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ORIGINAL ARTICLE

Maximizing the strength of calcium sulfate for structural bone grafts

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Abstract

Calcium sulfate (CS) combines remarkable properties of biodegradability, biocompatibility, and osteoconductivity but its low strength limits the range of its applications in orthopaedic surgery. In this study we have addressed this limitation by optimizing the fabrication process for pure CS, and by using mechanical testing procedures which are relevant for load carrying, or structural bone grafts (flexural tests in hydrated condition). By optimizing the processing parameters (pressure during setting, CS powder to water ratio, saturated solution) we produced CS samples with the highest flexural strength ever reported in hydrated conditions. Once these optimal conditions are used, the addition of "reinforcing" inclusions in the material decreased its strength because these inclusions actually act as defects instead of reinforcements. In addition, the CS can be formed in precise shapes while maintaining optimal processing conditions and provided a strength similar to that of bone with the same dimensions. Dense and porous materials can be combined to duplicate the trabecular and cortical architecture of long bones, with only a small loss of overall strength.

KEYWORDS
biomineral, bone graft materials, calcium sulfate, material processing, strength

1 | INTRODUCTION

Millions of people worldwide are in need of a treatment for bone loss and bone defects (Bohner, Galea, & Doebelin, 2012; Hall, DeFrances, Williams, Golosinskiy, & Schwartzman, 2010), but the treatment of segmental bone loss remains a major challenge in orthopaedic surgery. Whether these defects are from trauma, tumor resection, failed arthroplasty, or infection, the orthopaedic surgeon frequently has only imperfect treatment options. Traditional approaches (e.g., autograft, allograft) and newer strategies (e.g., recombinant human bone morphogenetic protein) each have limitations: donor site morbidity, insufficient autogenous quantity, viral transmission, immunologic incompatibility, long recovery time, and structural failure (Bohner, 2010). New strategies for the treatment of bone defects are therefore needed (Giannoudis, Dinopoulos, & Tsiridis, 2005; Parikh, 2002). The ideal bone graft must meet three major requirements (Bohner et al., 2012): (a) match the mechanical properties of healthy bone in terms of stiffness, strength, and toughness to prevent fracture and stress shielding; (b) be biocompatible/osteoinductive/osteoconductive to promote healing and transfer of mechanical stresses, and (c) degrade and resorb over time so healthy bone can take over. To this day, there is no nonautogenous material that can fulfill these three requirements simultaneously (Bohner, 2010; Bohner et al., 2012). Titanium and other metallic and polymeric materials are widely used for orthopaedic implants, but they are too stiff and do not resorb over time (Hahn & Palich, 1970). Bioglasses, a type of ceramics made of bioactive components CaO, Na_2O, SiO_2, or P_2O_5, have a high osteoinductive, osteoconductive, and osteointegrative potential (Pneumaticos, Triantafyllopoulos, Basdra, & Papavassiliou, 2010), but they have limited resorbability (Nasr, Aichelmann-Reidy, & Yukna, 1999) and they are brittle (Rahaman et al., 2011). Polylactic acid, polyglycolic acid, and their co-polymer Poly Lactic-co-Glycolic Acid (PLGA) are used in the making of sutures, screws, and rods but also to heal large segmental bone defects. They are biodegradable and biocompatible but their mechanical properties are too weak and compliant when compared to those of natural bone (Pneumaticos et al., 2010). Collagen-derived biomaterials have excellent biocompatibility, but their stiffness is orders of magnitude lower than bone so that they cannot support the loads usually carried by bones.

