Biomaterial-mediated Controlled Release of Inflammasome Modulators for Diabetic Tissue Repair

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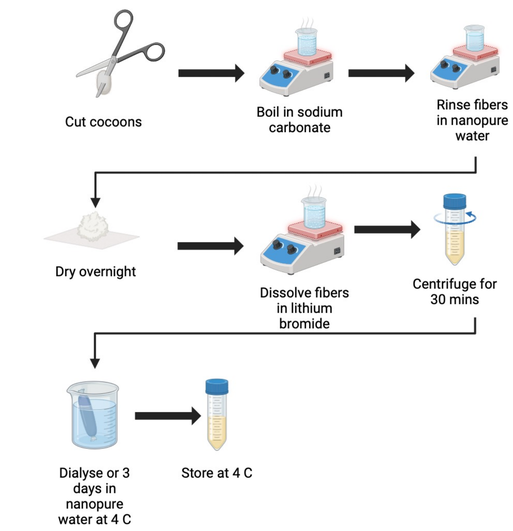
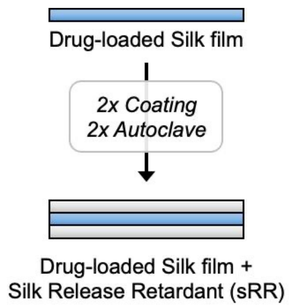
Introduction

Complex wounds are a significant health and economic burden affecting 1 in 38 adults in the US. Chronic wounds, such as diabetic ulcers, exhibit delayed healing and an increased risk of infection and amputation, with a 5-year survival rate of only 30% (Sen et al., 2020). Sustained inflammasome-driven inflammation in diabetic wounds represents a druggable target to promote healing (Mirza et al., 2014). Our previous studies showed that single-layer 60 µm silk films released A438079 rapidly, with a burst release on the first day, which may limit the duration of therapeutic effects (Yaron et al., 2024). In this study, we introduce an additional silk layer to slow down and extend the release, aiming to provide a more controlled and sustained drug delivery. This research focuses on the biomaterial engineering of silk fibroin-based wound dressings to create a controlled, sustained release platform for the inflammasome pathway inhibitor A438079, potentially enhancing healing in diabetic wounds."

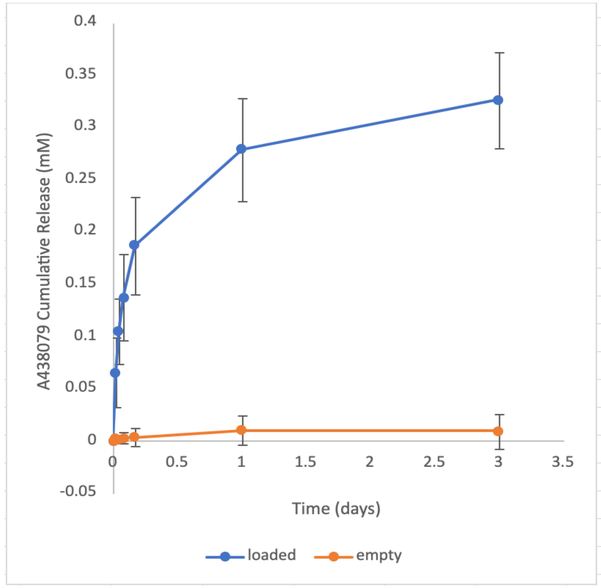
Methods





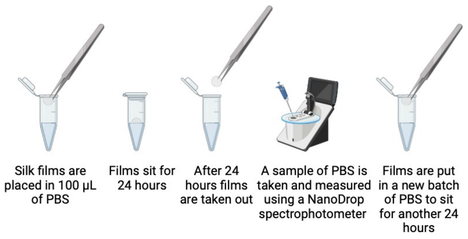
- The silk solution was then placed in a pertri dish to cast films. These films were cut to a 6 mm diameter, measured, and autoclaved to make them water insoluble.
- The autoclaved films were loaded overnight with A438079.
- Layered films were dipped in silk solution, redried and autoclaved.
- Drug loaded films were placed in 1x PBS solution with the absorbance measured over 7 days.

Previous Studies

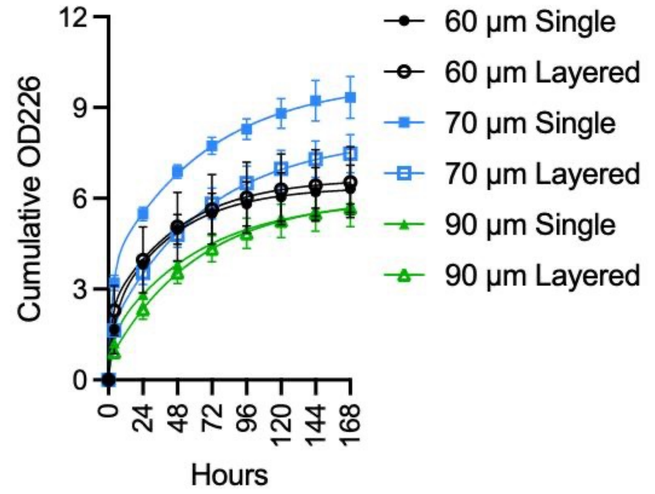


Loaded A438079 and unloaded films were placed in a 1x PBS solution with the absorbance measured at the 4-, 6-, 24- and 72-hour mark. The graph shows the silk films ability to gradually release A438079 over a period of days.

6 mm film after autoclave



Results



Loaded A438079 films of different thickness (60 µm, 70 µm, and 90 µm) were placed in a 1xBS solution with the absorbance measured every 24 hours for 7 days.

Conclusion

Comparing single and layered films, our results indicate that the 70 µm layered films demonstrated a significantly slower release rate, while the 60 µm and 90 µm films showed minimal differences between single and layered formats. Future studies will further investigate how variations in film thickness influence the release dynamics, aiming to optimize film design for controlled release applications.

References

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