DEVELOPMENT AND EVALUATION OF NOVEL NON-BIOLOGICS-BASED HEMOSTATIC DRESSING

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BACKGROUND

Lidocaine with epinephrine is standard for local anesthesia in cutaneous procedures, providing hemostasis via vasoconstriction. Common formulations use 1–2% lidocaine with epinephrine at 1:100,000 or 1:200,000. However, a nationwide epinephrine shortage beginning in 2017, worsened by COVID-19, alongside concerns about systemic adverse effects (tachycardia, palpitations, sweating), particularly with large surface areas or cardiotoxic anesthetics, has driven interest in alternatives. Midodrine, a prodrug converted to the selective α1-adrenergic agonist desglymidodrine, offers vasoconstriction without β-adrenergic stimulation or heart rate changes, suggesting a safer hemostatic profile.

Our group previously showed that injectable 2% lidocaine with 50 μM midodrine significantly reduced bleeding versus lidocaine alone ($P < 0.05$). To expand its utility, we developed topical midodrine formulations avoiding the need for injection and evaluated drug release across four delivery matrices: PEG-ODEX hydrogel, Vanicream, alginate hydrogels, and Kerracel (carboxymethylcellulose). Release was quantified in phosphate buffer via UV-Vis spectrophotometry using dialysis and Franz Cell assays, with Kerracel assessed on 3D-printed scaffolds to simulate wound conformity. These formulations represent a promising non-invasive option for bleeding control in outpatient dermatologic care.

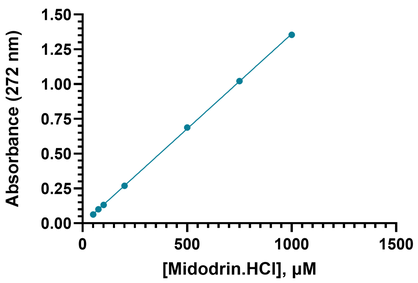
Study goal:
Identify the topical matrix that best combines rapid early release, wound-bed contact, biocompatibility, and practical handling for rapid hemostasis.

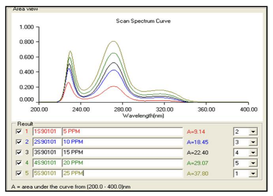
RELEASE ASSAY AND WORKFLOW

Target performance for an ideal dressing

- Rapid release within 5-10 min to match active bleeding.
- Strong adhesion/contact on moist, irregular wound beds.
- Biocompatibility without local toxicity.
- Easy handling for real clinical use.

UV-Vis Spectroscopy-Based Quantification





Calibration curve at 272 nm used to quantify midodrine release from each formulation.

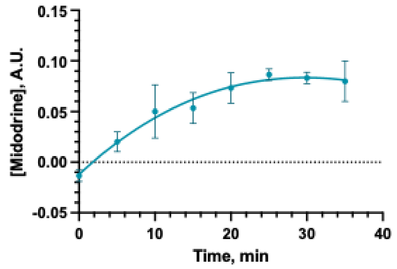
MATRIX SCREENING RESULTS

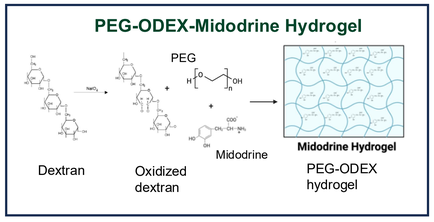
PEG-ODEX Hydrogel

Strengths: Wet adhesion, conformal coverage, tunable network for localized delivery.

10-min release: ~50 μM, below the minimum rapid-release target, likely due to covalently crosslinked nature

Interpretation: Useful sustained-delivery behavior, but too slow for acute hemostasis.



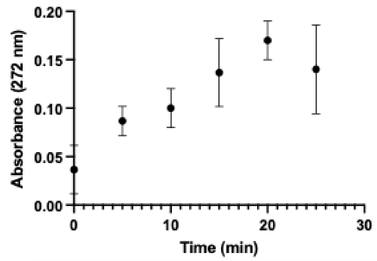


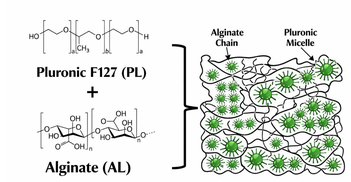
Alginate - Pluronic F127

Strengths: Thermoresponsive gelation, better early diffusion, good topical handling.

10-min release: ~100 μM, improved over PEG-ODEX but still below the higher release goal.