One route is to mineralize collagenous biomaterials, but this approach remains difficult (Habibovic et al., 2010). Hard minerals such as hydroxyapatite (HA), calcium sulfate (CS), or calcium phosphate (CP) have been used in the treatment of segmental bone defects because of their chemical composition close to the biominerals in bones (Bohner, Galea, & Doebelin, 2012; Maeda et al., 2007; Turner, Urban, Gitelis, Haggard, & Richelsoph, 2003). HA is biocompatible and osteoconductive but has a poor resorbability (Bohner et al., 2012). CP is osteoconductive but osteoinductive only in some cases (Jeong, Kim, Shim, Hwang, & Heo, 2019). CS is one of the oldest bone graft materials still in use, and also one of the most promising bone graft material because of its remarkable combination of biodegradability, biocompatibility, osteoconductivity (Maeda et al., 2007; Pietrzak & Ronk, 2000; Turner et al., 2003), and its ability to regenerate bone (Coetzee, 1980; McKee & Bailey, 1984). CS is a highly crystalline version of gypsum with intermeshed crystals that confer a rigid structure (Pietrzak & Ronk, 2000). Such structure is formed after the chemical reaction of water with hemihydrate CS. Hemihydrate CS powder is obtained from the calcination of gypsum or dihydrate CS, the hydrated form of CS. The calcination process produces various forms of hemihydrate CS powder. These types of form are, from the weakest to the strongest: Type I (impression plaster), type II (plaster of Paris), type III (dental stone), type IV (high strength dental stone), and type V (ultra-high strength dental stone) (Pietrzak & Ronk, 2000). Impression plaster (type I) is obtained simply by mixing additives to gypsum and is the most porous form of CS. Plaster of Paris (type II) is obtained from calcination at 110–130°C. This form still exhibits irregular particles but its higher density and better crystal uniformity result in a higher strength (Sakaguchi & Powers, 2006). Type I and II are the forms of CS with a poor level of crystal uniformity, called β-forms. The purer and stronger types (III–V) are the α-forms, or "dental stones" because of their use in denture molds, inlays, crowns and bridge casts. They are obtained by autoclaved calcination where the powder particles crystallize slower, are more uniform, and the final material is less porous. Dental stone type IV has crystals with cuboidal shape obtained by using an additive in the autoclaved calcination process (calcium chloride) that produces particles with a reduced surface area. Finally, the strongest form of CS (type V) is a dental stone obtained in a similar process than type IV, but with retardants and surface tension reducing agents that are added to increase the density and the crystal uniformity (Sakaguchi & Powers, 2006). The difference between each form therefore resides in the purity and shape uniformity of the powder grains (Sakaguchi & Powers, 2006). Once the powder has reacted with water, these differences also impact the mechanical properties of the final material (Pietrzak & Ronk, 2000). During this setting reaction, hemihydrate CS particles are first hydrated to form a solid gel. Hydrogen bonds then form on sulfate groups, and crystals interlock as they grow, which provide the cohesive structure of CS dihydrate (Sakaguchi & Powers, 2006). Figure 1 shows the compressive strength of different types of CS. Compressive strength varies from 4 MPa (Anusavice, 2003) (type I) to 90 MPa (Azer et al., 2008) (type V). The data for the mechanical properties of CS are mostly available in compression, which does not reflect the brittleness of these materials (the tensile strength of brittle ceramics is typically only 1/15 of the compressive strength [Ashby, 2010]). In addition, the mechanical properties reported in the literature are in dry conditions, and they do not reflect the hydrated condition of a bone graft material in-situ. While CP and HA require to be sintered at high temperatures (>1,200°C) which prohibits the addition of proteins or therapeutic drugs that would enhances their efficacy as bone graft, hard CS is formed from a chemical reaction with water at room temperature. Therefore, additives that can enhance the biological or mechanical performance of the material, but that would be destroyed with high temperatures, can be incorporated in CS. Historically, several types of reinforcing inclusions were explored for CS including wood fibers (Coutts, 1986), gelatin (Gao et al., 2012), viscous polymers (carboxymethylcellulose and hyaluronan) (Park, 2007), or cellulose fibers (Thomas, 1955). In all cases, the inclusions successfully improved the strength and/or the toughness of the bone graft material. Chemical ways also exist to improve the strength of CS: mixing with potassium sulfate (K_2SO_4), saturated solutions of CS (Shen, Mohammed, & Kamar, 1981), calcium oxide (CaO), or calcium hydroxide (CaOH) (Pietrzak & Ronk, 2000). Sanad, Combe, & Grant, (1982) reported a doubling of the strength of CS by mixing arabic gum and calcium oxide or hydroxide. Despite these recent improvements, the flexural and tensile strength of CS remains lower than those of natural bone. As a result, calcium based cements are used only as nonweight bearing structures, to fill defects, or to coat hip implants (Mumford & Simpson, 1992). In this work we optimize the preparation and processing of calcium sulfate minerals. We show that with optimal parameters, calcium sulfate implants can be as strong as natural bone in flexion. We also demonstrate that calcium sulfate can be manufactured in any shape, including hollow features which are known to promote osteoconduction (Yoshikawa, Tsuji, Shimomura, Hayashi, & Ohgushi, 2008). We logically worked

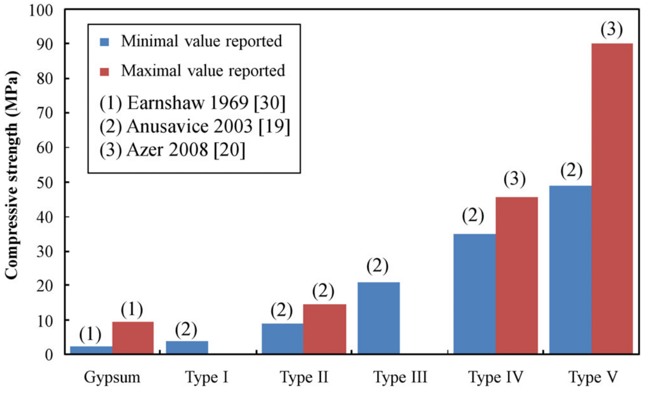

FIGURE 1 Comparison of the compressive strengths of various types of calcium sulfates (Anusavice, 2003; Azer, Kerby, & Knobloch, 2008; Earnshaw, 1969)

with the strongest form of calcium sulfate (type V) in order to develop the most mechanically interesting material.

