

256f Bioresorbable Composite Films for Antibiotic Release

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The purpose of this study was to develop a bioresorbable film to aid in wound healing through controlled release of antibiotic drugs. The antibiotic film would act as a barrier layer between the abdominal and uterine walls upon surgical closure to separate the two healing processes and administer the needed antibiotics to the site over an appropriate period of time, ideally 2 to 4 weeks. The films are composed of biodegradable microparticles containing drug within a fast-resorbing film of gelatin.

The first stage in this process was to create gelatin films of 10-20wt% gelatin. The mechanical properties of these films were then tested using an Instron In-Spec mechanical testing system. Proposed storage of the finished films include a freeze drying process that allows for full re-hydration over a time comparable to surgical preparation time in the operating room. The mechanical properties were evaluated on still-hydrated films as well as for films that had been freeze-fried and then rehydrated. This is to ensure that the films are strong enough and do not deteriorate beyond use while they are being used or before they are needed to be used. The rehydration was checked at regular intervals (30 minutes, 1 hour, 2 hours, 4 hours, etc.) until the films had regained their initial weight.

The next step was to create blank microparticles which were placed within the gelatin films to evaluate the effect of inclusion of the microparticles on the mechanical properties of the film. The physical properties, such as size and shape, of these microparticles were analyzed. These particles were incorporated into the gelatin films at a 5 wt% loading. Again the mechanical properties of these composite gels were tested as prepared and after freeze-drying and rehydration.

Studies were then conducted with varying the microparticle preparation methodology to increase the particle capacity for erythromycin incorporation. Erythromycin was incorporated in poly(lactic-co-glycolic acid) (PLGA, Medisorb 50-50 DL 2A, MW 12, 000) microparticles using an oil-in-water solvent evaporation method with dichloromethane as the organic solvent and 0.4 wt% poly(vinyl alcohol) as the aqueous solution. The erythromycin was incorporated at levels up to 40 wt%. After the best preparation conditions were experimentally determined, release studies were completed in saline at 37 °C for both free loaded particles and loaded particles embedded in a bioresorbable gelatin matrix to determine the rate and reproducibility of drug release over time. Studies were conducted on the films as prepared and also after freeze-drying and rehydration, following the rehydration timeline previously determined.

It was found that the freeze-dried gelatin films would take 12 hours or more to completely rehydrate, but that, depending on the exact composition, they would rehydrate enough within 30 minutes to be flexible enough to use. Therefore, it was this 30 minute time that was used in later studies to mimic the time that the films would be rehydrated prior to actual insertion and use, therefore prior to the start of release studies. Gelatin films prepared at 10 and 15 wt% gelatin were determined to be optimal for mechanical properties, with the 15 wt% gelatin giving much stronger films both before freeze-drying and after rehydration. Inclusion of microparticles up to 5 wt% did not affect the mechanical properties of the films. The gelatin films at 10 wt% gelatin lost a greater percentage of their strength with freeze-drying and rehydration, up to 15%, while the 15 wt% gelatin films lost less than 8% of their strength.

Release studies from free particles and particles within a gelatin matrix showed nearly identical release profiles, with release being followed for at least 14 days. A faster rate of release was seen for the first 12-24 hours with a constant, slower rate of release for the duration of the studies.

This study showed that gelatin films maintain their mechanical integrity when they are freeze-dried and rehydrated. This is ideal for long term storage and use of these films. In vitro release from these films compares well with that from free microparticles and should last for the targeted range of 2-4 weeks.