

Antibiotic-Eluting Bioresorbable Composite Fibers for Wound Healing Applications: Microstructure, Drug Delivery and Mechanical Properties

Jonathan J Elsner¹, Israella Berdicevsky², Moran Shohat¹, Metial Zilberman¹.

¹Tel-Aviv University, Tel-Aviv, Israel

²Technion – Israel Institute of Technology, Haifa, Israel

Statement of Purpose

Wound dressings aim to restore the milieu required for skin regeneration and for protection of the wound from environmental threats and penetration of bacteria. Although traditional dressings offer some protection against bacteria, this protection is lost when the outer surface of the dressing becomes moistened by wound exudate or external fluids. Other major drawbacks associated with most of the dressing solutions presented to date are the discomfort and potential harm to vulnerable underlying skin caused by the removal of dressing and concerns regarding safety issues related to the silver ions that are included in most of these products as a germicidal agent.

The current study focuses on the development and investigation of bioresorbable core/shell fiber structures loaded with the antibiotics gentamicin sulphate, ceftazidime pentahydrate and mafenide acetate. Wound dressings comprised of such fibers would not require removal once they have fulfilled their role, and the local antibiotic release profile from these fibers could be tailored to exhibit a considerable initial release rate in order to respond to the elevated risk of infection from bacteria introduced during the initial shock, followed by a release of antibiotics at an effective level long enough to inhibit latent infection. We therefore hypothesize that our fibers may better control the bio-burden in the wound bed and thus prevent infection and accelerate wound healing.

Methods

The composite fiber structure composed of a polyglyconate core and a porous PDLGA shell loaded with the various antibiotic agents was prepared using freeze-drying of core fibers which were dip-coated in inverted emulsions. This fabrication process is advantageous in that it enables the combining of good mechanical properties with the desired drug release profile and preservation of the drug's activity in the surrounding shell. Fiber characterization focused on the effects of the emulsion's formulation parameters on the shell microstructure (SEM), the resulting drug release profile (HPLC), bacterial inhibition of relevant strains (*Staphylococcus aureus*, *Staphylococcus epidermidis* and *Pseudomonas aeruginosa*) and mechanical tensile properties.

Results

The release profiles generally exhibited an initial burst effect accompanied by a decrease in release rates with time over periods ranging from several days to 50 days, depending on the emulsion's formulation. Albumin was found to be the most effective surfactant for stabilization of the inverted emulsions and its incorporation in the aqueous phase resulted in a lower burst release, which is probably related to its function as a predominant drug-

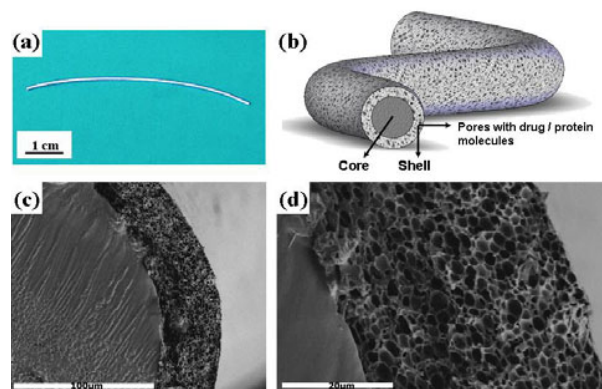


Figure 1 The structure of the composite core/shell fiber structures: (a) general view (photograph) of the fiber, (b) schematic representation showing the composite structure, (c) and (d) SEM fractographs of part of a core fiber coated with drug-loaded porous PDLGA shell (cross section).

binding protein. Higher organic: aqueous (O:A) ratios, polymer content and MW all reduced the burst release of antibiotics from the fibers and prolonged their release due to changes in the shell structure. A higher MW and polymer content demonstrated a larger effect on the microstructure and release profile than the O:A phase ratio. The release of antibiotics from our fibers resulted in a significant decrease in bacterial viability and practically no bacteria survived after 2 days when initial bacterial concentration of 1×10^7 CFU/ml was used. Hence, the fiber preparation did not affect the drug's potency as an antibacterial agent. Mechanical testing of the composite fibers demonstrated that the fibers were strong and flexible and still possess superior mechanical properties ($E=225\text{MPa}$, $\epsilon_f=42\%$, $\sigma_f=300\text{MPa}$) compared to monolithic and reservoir fibers.

Conclusions

Our fibers exhibited release profiles suitable for antibiotic release systems, i.e. with a considerable initial release that will combat the elevated bacterial concentrations during the initial shock, followed by a long-term relatively low release rate. In practice, a wound dressing can be woven from a combination of several types of fibers to create a resultant release profile which is the product of several release profiles or drug types. The diverse profiles achieved in this study with higher and lower burst release rates and with varying elution spans may serve as a good basis for further *in vivo* examination of the fibers in order to create the ideal profile for a particular wound healing application.