2 | MATERIAL AND METHODS

In this work we used hemihydrate CS type V (Suprastone, Kerr Dental, Charlotte, NC), the strongest form of CS (Figure 1). CS powder has the chemical composition $CaSO_4,{}^1/_2\ H_20$ (calcium sulfate hemihydrate). After reacting with water, CS becomes $CaSO_4,\ 2H_20$ (calcium sulfate dihydrate): $CaSO_4,{}^1/_2\ H_20 + {}^3/_2\ H_20 \rightarrow CaSO_4,\ 2H_20$. The manufacturer recommendation for mixing ratio is 1.86 g of water for 10 g of powder (we examined the effects of deviating from this ratio in this study). CS powder and water were mixed vigorously for several minutes until fully homogenous. The slurry was then poured into a rectangular polymeric mold to give the sample the desired rectangular shape (Figure 2). The mold and sample were compressed between two stiff metallic plates using a 25 tons capacity press (FW-4 tablet press, Joyfay, Cleveland, OH). The time elapsed between powder mixing and the application of the pressure in the press never exceeded 8 min, which ensured that the CS mix was still malleable when the pressure was applied on the mold. Samples were then left in the press for 12 hr to ensure complete setting. Once removed from the press, the samples were left in air for at least 12 hr before testing (which ensured full hydrated conditions, there was no difference in properties for samples left in water for a longer period of time).

In this study we examined the effects of processing on mechanical performance, with 3 to 5 samples tested for each condition (for a total of about 100 samples fabricated and tested). The samples were then tested using a small loading machine (MicroTester expert 4,000, Admet, Norwood, MA) in flexure in order to simulate the primary loading mode of long bones (three-point bending with 20 mm span). Force-displacement curves were recorded and stress–strain curves were computed using standard beam theory (Timoshenko, 1921). The flexural strength reported here was the maximal value of the flexural stress, just prior to fracture. The flexural modulus was the initial slope of the stress–strain curves while the sample was deforming in its elastic region. Three samples were also observed under scanning electron microscopy. These samples were coated with approximately 4 to 8 nm of gold before being observed under microscope (Inspect F-50 FEI, Hillsboro, OR).

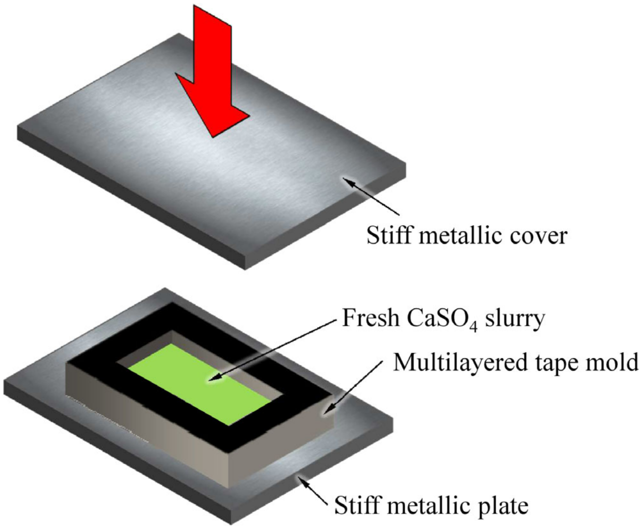

FIGURE 2 Preparation protocol for calcium sulfate (CS) samples requiring setting under hydrostatic pressure

3 | PARAMETRIC STUDY AND OPTIMIZATION

In this part of the work we systematically explored the effect of several key parameters: compressive pressure during setting, powder-water ratio, modified water composition, hydration, and reinforcements with inclusions.

3.1 | Pressure during setting

Reacted solid CS is in general porous (Sakaguchi & Powers, 2006). Porosity decreases the mechanical properties, especially with brittle materials whose strength is greatly reduced by stress concentrations. In this section we explore how the application of high pressure during setting can reduce porosity. For preparation we used the powder-water ratio recommended by the manufacturer: 10 g of CS powder for 1.86 g of water. Samples were prepared following this ratio and the slurries were compressed under various pressures from $p = 0$ MPa (i.e., no applied pressure) to $p = 250$ MPa. Figure 3c shows a sample prepared with $p = 0$. Large macroscopic pores are visible and scanning electron micrographs reveal a high porosity. By comparing the weight and volume between this type of sample and unreacted CS powder, we estimated at about 54% the relative density of the samples (porosity of 46% vol.). These samples had a flexural strength of 7 ± 1.8 MPa and a modulus of 12 ± 0.8 GPa. Increasing the applied pressure during setting decreased the porosity of the final material significantly for $p = 5$ MPa (Figure 3d), with a porosity of about 16% vol. At $p = 10$ MPa, the material was almost fully dense, with a porosity <2% vol. Higher pressures did not generate any further improvement in density. Dense CS had a darker appearance (Figure 3e). The whiter appearance of the porous samples is likely due to the scattering of light on the microscopic pores (Pae, Chu, Lee, & Kim, 2000). Increasing the pressure increased both modulus and strength (Figure 3a, b) up to $p = 10$–20 MPa, which we associated with the decrease in porosity. However, pressures greater than 20 MPa resulted in a decrease of the mechanical properties.

