Influence of TiO_2 and Ag_2O Addition on Properties of Tricalcium Phosphates

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Statement of Purpose: Tricalcium phosphate (TCP) is a resorbable bio-ceramic widely used in bone restoration and replacement. TCP forms strong bonds with natural bone tissue and show *in vivo* time dependent mechanical properties. When in the body, TCP degrades due to cellular activity and degradation by body plasma. This degradation of the ceramic allows new natural bone to grow into the implant site and eventually replace the artificial material. Regeneration instead of replacement is often thought of as an ideal restoration mechanism. It is intuitive that the rate at which the ceramic degrades will play a large role in how versatile this material can be, as natural bone grows at different rates depending on the implant site and patient. As of now, little is known about the degradation rate of TCP or what may be used to tailor it to specific applications. This research focuses on characterizing the influence of two select dopants (titania and silver oxide) on the degradation rate of TCP.

Methods: TCP ceramics reinforced with compositions of TiO_2 and Ag_2O were processed into two different sample shapes via uniaxial powder compression: disc compacts and compression cylinders. Four different compositions were created from these dopants, pure TCP, the two individual dopants, and a binary composition with both dopants. These green compacts were then sintered at 1250^0 C for 4 hours. After sintering, the weight and volume of each compact and cylinder were carefully measured and the density calculated. X-ray diffraction analysis was used to determine if the introduction of any of the dopants significantly altered the phases of the TCP after sintering at 1250^0C for 4 hours, compared to the pure TCP with the same conditions. Powdered samples of all the compositions were prepared by grinding sintered compacts in a mortar and pestle. The effect of the dopants on the microstructure of the TCP samples was studied via SEM. *In vitro* cytotoxicity tests on dense TCP compacts were used to study the influence of the selected dopants on cell attachment and proliferation. This analysis was carried out using a modified human osteoblast (HOB) with an osteoprecursor cell line (OPC 1). In order to characterize change in the ceramic's properties over time in a biological environment, sintered samples were soaked in a simulated body fluid (SBF) for up to 3 months. Compression strength as a function of time in SBF was chosen to test biodegradation of these materials. The ultimate compressive strength was measured using a screw driven Instron with a constant crosshead speed of 0.002 mm/sec.

Results / Discussion: Densification is presented normalized to the theoretical density of pure β-TCP (3.07 g/cm^3). The presence of TiO_2 in TCP improved densification by over 15% of the pure TCP, and increased compression strength from 70 (±25) to 145 (±40) MPa. The binary composition had the highest densification, increased by almost 20% of the theoretical density for pure TCP. Compression strength for this composition increased to 180 (±15) MPa. Ag_2O had very little influence on densification or compression strength. Micrographs on the surface of the samples are seen to correlate porosity viewed with density measured. XRD analysis showed that no significant phase change occurred due to the addition of dopants. Cytotoxicity tests confirmed that cells were able to attach, proliferate, and differentiate on the surface of TCP ceramic. The addition of the dopants appeared not to decrease this cell growth behavior and in some instances improved the cell-substrate interaction. Ag_2O-doped samples grew a Ca-P based apatite from the cell culture media on which the cells attached better than the underlying ceramic. All samples gained weight during the 3 months of SBF treatment suggesting that precipitation rate was prevailing over degradation rate for these samples. Weight change correlated inversely with sintered density. The samples which had a lower sintered density gained more weight during SBF treatment than did samples with higher density. This suggests that porosity provided free surfaces for precipitation and, therefore, had more weight increase. However, higher surface area could also lead to faster degradation, if degradation kinetics were faster than precipitation kinetics, which was not the case for these samples. Weight gain also correlated strongly with precipitation viewed in the inner-connected pores of the samples confirming that precipitation was the source of gained weight. After 2 months in SBF, pure TCP strength had degraded by 20 MPa, but for doped compositions, no noticeable degradation was noticed up to 3 months.

Conclusions: Results show that there is potential for tailoring properties with the addition of additives without hindering the excellent biocompatibility of TCP. The addition of TiO_2 significantly increased the densification of pure TCP. This increase of densification had a magnified increase in the mechanical properties of the ceramic more than doubling the ultimate compression strength. Strength degradation in pure TCP began after 1 month in SBF, but for the doped composition, no noticeable degradation was measured up to 3 months. All these properties were improved without hindering the excellent biocompatibility of pure TCP. Results such as these show promising improvements in the characteristics of TCP ceramics, which can be utilized in applications such as spinal fusion and dental augmentation to make TCP a more versatile biomaterial.