**Hydrating Calcium Phosphate/ Demineralized Bone Matrix Graft Material with Blood, Bone Marrow, and Antibiotics**

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**STATEMENT OF PURPOSE**:

There is a growing desire to enhance performance of bone graft substitutes (BGS) by mixing with human blood and bone marrow aspirate (BMA) to introduce osteogenic cells and autogenous growth factors or with antibiotics to prevent local infection. However, little is known about how these additives affect the physical or chemical properties and performance of these grafts. Calcium phosphate cement based products are of particular interest because they are provided as two component systems, a powder and hydrant, facilitating addition of the additive by replacement of the hydrant. One such commercial BGS, a CaP/DBM composite cement, which was previously shown to perform equivalently to autograft in both critically sized bone defect and spinal fusion models, was evaluated with multiple additives. Three different forms of antibiotics, blood and bone marrow aspirate were evaluated with the goal of determining the highest concentration of additive at which the graft performance is maintained.

**MATERIALS & METHODS**:

CPC/DBM product was mixed with either saline (control), human blood, human BMA, Tobramycin (5 to 40 mg/mL), Clindamycin (18 to 150 mg/mL) or Vancomycin (50 mg/mL). Mixing was achieved by replacing the indicated product hydrant with the specified solution at a fixed hydration volume of 0.7cc per gram powder. Samples were incubated at 37 C and tested for compressive strength and hardening time. Another set of samples were implanted in an intramuscular athymic rat model to test for osteoinductivity. Additional samples were incubated for 72 hrs in simulated body fluid and tested by FTIR to determine chemical composition. Samples were also tested for Injectability.

**RESULTS & DISCUSSION**:

A summary of testing results is given in Table 1. Mixing CaP/DBM with blood and bone marrow had no negative impact on the performance of the graft material even when all of the hydration was replaced with the additive. CaP/CMC was more sensitive to addition of antibiotics and the effect was dose dependent. Vancomycin had no negative impact on the performance of the graft material up to a concentration of 50 mg/mL. Tobramycin had no negative impact at a concentration of 5 mg/ml but delayed the setting reaction at higher concentrations. Clindamycin had the greatest negative impact, retarding setting time and inhibiting osteoinductivity at 18 mg/ml.

**CONCLUSIONS**:

Adding autogenous growth factors and/or antibiotics is a promising method for enhancing the performance of synthetic bone grafting materials. CPC/DBM combined with blood, BMA, and specific antibiotics at specific concentrations maintains its chemical, physical and performance characteristics.

**Table 1: Results Summary**

| Additive | Concentration | Setting Time (minutes) | Compressive Strength (MPa) | Chemical Composition | Osteo-inductivity | Injectability |
|---|---|---|---|---|---|---|
| Saline | 100% | 10 | 2 | NCHA | Inductive | Injectable |
| Blood | 100% | 10 | 2 | NCHA | Inductive | Injectable |
| BMA | 100% | 10 | 2 | NCHA | Inductive | Injectable |
| Tobramycin | 40 mg/mL | > 20 | - | - | - | - |
| | 20 mg/mL | > 20 | - | - | - | - |
| | 10 mg/mL | > 20 | - | - | - | - |
| | 5 mg/mL | 10 | 2 | NCHA | Inductive | Injectable |
| Vancomycin | 50 mg/mL | < 10 | 2 | NCHA | Inductive | Injectable |
| Clindamycin | 150 mg/mL | > 20 | - | - | - | - |
| | 37.5 mg/mL | > 20 | 0 | - | - | - |
| | 18 mg/mL | 20 | 2 | NCHA | Non-inductive | Injectable |