A biocompatible nanofibrous coating of prosthetic vascular graft as a drug delivery system for the treatment of vascular graft infections

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Introduction

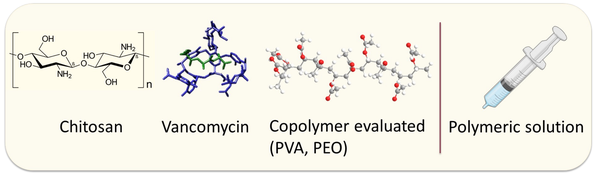
- More than 400,000 vascular grafts are implanted annually in USA, and vascular graft infection (VGI) is a major complication that affects 1-6% of the cases.[1-2]
- VGI is a serious complication with significant morbidity, mortality, and healthcare costs. The available treatments rely on administration of systemic antibiotics and debridement of the surgical wound. If not properly addressed, bacterial infiltration can lead to graft removal, major soft tissue defects, sepsis and eventually death.
- Here, we describe a nanofibrous coating made from chitosan, an antimicrobial polymer, as a reservoir for drug delivery.

Objectives

- Create a nanofibrous coating with chitosan using the electrospinning technique
- Encapsulate vancomycin in the nanofibrous coating and achieve a sustained release over time.

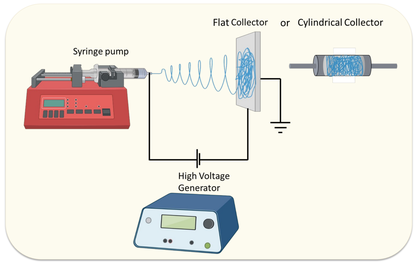
Methods

Polymeric solution composition



Electrospinning

Electrohydrodynamic process, during which a liquid droplet is **electrified** to generate a jet, followed by stretching and elongation to generate **nano-fiber(s).**



Results

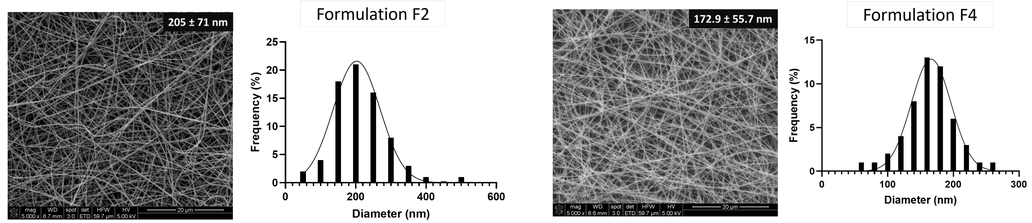
Characterization of the CNC

Formulation	Chitosan	PVA	PEO	Vancomycin
F1	✓	✓		Low
F2	✓	✓		High
F3	✓		✓	Low
F4	✓		✓	High

Table 1 (Left). Out of all the tested iterations, Formulations F1, F2, F3, and F4 were the most promising in regards to obtaining a proper nanofibrous coating. Poly(vinyl alcohol), PVA; poly(ethylene oxide), PEO.

Figure 1 (Below). Scanning electron microscopy (SEM) images of homogeneous deposition of nanofibers created from formulations F2 and F4 via electrospinning.

1



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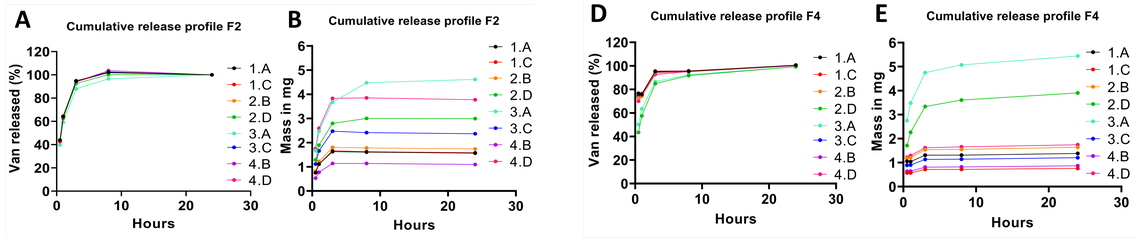

Figures 2A-E. Vancomycin release kinetics in F2 and F4 nanofibrous coatings, evaluated using high-performance liquid chromatography (HPLC).

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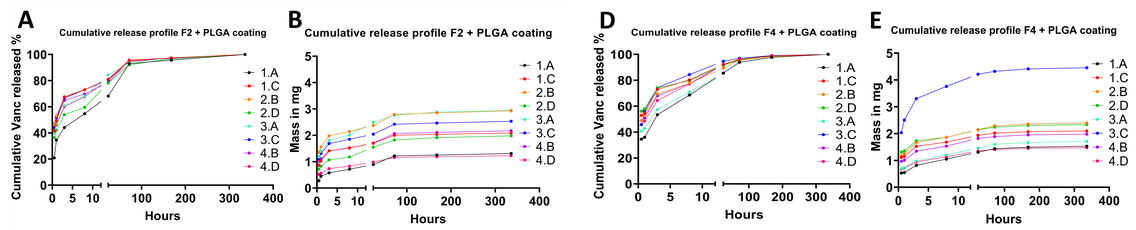

Figures 3A-E. Vancomycin release kinetics in F2 and F4 nanofibrous coatings with an additional poly(lactic-co-glycolic) acid (PLGA) coating, evaluated using HPLC.

Conclusions

- A major challenge was creating a nanofibrous coating with chitosan alone using the electrospinning technique, but the addition of PVA and PEO as copolymers made it possible to obtain homogeneous coatings (Figure 1).
- After successful encapsulation of vancomycin within the CNC using formulations F2 and F4, we observed a complete release of the antibiotic within a few hours.
- To address the rapid release of vancomycin, we explored the effects of an additional layer of poly(lactic-go-glycolic) acid (PLGA) after the coating was electrospun.
- PLGA proved to be beneficial in slowing down the release of vancomycin, achieving a sustained release for up to 7 days. Traces of vancomycin were found for up to 14 days.

Future Directions

- We aim to ultimately develop a novel, biodegradable CNC of vascular prosthetics that facilitates a local and sustained delivery of vancomycin to prevent VGIs for days to weeks after surgery.
- This is an exciting starting point for further optimization and implementation of strategies to achieve a sustained release at therapeutic levels of vancomycin for a target of 14 days. To achieve this goal, a crosslinking phase could be beneficial in slowing down the release.
- Future studies include evaluation of release kinetics and dynamics and vancomycin encapsulation within the CNC and evaluation of the antimicrobial properties of the coating (antibacterial efficacy assessment), against different strains of bacteria such as *E. Coli* and *MRSA*.

References

1. Wilson WR, Bower TC, Creager MA, et al. Vascular Graft Infections, Mycotic Aneurysms, and Endovascular Infections: A Scientific Statement From the American Heart Association. *Circulation*. 2016;134(20):e412-e460. doi:10.1161/CIR.0000000000000457
2. Sousa, JV, Antunes L., Mendes C, et al. Prosthetic vascular graft infections: a center experience. *J Angiologia e Cirurgia Vascular*. 2014;*10*(2):52-57. doi:10.1016/S1646-706X(14)70050-3