This decrease in properties suggests that higher pressures for processing induce damage to the material that reduce mechanical properties when compared to samples prepared at optimal pressure. It is also possible that under high hydrostatic pressure, the reaction between CS and water is not complete, or that the optimal powder–water ratio becomes different under very high pressures. The lack or

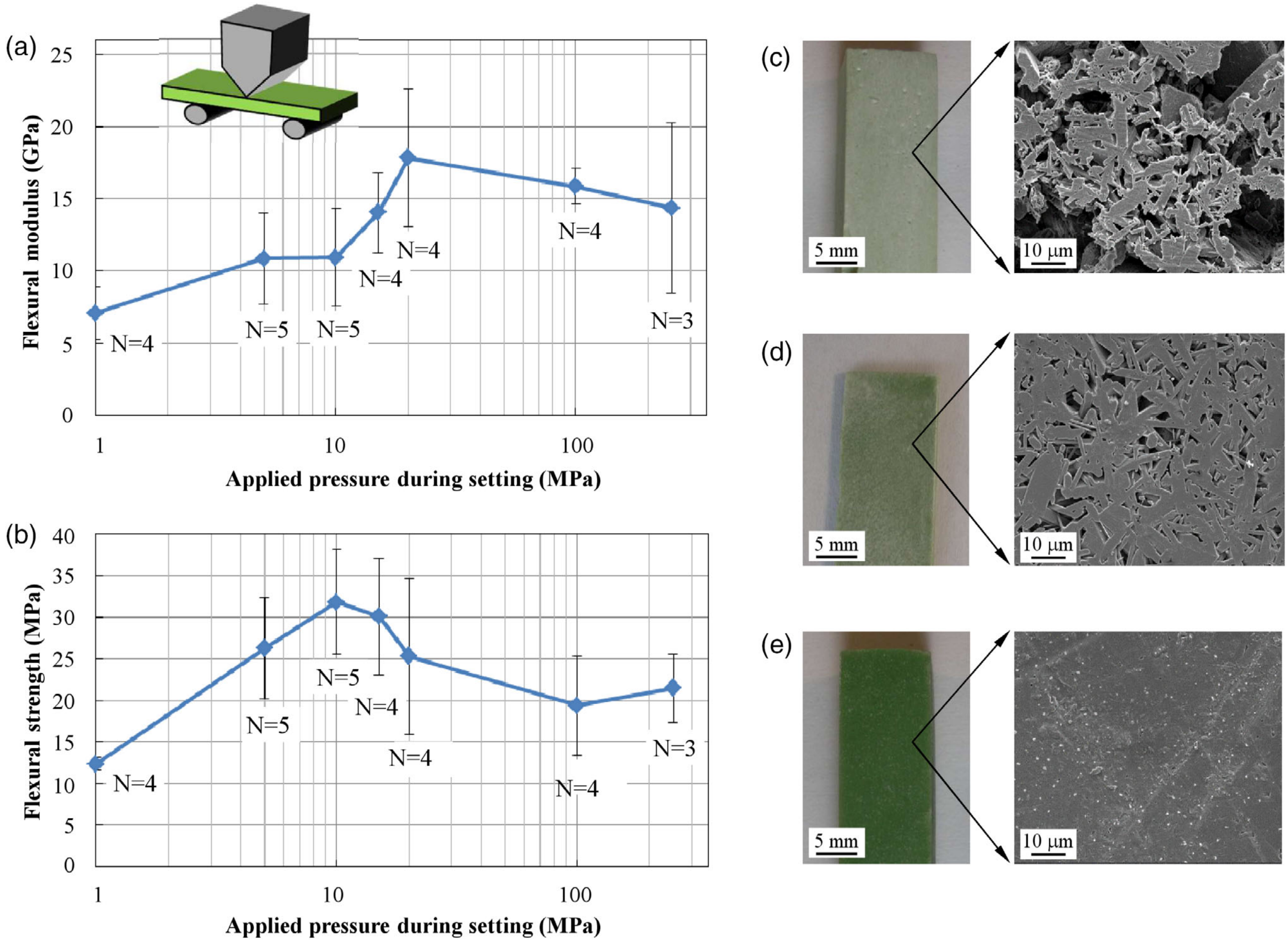

FIGURE 3 (a) Flexural modulus and (b) flexural strength as function of applied pressure during the setting of the calcium sulfate (CS) samples (3 to 5 samples tested for each condition); (c–e): optical images and scanning electron microscopy (SEM) images of three CS beams prepared with (c) no pressure during setting; (d) prepared with 5 MPa pressure during setting; (e) prepared with 10 MPa pressure during setting

the excess of water, or the presence of damages may not counterbalance the gain due to pore reduction after a certain amount pressure (more than 20 MPa). Figure 4 shows typical stress–strain curves obtained from samples prepared at different pressure. The stress strain curve for a sample prepared under a pressure higher than 10 MPa indicates a more brittle behavior and a lower strength. We chose *p* = 10 MPa as the optimal pressure to prepare the samples for the rest of the study.

