Delivery of Doxycycline from PLGA-Coated Hernia Meshes

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Statement of Purpose

Worldwide, over 20 million hernias are repaired each year, with approximately 700,000 of those occurring in the U.S. alone.[1] The high recurrence of hernias, from 32-63%, has been linked to overexpression of matrix metalloproteinases (MMPs).[2] Doxycycline inhibits the expression of MMPs and can aid healing of incisional hernias.[3,4] The goal of the present studies was to develop coated surgical meshes for local and sustained delivery of doxycycline over a period of two months. Two types of poly(lactic-co-glycolic acid) (PLGA) coatings were examined, and retention of bioactivity was verified.

Methods

Polypropylene surgical meshes were cut into 2.5 x 2.5 cm squares and dip-coated in a mixture of 10 mL of acetone, 20 mg of doxycycline, and 2 or 5 g of PLGA. Two types of PLGA were tested: 50:50 (ester terminated, IV:0.55-0.75 dL/g, 30-40 kDa) and 75:25 (ester terminated, IV: 0.55-0.75 dL/g). Dip-coatings were repeated, with drying in between, until each dry mesh was 0.35-0.4 g. Coated and dried meshes were placed in 6 mL tubes with 5 mL of phosphate-buffered saline, pH 7.4, (PBS) and gently shaken during incubation at 37°C. At selected time points, meshes were then transferred to new tubes with fresh PBS and the supernatants stored. Supernatants were analyzed using HPLC to quantify the amount of doxycycline released.

At selected time points, in a separate experiment, samples were cut from meshes, dried, and analyzed using Kirby-Bauer tests. Staphylococcus aureus were plated on blood-agar plates at a density according to the 0.5 McFarland standard. Meshes were placed on the plates and incubated at 37°C for 24 hours prior to measuring the zones of inhibition.

Results

As seen in Figure 1, 75:25 PLGA coated meshes released doxycycline in a small initial burst and then had a steady release of approximately 20 µg per week for 5 weeks. For the 50:50 PLGA meshes, there was also a small initial burst of doxycycline released within 4 days and then a major release from two weeks until one month. Over the course of 43 days, 62% of the doxycycline loaded into the 50:50 PLGA mesh was recovered, while only 8.5% of the drug was recovered from the 75:25 PLGA coated mesh. This may be due to the greater hydrophobicity and slower degradation of the 75:25 polymer.

The Kirby-Bauer tests revealed that the 75:25 PLGA meshes retained their activity, as reflected by antimicrobial properties, over the course of a month (Figure 2).

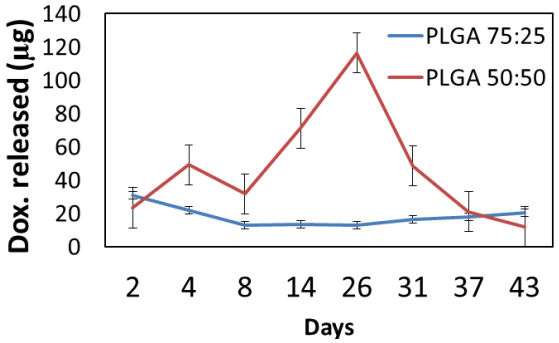

Figure 1. Release of doxycycline from PLGA-coated surgical meshes. (Data are mean ±standard error)

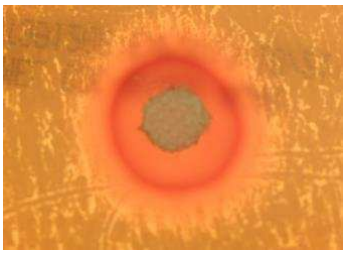

Figure 2. Agar plate after Kirby-Bauer test using mesh degraded for 26 days. Note the clear zone around the mesh.

Conclusions

Both types of coated meshes are viable options for local and sustained release of doxycycline. With additional mechanical testing of different PLGA coatings, we will be able to identify a coated mesh that can be used for delivery of doxycycline for enhancing healing of hernias.

References

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