The Effect of Surfactant on the Elution of Gentamicin from Orthopaedic Cement

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Introduction: Increasing the delivery of hydrophilic antimicrobials from the hydrophobic bulk of the cement was explored using a surfactant to emulsify a solution containing deionized water and methylmethacrylate monomer to produce a porous cement. We hypothesized that the emulsified cement when made with liquid antimicrobials in the emulsion would show improved antimicrobial delivery while maintaining the compressive strength.

Methods:

Preparation of Standard Antibiotic Loaded Beads
2 g of gentamicin powder (Fujian Fukang Pharmaceutical Co., Fuzhou, China) was mixed manually using a metal spatula with 40 g powdered polymer of Simplex® bone cement (Stryker, Kalamazoo, MI), prior to adding the monomer. The cement was mixed as per the manufacturers’ instructions. Cylinders of radius 6mm and length 12mm (ASTM 451-99) were prepared using a Teflon mold.

Preparation of Emulsified Antibiotic Loaded Beads
The monomer solution contained by volume 6% deionized water, with 2g gentamicin powder dissolved in the deionized water, per 40 g powdered polymer of Simplex® bone cement, 14% F 127(Sigma, St. Louis, MO), and 80% monomer. The cement was mixed as per the manufacturers’ instructions. Cylinders of radius 6mm and length 12mm (ASTM 451-99) were prepared using a Teflon mold.

Elution Studies
Both formulations of the antibiotic loaded bone cement cylinders were immersed in 5 mL deionized water at 37°C. The elution study was repeated in triplicate. The eluant was changed at 1, 7, 15, and 30 days. The concentration of gentamicin in each eluant sample was determined by agar-diffusion bioassay. Kocuria rhizophila strain 9341 (American Type Culture Collection, Manassas, VA) was used as the test organism. Known standard concentrations of each antimicrobial were diluted in deionized water and tested simultaneously with the samples ranging from 6.25 µg/mL to 600 µg/mL. Each sample of eluant assayed in triplicate. Inhibition zone diameters were measured and a standard curve was produced. The zone radius was measured to find the concentration. The antimicrobial concentration in each eluant was determined and expressed in micrograms of antibiotic released per hour, per cylinder, over each time period.

Compression Testing
The compressive strength of both formulations was measured under dry conditions at 23°C. Specimens were eluted in deionized water at 37°C for 30 days (n=5) and dry beads(n=5) were subjected to compressive loads, using a Syntech 1/S mechanical testing machine (Syntech Inc., Metairie, LA) at a cross-head speed of 24.0 mm min⁻¹. The peak compressive load was determined in accordance with ASTM 451-99 using a MATLAB algorithm.

Statistics
The data is reported as the mean ± standard deviation. Data are analyzed with ANOVA for comparison at given time points, with Tukey’s Multiple Comparison Test used as a post-hoc test to evaluate differences between groups.

Results:
Cylinders prepared with F 127 surfactant showed improved antibiotic delivery over control cylinders. (Fig 1). ANOVA showed the presence of surfactant to be a significant factor determining the cumulative mass of antibiotic released at Day 30 (p<0.001).

Discussion:
While the cement proved to be weaker than control cement, the emulsification did noticeably increase the amount of drug released. Additionally, the emulsified cement lost less compressive strength over time than the standard mix cement. Further study of this technique in combination with other cement modifications will be necessary before it can be used clinically.

Figure 1: Cumulative Delivery from Emulsified (white diamonds) and Standard Mix (Black Squares) Bone Cement

Cylinders containing surfactant showed reduction in Compressive Strength relative to control, but less than the standard mix cylinders did over 30 days of elution (Fig 2). ANOVA showed Surfactant to be a significant determinant of compressive strength at both day 0 and day 30 (p<.001).

Figure 2: Compressive Strength at 0 and 30 days for Emulsified and Standard Mix Bone Cement. 2a shows the Compressive Strength on Day 0, and the bottom shows the compressive strength on day 30.

Subsequent fracture and examination of the cylinders created for the experimental group in this study revealed pores throughout the cement characteristic of emulsified water, (Fig 3).

Figure 3: ESEM showing Pore Structure in Emulsified Bone Cement

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