3.2 | Powder–water ratio

The manufacturer recommends the following ratio for optimal mixing: 10 g of CS powder for 1.86 g of water (10:1.86). In this part of the work we explored the effect of the proportions of CS powder to water with 10:1.7, 10:1.86, 10:1.9, and 10:2.1. A pressure of 10 MPa was applied on the samples during the setting. The results in terms of flexural stiffness and flexural strength are shown on Figure 5.

Among the different ratios tried here, we found that the ratio recommended by the manufacturer (10:1.86) provided the highest modulus and strength. For higher ratios (i.e., less water), the water starved in the reaction which leaves some regions of CS unreacted, which led to inferior strength and stiffness. In contrast, for lower ratios (i.e., more water), the excess of unreacted water in the material

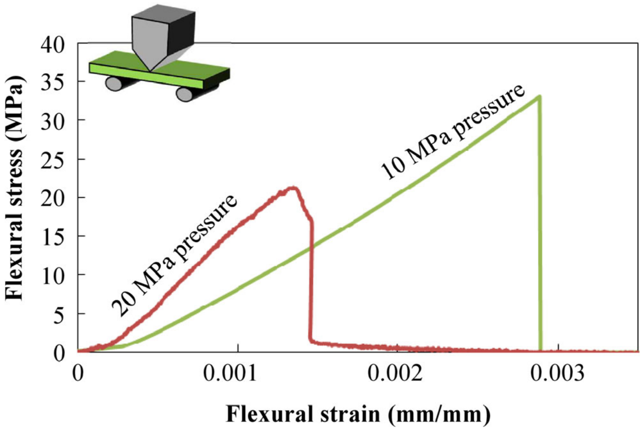

FIGURE 4 Typical flexural stress–strain curves for calcium sulfate (CS) samples prepared under 10 MPa pressure and 20 MPa pressure

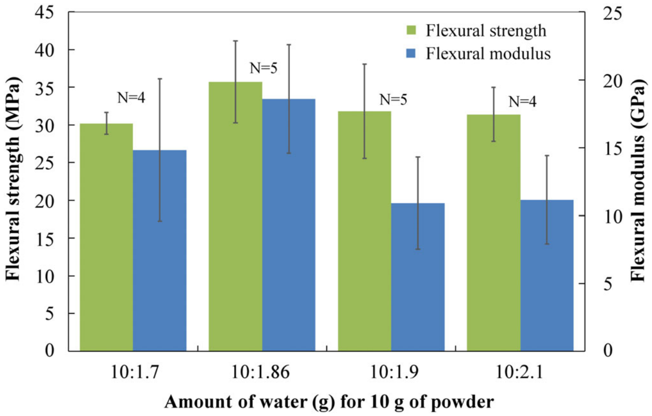

FIGURE 5 Flexural modulus and flexural strength for four different water:CS ratios. CS, calcium sulfate

generated pores in the final material, which also decreased strength and stiffness. In the rest of the study, the samples will be prepared following the optimal ratio 10:1.86.

3.3 | Effect of $CaSO_4$ saturated water

A previous study by Shen et al., (1981) showed that one of the best technique to improve the strength of CS is to replace the water in the mixing by a solution saturated with Ca^{2+}. Following this finding we prepared CS slurries using a Ca^{2+} saturated solution. The rest of the fabrication protocol and testing method was strictly identical to those of previous parts. Figure 6 shows that these samples showed an increase of 19% for flexural strength and 16% for stiffness compared to samples prepared with distilled water. Data series for the strength were found significantly different (p-value = .09) but not for stiffness (p-value = .193). Based on scanning electron microscopy observations, Shen et al., (1981) suggested that the saturated water modifies the shape and the size of the mineral crystals so that their formation and packing are improved.

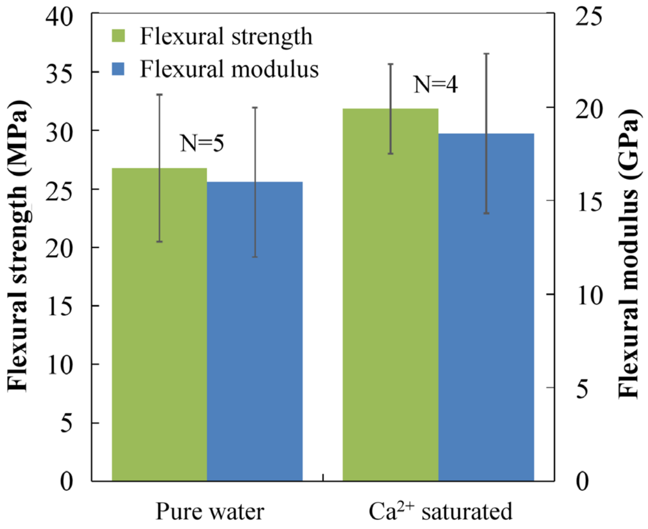

FIGURE 6 Flexural modulus and flexural strength for calcium sulfate (CS) beams prepared in pure water and in Ca^{2+} saturated water

