Innovative Vascular Balloon Coating Strategies for Below-the-Knee Peripheral Arterial Disease

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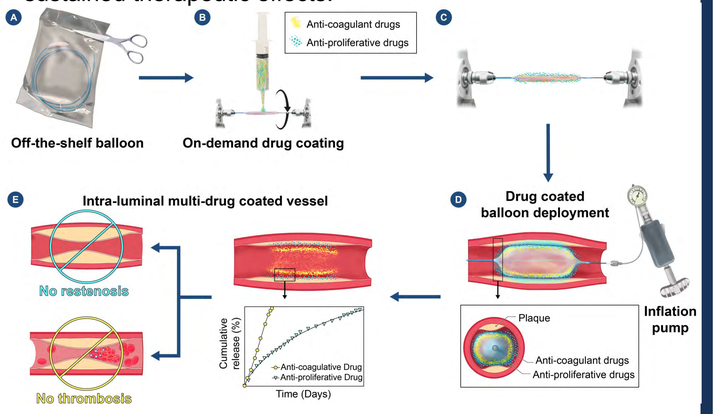
Introduction/Background

Peripheral Arterial Disease (PAD) affects >200 million people worldwide[1], causing narrowing or blockage of peripheral arteries due to atherosclerosis. It poses a major public health concern, increasing the risk of heart attack and stroke. Current treatments include percutaneous transluminal angioplasty and stenting, with or without drug coatings, yet these often require reintervention (35-40% within 6 months)[2] due to vessel dissection, acute thrombosis, and restenosis. While commercial drug-coated balloons (DCBs) reduce lesion failure rates compared to uncoated balloons (28.6% vs. 17.9%)[3], they still carry risks of thrombosis (3%-10%)[4] and restenosis (20%-45%)[5] within 6 to 12 months after below-the-knee (BTK) intervention. DCBs typically deliver a single drug at a pre-determined concentration, addressing restenosis but not acute occlusions, and current drug coatings are often uneven, lacking sustained delivery.

Objective

To develop an on-demand multilayer coating for vascular balloons enabling precise, tailored release for immediate and sustained therapeutic effects.



Scheme 1: Workflow for on-demand coating strategy.

Methods

Stock Solution 1: 2% Sodium alginate + (30-150 mM, 1x-5x) $CaCO_3$ in water
Stock Solution 2: 10% PVA in water

Prepare 3mL of 1:1 composite of the two stocks. Add 0.075 mg Paclitaxel $USP_{[aq]}$ and/or 0.07 mg Blue #1 dye, then degas

Add 2:1 GDL:$CaCO_3$ to initiate cross-linking

Coat the balloon and set for 10 mins @ -20°C. Then, dry the coating in the oven for 20 mins @ 55°C

Insert the DCB in a dynamic mock vessel filled with MilliQ water

Quantify drug release with UV-vis spectroscopy

Results

Rheological analysis

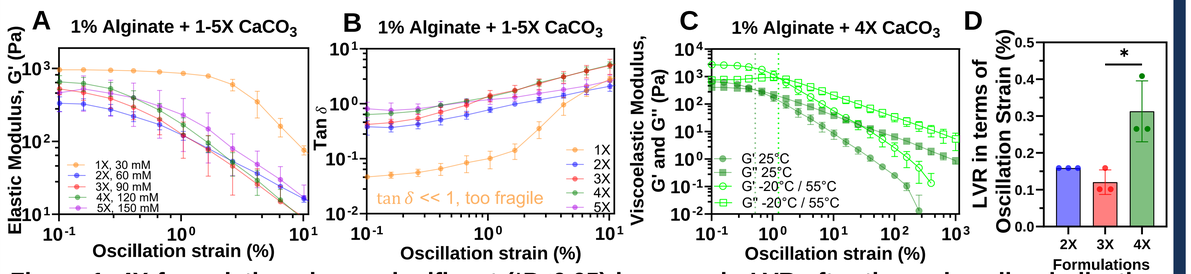


Figure 1: **4X formulation shows significant (*P<0.05) increase in LVR after thermal cycling indicative of enhanced stability.** (**A**) G' and (**B**) Tan δ (G''/G') for alginate formulations with varying (1X–5X) $CaCO_3$ concentrations. (**C**) G'' and G' from amplitude sweep analysis for the 4X formulation at 25 °C or cycled between -20°C/55°C. (**D**) Linear viscoelastic region (LVR) after -20°C/55°C cycling for formulations 2X, 3X, and 4X (n=3).

