr>
<td>Ca-silicate</td>
<td>30</td>
<td>130</td>
<td>105</td>
<td>105</td>
</tr>
<tr>
<td>Ca-phosphate</td>
<td>10</td>
<td>40</td>
<td>35</td>
<td>30</td>
</tr>
</tbody>
</table>

3.3 Bioactivity.

On all the tested cements and at all time-points surface films could be found. The structure and appearance of the films changed with storage time, although the film thickness was established early in the process. After 7 days, especially for the CA-system, crystalline apatite could be detected. For the CS system the presence of crystalline apatite was not as clear, i.e. the possible apatite was more amorphous in nature. For both the calcium silicate cement and the calcium aluminate cement, even after 1h, the presence of phosphorus could be detected at the surface using EDX.
4. DISCUSSION

The bioactivity of Ca-phosphate materials is well documented. The chemistry involved in the hydration of Ca-aluminate and Ca-silicate materials, and interaction with body liquid also point at bioactivity.

Two features contribute to perfect sealing of interfaces of the Ca-aluminate and the Ca-silicate systems; first the general dissolution and precipitation of nanosize hydrates in microvoids between particles and between particles and tissue, and second the zone formation including apatite formation upon which bioactive-induced formation of new tissue including apatite formation. Thus, both a pure chemical integration and a biologically induced integration contribute to sealing of biomaterial-tissue interfaces. This has been proven also in animal studies [6]. The interface between the surface zone and new hard tissue formed has been studied in some details using SEM and high-resolution TEM. In these, total closure of the gap between the biomaterial and tissue has been found, see Fig. 3.

![Figure 3. Chemically and biologically induced integration of Ca-aluminate based material and tissue – implantation in tibia, female adult New Zealand White rabbit (black bar = 500nm)](image)

High and early strength developed in the Ca-aluminate and silicate systems reflect the high water up-take, leaving the initial space between particles and microvoids filled with nano-size hydrates.

5. CONCLUSIONS

Comparing Ca-aluminate and Ca-silicate based cements to the more established biomaterial Ca-phosphate based cement; the property profile of these systems can be summarized as follows:

- Bioactivity, i.e. ability to form chemical bonds to new bone tissue
- High and early strength

6. ACKNOWLEDGEMENT

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REFERENCES