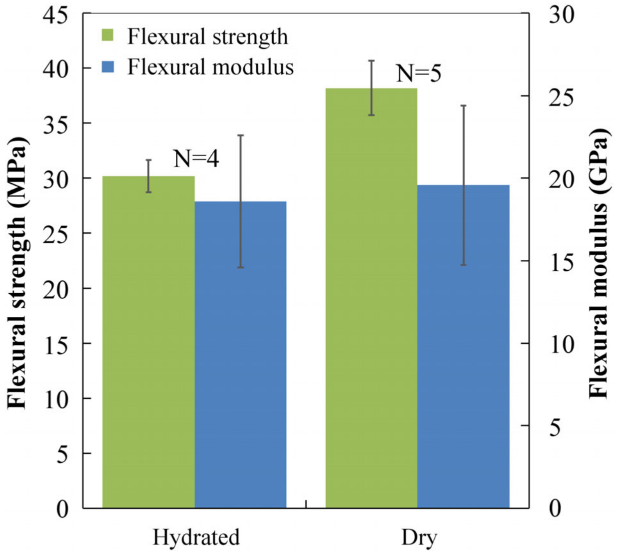

FIGURE 7 Flexural modulus and flexural strength for calcium sulfate (CS) beams tested in dry and hydrated conditions

3.4 | Effect of hydration

In this section we explored the effect of hydration on the mechanical properties. "Dry" samples were left in air for 12 hr after preparation and "hydrated" samples were left in Ca^{2+} solution for at least 12 hr before testing. Hydrated and dry samples displayed no statistically significant difference in moduli (Figure 7). However the strength decreased from 38.2 MPa (dry samples) to 30.2 MPa (hydrated samples) (p-value <.05). The loss of 26% of the strength due to the hydrated conditions can be attributed to ions exchanges between the Ca^{2+} saturated solution used to hydrate the material, and the material itself. Even if these exchanges were limited because of the saturation of the solution, they may have dissolved the material enough to damage its microstructure and create flaws that decreased the strength but not the modulus. Since the samples exhibited no changes in strength or modulus after hydrating 24 or 48 hr as mentioned earlier, the mechanical properties probably do not decrease any more after a certain amount of damage in the microstructure is reached.

3.5 | Effect of inclusions

Several previous studies have reported increases in CS mechanical properties by adding reinforcing inclusions in the material (Coutts, 1986; Gao et al., 2012; Park, 2007; Thomas, 1955). Here we explored the effect of adding different inclusions in CS samples prepared following the optimized fabrication protocol (compressed at 10 MPa during the setting, powder–water ratio of 1.86:10 and saturated solution in the slurry). All samples were tested in hydrated conditions. We tested alumina tablets (Antaria Limited, Bentley, Australia), glass fibers (McMaster-Carr, Aurora, OH), hydroxyapatite whiskers (Himed, Old Bethpage, NY), kaolin tablets (Imerys, Paris, France), silica beads (Sigma-Aldrich, St. Louis, MO), and wollastonite whiskers (Bonding Chemical, Katy, TX), at volume fractions of 5 and 10% (which are commonly reported in literature). Silica sand was also investigated but at volume fractions closer to sand reinforced cements (10 and 15%). The results (Figure 8) show that in all cases, the inclusions decreased the strength of the material between 10 and 74%. These decreases were found statistically significant ($p < .017$) except for HAW-5%. Ten percent was the volume fraction where the decrease was the most important. In general, the trend appeared to be the more volume of inclusions in the material, the larger the decrease in strength. Inclusions probably disrupt this microstructure and can be assimilated as defects. On the other hand, for CS samples not compressed during the setting, the presence of flaws from various sizes explains why additional stronger or stiffer inclusions have a toughening and strengthening effect. These results also suggest that in order to keep the advantage of the high density of the optimized CS, any alterations of the microstructure such as embedded inclusions must be avoided.

4 | NET SHAPE FORMING OF CS WITH COMPLEX GEOMETRY

Implants for segmental bone must conform to the requirements of specific patients and cases, which means that they may have complex shapes. In this section we explore the possibility of shaping CS materials into complex geometries using relatively easy and fast net shape fabrication methods, while maintaining the optimum preparation conditions established above. For reference in terms of geometry and mechanical properties, we used tibias and femurs from chicken. Chicken legs were acquired from a local butcher shop. Tibias and femurs were extracted from the chicken legs and the soft tissues were carefully cleaned with a razor blade. The samples were kept hydrated in water until testing. The bones were approximately 50 mm in length. The shaft of the bone had an outer diameter of 11 to 12 mm, and a cortical shell thickness of 1 to 1.7 mm (Figure 10). The flexural properties of the bones were evaluated using a three-point bending configuration, with a span of 40 mm. Figure 10 shows the flexural force at failure and the flexural stiffness of these bones. Using standard stress analysis, beam theory and the hollow cross section of the bone, we found a tensile strength of 40–70 MPa and a modulus of 0.71–-1.55 GPa, which are the typical values for cortical bone (Patterson, Cook, Crenshaw, & Sunde, 1986). We fabricated CS rods with a bone like geometry using the setup shown on Figure 9. The first step of the fabrication process was the 3D printing of a cylinder with the desired shape and dimension. Here the overall dimensions were slightly larger