Single layer coated balloon (SCB) deployment in a mock vessel setup

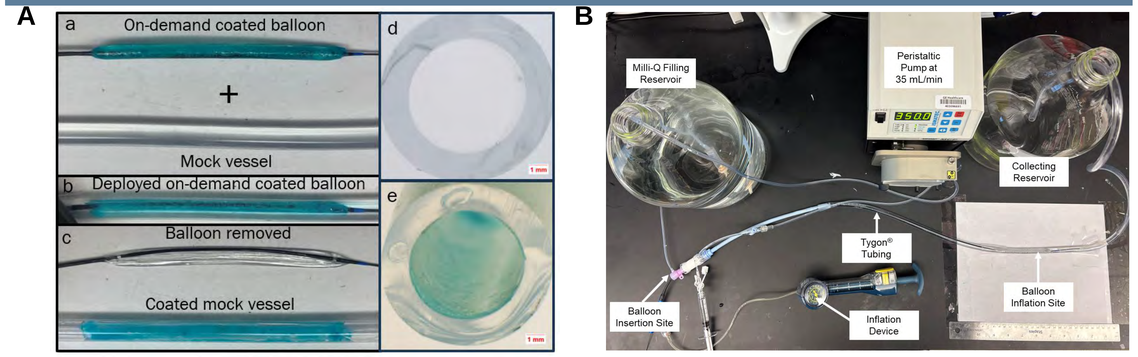


Figure 2: **Coating of mock vessel.** (**A**) On-demand coated balloon (4X formulation) deployed in a mock vessel with pulsatile flow (35 mL/min, peristaltic pump) (a, b). After 3 min, the balloon was removed, leaving the coating adhered to the vessel (c). Cross-section of the empty vessel (d) and after deployment (e) with coating thickness of 103 µm. (**B**) Complete dynamic mock vessel release setup used for the experiment.

Drug release of the SCB in the mock vessel

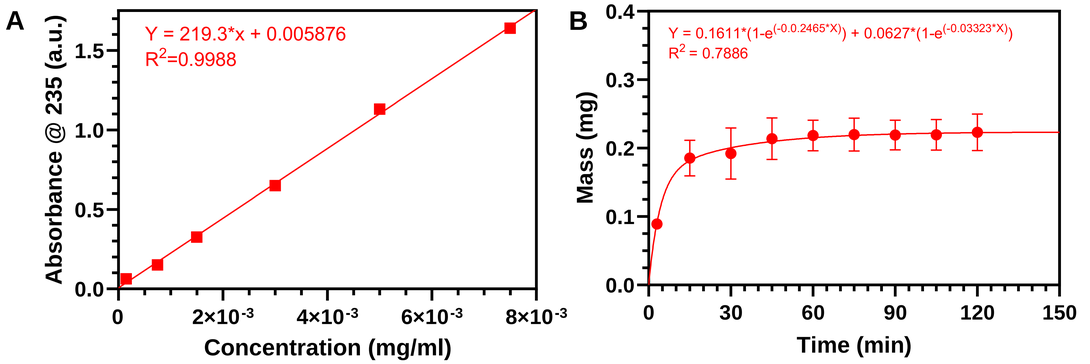


Figure 3: Drug release in the mock vessel. (**A**) Absorbance vs. concentration for Paclitaxel measured @ 235 nm. (**B**) Release profile of Paclitaxel from the coated mock vessel for over 120 min (n=3).

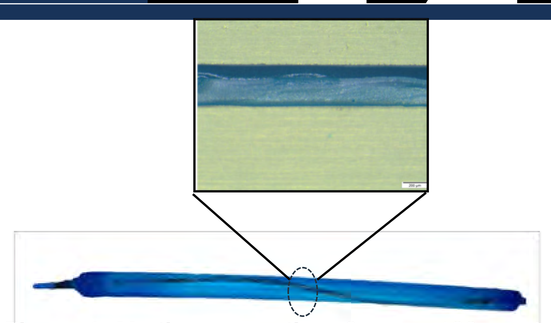


Figure 4: Multi-layer coating. 6 mm × 100 mm balloon coated with two layers. Inset shows the cross-section with the inner Blue #1 dye layer (top) and an outer Paclitaxel layer (bottom).

Conclusions

- ✓ A cycle of 10 min at -20 °C, followed by 20 min at 55 °C, shifted the crossover point toward higher oscillation strains and higher viscoelastic modulus.
- ✓ Rheological analysis confirmed that the 4X formulation optimally achieves the desired mechanical properties in terms of LVR ($p < 0.05$).
- ✓ The 4X coating detached completely from the SBC balloon while remaining adherent to the mock vessel, effectively simulating angioplasty procedures.
- ✓ The SCB's release profile showed sustained release for 60 min, followed by a plateau phase.
- ✓ A coating thickness of 103 µm maintained normal flow dynamics without clot formation.
- ✓ MCB enables multi-layer structures encapsulating different agents.

Future Direction

1. Test for biocompatibility with cell viability, cytotoxicity, and hemocompatibility
2. Optimize the release profile to achieve sustained drug release over longer periods (*i.e.* days/weeks)

Acknowledgments/References

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