The Effect of Poragens on Elution and Compressive Strength of Antimicrobial Loaded Bone Cement
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Background
Antimicrobial Loaded Bone Cement (ALBC) is used for prophylaxis to prevent orthopaedic infections with low dose antimicrobials and to treat orthopaedic infections with high dose antimicrobials. Antimicrobials cause pores to form in ALBC (poragen). Inert fillers can be used as poragens to increase pre formation and increase antimicrobial release but this happens at the expense of decreased mechanical performance. Xylitol has been proposed as a soluble particulate poragen for ALBC due to its inherent antimicrobial properties against dental flora that cause carries with the expectation that it will add inherent antimicrobial activity to its role and a poragen. The increase in elution relative to the decrease in mechanical properties with poragens is unknown and it is likely that the mechanical degradation will progress as the particulate material is removed from the pores by elution

Purpose/Hypothesis
The purpose of this investigation is to study the relationship between increased elution and decreased mechanical performance of ALBC caused by adding poragens. We hypothesize 1) that adding poragen to ALBC will increase the antibiotic delivery, and 2) that adding porogen will lead to progressive loss of compressive strength with elution.

Methods:
ALBC test cylinders 12 mm in length and 6 mm in diameter (ASTM 451-99) were made using ALBC formulated with Simplex P bone cement (Stryker ®), 1 gram of tobramycin and xylitol as the poragen in the following doses: 0, 1, 2, 4, 8 and 16 grams. The powdered polymeric PMMA, tobramycin and xylitol were first mixed homogeneously using a commercial bone cement mixing bowl. The monomer was then added and the ALBC mixed by hand without vacuum. In the dough phase the ALBC was introduced into a Teflon mold. Three batches of cylinders were formulated and studied for each filler concentration.

Three groups of 5 cylinders for each xylitol dose were eluted in 20 ml of de-ionized water. Total eluant exchange was performed on days 1, 3, 7, 15 and 30. The tobramycin concentration was measured using disc diffusion bioassay. Total recovered tobramycin was calculated.

Three groups of 5 cylinders for each xylitol dose for 4 time periods (0, 7, 15, and 30 days) were eluted following the above protocol. Cylinders were tested to failure in axial compression at 24 mm /min in an MTS Sintech 1/S material test frame. A custom Matlab algorithm was used to calculate the compressive strength in accordance with standards (ISO 5833).

Data was subjected to statistical analysis using repeated measures ANOVA with P<0.05 defined as significant. Tukey’s multiple comparison test (P<0.05) was used as a post-hoc test to identify differences between groups.

Results:
Tobramycin elution increased with time in days (p<0.05) and grams of xylitol per batch (p<0.05), following first order kinetics. For 1 gram of xylitol, 440 µg was recovered by 3 days and 816 µg after 30 days. For 16 grams of xylitol, 1043 µg was recovered by 3 days and 2722 µg after 30 days. Elution results for tobramycin sulfate n (Fig 1).

Discussion:
Our data shows that addition of xylitol as a porogen increases the amount of antibiotic eluted. Compressive strength decreases as filler fraction increases. For 0,1 and 2 grams of xylitol the compressive strength stayed above the ISO standard during the study (4 grams at 20 days, 8 grams at 6.5 days and 16 grams at 2 days).

There are several limitations to our study. The first of which is that this is an in vitro experiment, and actual use of xylitol as a poragen would need to be tested as an in vivo model before recommending this for clinical treatment. Although xylitol’s clinical safety has been well documented in the dental literature, its use in orthopaedic applications has not been studied. Our study design employs hidden replication to estimate the difference in antibiotic release based upon different xylitol formulations. Since we measure our cylinders in groups of 5, our elution data does not estimate within batch variability. Since the compression data is higher powered, we can use that data to identify appropriate ranges of fillers. Additionally, we only tested the cylinders in uniaxial compression. The mechanical strain any implant goes through in vivo is much more complicated. Any formulation change would need to be tested in torsion and fatigue and corroborated against the published standards before it could be recommended clinically. Adding particulate poragens to ALBC more efficiently and cost-effectively delivers high concentrations of antimicrobials from ALBC. The structural aspects of the study show that, at least in compressive strength, adding poragens at lower doses does not decrease the compressive strength to below the ISO standard. The use of xylitol can also be seen as a cost cutting measure, by allowing a significantly higher release of antimicrobials from ALBC, while using a lower dose.

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