Calcium Phosphate Cement as a Carrier for the Local Delivery of Antibiotic

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Introduction: Infection in and around bone is a rare but serious condition[1]. When infection is present the targeted delivery of antibiotic decreases the possible systematic toxicity and increases the amount of antibiotic locally available to fight the infection[2].
This study aims to determine the ability of Calcium Phosphate Cement[3] (CPC), as a bone void filler, to incorporate and release antibiotic at a level to inhibit bacterial growth. A modified Kirby-Bauer susceptibility test was used to evaluate the potential of the combination of CPC and the antibiotic tobramycin.

Methods: The CPC powders (BoneSource®, Stryker Orthopaedics, Mahwah, NJ) were mixed with three levels of antibiotic (Tobramycin, Alpharma, Copenhagen, Denmark) for testing: low, medium, high. A standard CPC without tobramycin was included as one control. As a positive control, PMMA with antibiotic (Simplex P with Tobramycin, Stryker Orthopaedics, Mahwah, NJ) was included in the test matrix (Table 1).

Table 1. Cements composition tested

Cement	CPC	CPC	CPC	CPC	PMMA
Amount Cement (Grams)	10	10	10	10	40
Amount Tobramycin (grams)	0	0.036	0.172	0.430	1.0
Weight %	0	0.36	1.72	4.3	2.5
Designation	CPC_0 None	CPC_L low	CPC_M medium	CPC_H high	$PMMA_T$ standard

The CPC powders were hand mixed with 0.25M sodium phosphate solution (liquid : powder = 0.36) to form a paste, which was cast into aluminum molds to produce 14mm diameter by 2mm thick disks. The PMMA was cast into the same molds as the CPC to produce the same size disk. After one hour, the cured cements were placed in an agar plate seeded with Staphylococcus aureus ATCC 6538 in a modified Kirby-Bauer susceptibility test. The petri dish was incubated overnight at 37°C. The zone of bacterial inhibition, defined as the distance between the edge of the test disk and the edge of bacterial growth (excluding areas of partial inhibition) around each disk, was measured in millimeters. Seven replicates of each composition were tested.

Results/Discussion: All CPC samples without tobramycin additions had no zone of inhibition around the cement (Table 2).

Table 2 Results of zone of inhibition testing (n=7)

	CPC_0	CPC_L	CPC_M	CPC_H	$PMMA_T$
Zone (mm)	0.0	5.14	7.21	9.79	5.57
Stand. Dev.	0.0	0.244	0.567	0.994	0.607

The zone of inhibition for the PMMA with tobramycin was very similar to the values found in previous testing using this model[4]. Including tobramycin with the standard CPC composition resulted in a more fluid paste than CPC without tobramycin. Some of the CPC disks made with the high level of tobramycin did not stay intact during removal from the mold, but still generated large zones of inhibition.

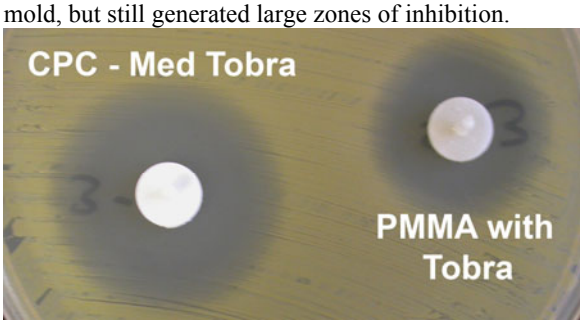
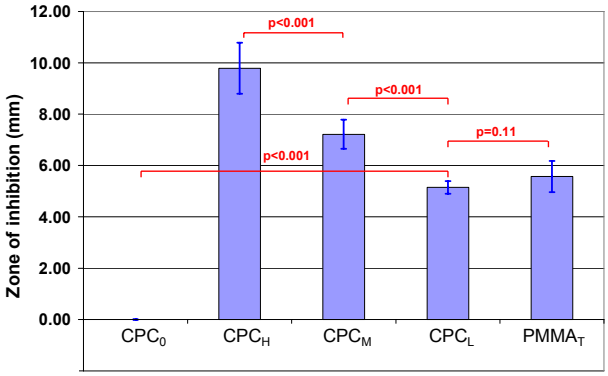


Figure 1. CPC + medium dose Tobra and Simplex + tobra

Both CPC and PMMA containing tobramycin had statistically significant larger zones of inhibition than CPC without tobramycin. The zones of inhibition around CPC with a low dose of tobramycin and the PMMA with tobramycin ($p=0.11$) were equivalent. Both medium ($p<0.001$) and high ($p<0.001$) doses of tobramycin in CPC had significant larger zones of inhibition than PMMA with tobramycin or a low dose CPC.



Conclusions: In this in-vitro study calcium phosphate cement was an acceptable carrier; capable of incorporating tobramycin antibiotic and releasing it in quantities sufficient to inhibit bacterial growth in a modified Kirby-Bauer susceptibility test.

References:

1. Bauer, T. JBJS 2006:88-A:869-882
2. Witsø, E. Acta Orthop Scand. 2004:75-3:339-346
3. Brown, W. Cement Res Prog. 1986:351-379
4. Scott, C. JBJS BR 1999:81-B:440-443