Mechanical and Physical Properties Effects through Material Selection for a Surgically Adaptable Chitosan Implant

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Statement of Purpose: The natural polysaccharide, biopolymer chitosan (CS) in the film form is intrinsically hemostatic and bacteriostatic which has led CS to excel as a wound healing bandage. Its additional abilities to act as a chemical depot and to biodegrade have led to its investigation as a wound healing drug delivery implant.[1] Antibiotic (AB) pre-loaded CS film's ability to inhibit and abate local infection has been previously researched.[2] The current research seeks to optimize two integral CS variables, the degree of deacetylation (DD) and acid solvent, to develop a pliable CS film able to be AB loaded immediately before use and applied to an implantable device or complex wound.[3] CS films are characterized and optimized based on AB uptake, swelling ratio, ultimate tensile strength (UTS), Young's modulus and percent elongation.

Methods: 1.5wt% CS (Primex, Iceland) having 61, 71 and 80% DD was dissolved in 1% lactic acid (LA) or acetic acid (HAc) solutions. The solution was filtered to remove insolubilities, placed in a glass mold and transferred to a convection oven at 60°C until dry. The dehydrated film was removed and neutralized by placing it in a NaOH solution followed by rinsing in water. This neutralized film was allowed to dry at 25°C. An uptake study was performed to determine the quantity of AB solution that each variation could absorb. The AB, daptomycin (Cubist, MA), was dissolved in solution at 1mg/ml. The film was then submerged in the AB solution for thirty seconds and removed. The remaining solution was tested using a high pressure liquid chromatography (Varian, CA) method to determine the AB concentration. Absorbed AB quantity was determined using differences in concentrations. Concurrent with the uptake study, film dimensions were measured using digital calipers in order to calculate film volume differences, yielding the swelling ratio. CS film swelling ratio quantifies the increase in volume as the film rehydrates. Neutralized films were also subjected to tensile testing using a Universal Materials Testing Machine (Instron, MA). Test specimens were cut uniformly with gauge lengths and widths of 12.7mm and 3.5mm respectively. The testing device software was configured to output UTS, Young's modulus and the breaking point % of elongation. All experiments were performed with $n \geq 5$. Tukey's HSD statistical analysis was performed with $\alpha = 0.05$ to determine statistical differences between film variations.

Results: In figures 1 and 2 variations are labeled as the DD followed by the acid solvent with significant differences indicated. For AB uptake in figure 1, LA variations were significantly higher than HAc variations. Negative uptakes show that some HAc variations excluded AB, only absorbing water. 80LA and 71LA swelling ratios were significantly higher than others. In figure 2, UTS analysis revealed 71 and 80% DD HAc films were significantly stronger than all other variations. Statistical differences for Young's modulus data were similar to UTS. There were no significant differences in the % elongation at the breaking point.

Figure 1: Antibiotic Uptake

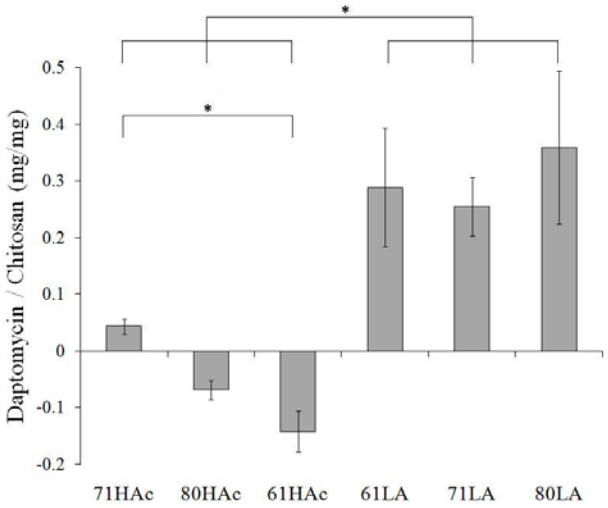
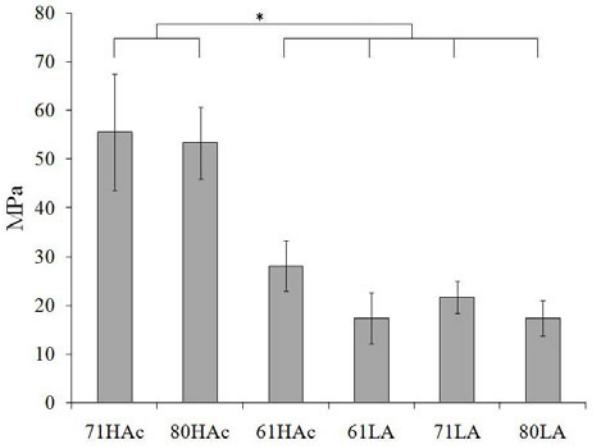


Figure 2: Ultimate Tensile Strength



Discussion/Conclusions: Negative uptake results lead to the rejection of all HAc CS film variations as candidates. Based on the fact that there are no significant differences between LA variations in UTS, Young's modulus, or the breaking point % elongation, and because 80% DD CS in LA solution has a significantly higher swelling ratio than other variations, 80% DD CS film in LA solvent is considered the currently optimized composition suited for a surgeon's need of a mechanically pliable drug delivery implant. Ongoing work will include additional material characterization, drug elution, film degradation, and AB activity experiments to further optimize a customizable CS film implant.

References: [1]Cárdenas G. J Mater Sci. 2007;19:2397-2405. [2]Noel S. Clin Orthop Relat Res. 2008;466:1377-1382. [3]Wenling C. J Biomater Appl. 2005;20:157-177.

Acknowledgements: Funded by Army Grant USAMRMC OTRP W81XWH-08-1-0312. Antibiotics donated by Cubist Pharmaceuticals.