PLGA Microsphere Spray System for Wound Coverage

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Introduction

For spinal procedures, there is significant post-surgical blood loss and a risk for infection in the surgical site [Spine 37:1340, 2012; J Bone Joint Surg Am 93:1268, 2011]. There is no current technology to simultaneously prevent/treat infection and control blood loss after surgery.

Poly(lactic-co-glycolic acid) (PLGA) is a commonly used and FDA-approved polymer for certain drug delivery applications. PLGA be used to form microspheres encapsulating an antibiotic for infection prevention and treatment as well as an antifibrinolytic compound to reduce bleeding at the surgical site. The PLGA microspheres must be distributed across the surgical site to ensure delivery of the bioactive compounds to the targeted area. Furthermore, PLGA microspheres have been shown to have a sustained release of their contents, which allows the antibiotic to be delivered over a course of several weeks.

The goal of the present research was to create a sprayable delivery system for PLGA microspheres loaded with both an antibiotic and antifibrinolytic compound to prevent infection and reduce blood loss in a surgical site, respectively.

Methods

PLGA microspheres (75:25, ester-terminated, MW ~90 kDa) loaded with vancomycin and tranexamic acid (TXA) were prepared by a double emulsion procedure. The microspheres were placed in 6 ml of phosphate-buffered saline (PBS). The solution was collected and changed every day. The supernatants were read at 280 nm to determine vancomycin concentrations, and aliquots were reacted with ninhydrin for analysis of TXA.

A commercially available water spray bottle was adapted for the delivery of the microspheres. The spray system was loaded with 50 mg/ml (microspheres in PBS) to measure the area covered for repeated sprays and the mass of microspheres sprayed. The area covered was analyzed using ImageJ.

Results and Discussion

Because the goal of this project is to develop a two drug spray system that can cover a surgical site with drug-loaded microspheres, the "sprayability" of the system was examined. Five different sprays were measured to determine the area coverage as well as demonstrate that a greater amount of microspheres could be delivered with an increasing number of sprays (Figure 1). A single spray and five sprays covered approximately 15 cm^2 and 90 cm^2 of the given area, respectively. Each spray delivered approximately 0.9 ml per spray, and when the system was loaded with a 50 mg/ml suspension of microspheres, approximately 45 mg were dispersed with each spray. This was confirmed by measuring the mass of microspheres, with the slope of the trendline between mass and sprays being 43 mg per spray.

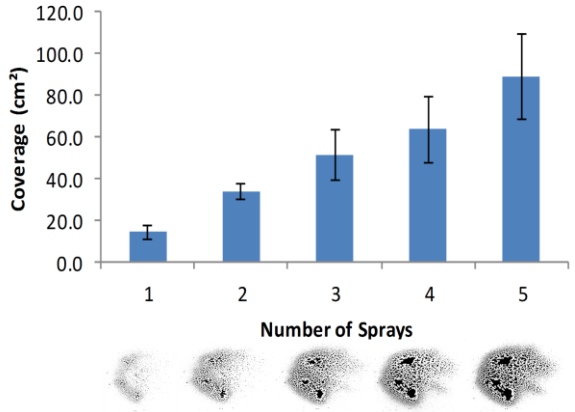

Figure 1: Area coverage for repeated sprays at the same location (data are mean ± SD, P = 0.0001)

For effective treatment of clinical surgical site infection, antibiotics are administered for 6 to 8 wk intravenously. Figure 2 shows the release of vancomycin from PLGA microspheres. Although there was an initial burst, the rate of release decreased steadily after 10 d and stayed above the MIC (2 µg/ml) for most bacteria for 42 d. TXA was encapsulated in microspheres with a loading of 1.2%. During incubation at 37ºC, TXA was exhausted over the first 2 d, a period critical for controlling bleeding.

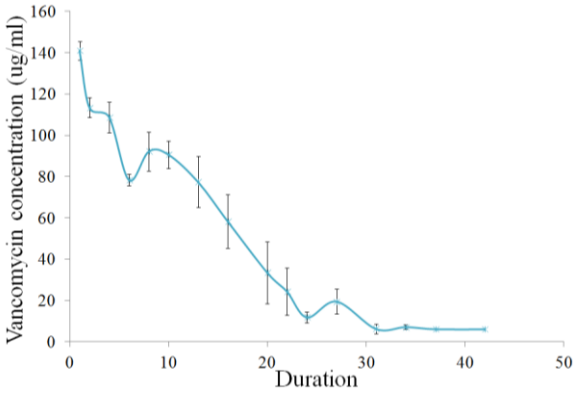

Figure 2: Instantaneous release of vancomycin from PLGA microspheres (data are mean ± SD)

Conclusions

The present results demonstrate a simple, sprayable system to efficiently cover a wound site with drug-loaded microspheres to potentially prevent/treat infection and control blood loss.