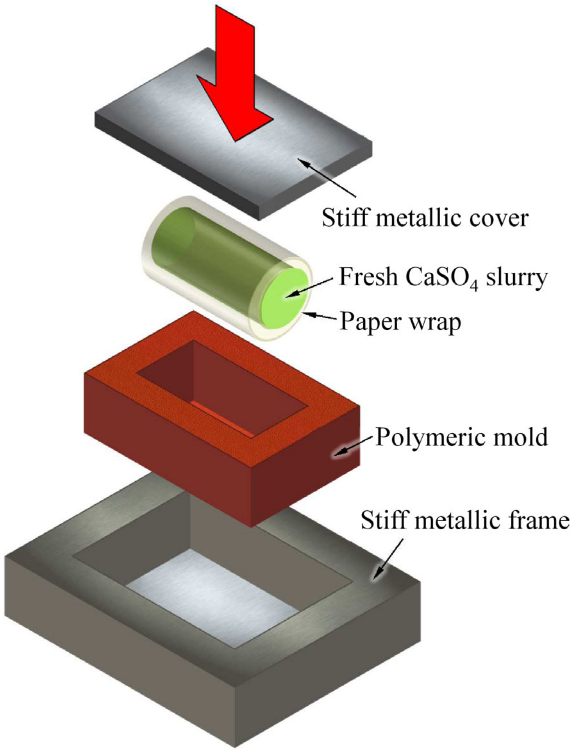

FIGURE 9 Preparation protocol for cylindrical calcium sulfate (CS) samples requiring setting under hydrostatic pressure

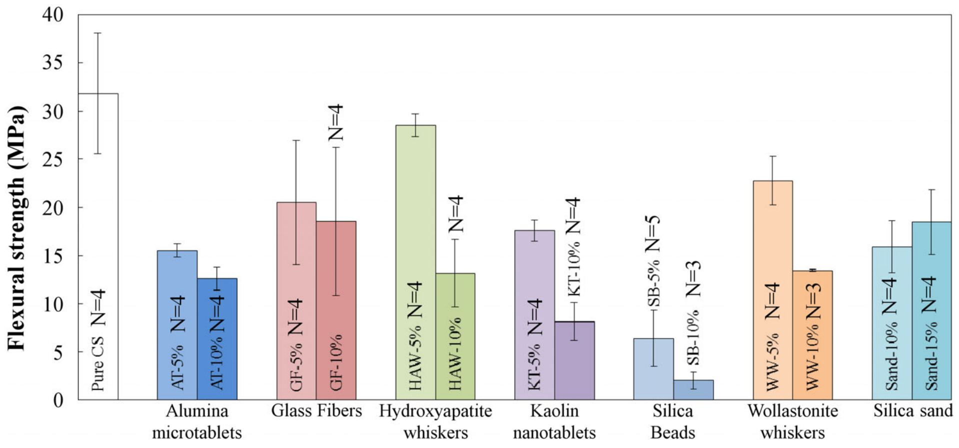

FIGURE 8 Flexural strength for pure calcium sulfate (CS) beams and for CS beams reinforced with seven types of inclusions

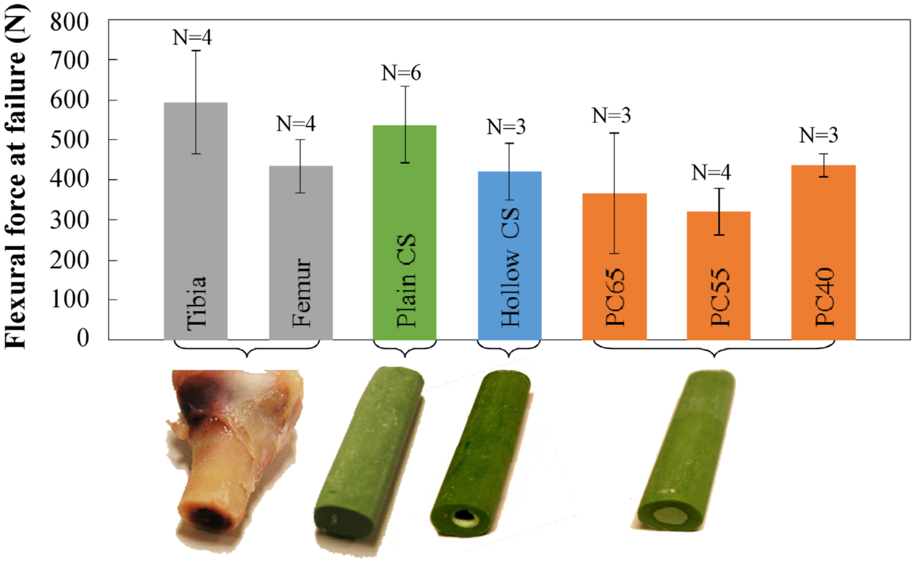

FIGURE 10 Flexural force at failure for natural bone, and for three bone-like calcium sulfate (CS) design: Plain, hollow, composite with porous core, and dense shell (samples and cross sections are shown). All samples have the same outer diameter