Interpretation: A stronger acute-delivery candidate, yet still not the best performer and gel creation takes 2 days.



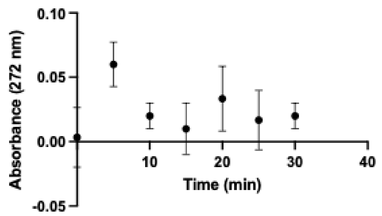


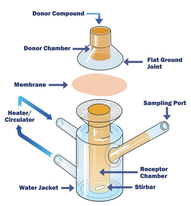
Vanicream

Strengths: Simple handling, skin-compatible base, broad familiarity in dermatology.

Release profile: Poorest release performance among tested formulations.

Interpretation: Helpful comparator, but not well suited for rapid wound hemostasis.



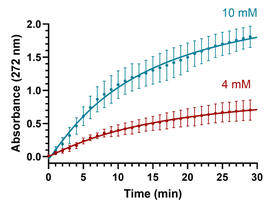


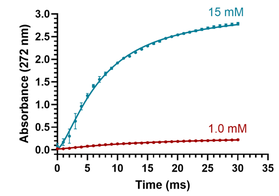
Kerracel (CMC Fiber)

Strengths: Close wound-bed contact, vertical wicking, cohesive gel formation, favorable release of hydrophilic drug.

10-min release: 15,000 μM loading -> ~1,000 μM released; 1,000 μM loading -> ~100 μM released.

Interpretation: Best alignment with the target product profile and selected as the lead matrix.

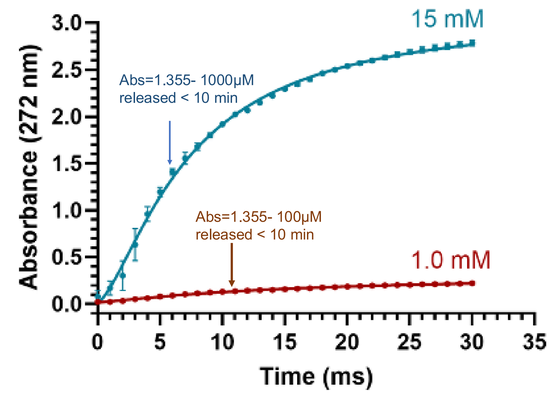




OPTIMAL MATRIX - KERRACEL

- Assay optimized across pilot runs to better mimic wound packing and improve consistency.
- 15,000 μM loading achieved the target window: ~1,000 μM released within 10 minutes.
- 1,000 μM loading released ~100 μM at 10 minutes, demonstrating dose-dependent scaling.

Dose-dependent rapid early release from Kerracel



Criterion	PEG-ODEX	Alginate	Vanicream	Kerracel
Fast 5-10 min release	Limited	Moderate	Low	**Best**
Moist wound-bed contact	Strong	Strong	Moderate	**Strong**
Clinical handling	Good	Good	Easy	**Easy**
Fit for acute hemostasis	No	Partial	No	**Yes**

Selected for in vivo testing

CONCLUSION

- Kerracel best satisfied the predefined product profile for acute dermal hemostasis.
- PEG-ODEX provided sustained, but slow delivery.
- Alginate - Pluronic F127 provided the benefit of thermo-responsiveness, but preparation is lengthy, and release is not optimal.
- Vanicream has the benefit of skin-compatibility, but traps the drug within its matrix.
- Kerracel was the first platform to combine wound-bed practicality with the rapid burst release needed for real-time bleeding control.
- In-vivo studies are now underway.

- Dong J, Issa NT, Kaiser M, Gaumond SI, Solis M, Gil J, Kirsner RS, Davis SC, Jimenez JJ. Use of Midodrine for Intraoperative Hemostasis in Cutaneous and Percutaneous Surgery. JID Innov. 2024 Dec 3;5(2):100335. doi: 10.1016/j.xjidi.2024.100335. PMID: 39944289; PMCID: PMC11815705.
- Larrabee WF Jr, Lanier BJ, Miekle D. Effect of epinephrine on local cutaneous blood flow. Head Neck Surg. 1987 May-Jun;9(5):287-9. doi: 10.1002/hed.2890090507. PMID: 2957344.
- Max Seaton, Anne Hocking, Nicole S. Gibran, Porcine Models of Cutaneous Wound Healing, ILAR Journal, Volume 56, Issue 1, 2015, Pages 127–138, https://doi.org/10.1093/ilar/ilv016