than chicken bone with a length of 50 mm and outer diameter 14 mm. This template was then embedded in a silicone solution and left to curing for 1 hr. The template was then removed from the cavity by deforming the silicone. A silicon mold with a perfect negative replica of the template was thus produced. To prepare CS samples, the CS slurry was poured into the silicone mold (Figure 9) and placed in the hydraulic press. The volume of CS was larger than for the thin plates used in the previous section, so that excess water could not be expelled from the material. To resolve this problem, we lined the mold with a layer of 1 mm of scientific grade blotting paper (Fisher scientific, Hampton, NH) to absorb the excess water expelled from the material during compression. The silicone mold was placed into a confining steel chamber and submitted to a compressive load using a 25 tons capacity press (FW-4 tablet press; Joyfay, Cleveland, OH). Silicone has a very low shear modulus, but a very high bulk modulus because it is nearly incompressible. As a result, uniaxial compression translated into a hydrostatic state of compressive stress because of the confinement. The pressure applied on the surface of the calcium sulfate material was therefore uniform, and produced materials with homogenous properties. Once the blotting paper layer removed, the diameter of the samples matched those of natural bones (11 to 12 mm). These samples were tested in hydrated conditions. We fabricated plain rods, as well as hollow rods with inner diameter of 6.6 to 7.4 mm (corresponding to a cortical shell of 1.8 to 2.7 mm). There is a particular interest in hollow rod, because this geometry has been demonstrated to promote bone formation (Yoshikawa et al., 2008). For these samples, a hole was drilled through the central axis of cylindrical samples made of pure optimized CS and the samples were tested in hydrated conditions.

We also fabricated hybrid rods, with a fully dense cortical shell and an inner core made of porous CS (relative porosity approximately 50%). These samples were obtained by inserted a smaller porous CS rods already set inside the fresh slurry before compressing in the press. We tested three different diameters of core, in hydrated conditions, and reported the results as a function of the ratio diameter of the core—diameter of the sample: PC65 (respectively PC55 and PC40) refers to cylindrical samples with a core with a diameter that is 65% (respectively 55 and 40%) of the diameter of the sample. The difference between the total diameter of any of these samples and those of chicken bones was always within 8%. Figure 10 shows images of the different materials tested here, together with mechanical properties. All CS samples were tested in the same conditions than natural bones (span = 40 mm). Plain CS samples a strength of 39.33 MPa (±7.55 MPa) which was higher than for the rectangular beams, probably because modifications of the span-to-thickness ratio of the samples can affect their apparent strength (Alander, Lassila, & Vallittu, 2005).

Plain CS samples exhibited an average force at failure of 537.8 N which is similar to chicken bones. Hollow cylindrical samples and samples with porous core only lost a small fraction of strength compared to plain cylindrical samples. This was expected, because in flexion the region near the neutral axis does not carry stress, largest stresses occurring at the surface of the sample. Simple stress analysis predicts that the flexural strength a tube with the inner diameter equal to half of the outer diameter is only 6% smaller than the flexural strength of a plain rod with the same outer diameter. For the same reason, the hybrid samples with a porous core (PC65, PC55, PC40) had about the same strength as the hollow sample. These results demonstrate that the CS materials prepared with our optimized protocol can be formed easily in a desired shape, and provide mechanical strength on par with natural bones.

5 | CONCLUSIONS

Calcium sulfate provides many advantages over the other types of ceramics used as bone graft materials: CS is biocompatible, osteoconductive and biodegradable, and it can be processed at room temperate. The main drawback of CS is its low tensile and flexural strength. In this study we have addressed this limitation by optimizing the fabrication process for pure CS, and by using mechanical testing procedures which are relevant for load carrying, or structural bone grafts (flexural tests in hydrated condition). In particular we found that applying large compression during the setting significantly reduced its porosity and increased its strength, an important fabrication step which to the best of our knowledge has never been reported in the literature on CS. This key parameter, together with other optimized processing condition (CS powder to water ratio, saturated solution) produced the CS materials with the highest flexural strength ever reported in hydrated conditions. Interestingly, we found that once these optimal conditions are used, the addition of "reinforcing" inclusions in the material actually decreases its strength, probably because these inclusions actually act as defects instead of reinforcements. Finally, we demonstrate how CS can be formed in precise shapes while maintaining optimal processing conditions. The CS cylindrical rods we made were as strong as chicken bone for the same overall dimensions.

A new question that may rise from this study is the effect of the decreased porosity on the osteoactivity of a bone implant made of optimized CS. It has indeed been demonstrated that a large pore size in bioceramics is beneficial for the vascularization and tissue ingrowth (Bai et al., 2011). We proposed at the end of this study an architectured bone implant in which dense and porous materials are combined to duplicate the trabecular and cortical structure of long bones. Such implants exhibited only a small loss of overall strength, while their osteoconductivity could be superior to that of monolithic fully dense CS material. Future investigations on the osteoconductivity of fully dense CS, porous CS and architectured CS will be crucial to assess the suitability of optimized CS as a bone graft material.

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