


Skin Substitutes to Promote Venous Leg Ulcer Healing


What is the Evidence?

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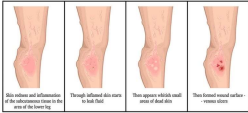
Disclosure

- No disclosures




Introduction

- Venous leg ulcers (VLUs): chronic, hard-to-heal wounds
- Affecting millions globally
- Impact: reduced quality of life, high recurrence rates
- Skin substitutes: an innovative therapy to improve healing

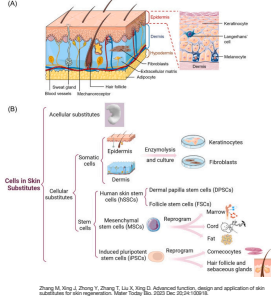



Stages of Development of Venous Ulcers



What Are Skin Substitutes?

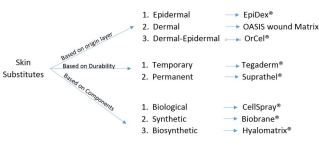
- **Definition:**
 - Skin substitutes are bioengineered products designed to replace or support the function of damaged or missing skin.
- **Purpose:**
 - Promote wound healing by mimicking the properties of natural skin.
 - Enhance extracellular matrix repair and support cellular proliferation.
 - Reduce the risk of infection and improve healing outcomes.






Types and Classification of Skin Substitutes

- **Types**
 - Biological (e.g., AlloDerm, CellSpray®)
 - Synthetic (e.g., Integra, Biobrane®)
 - Hybrid/Biosynthetic (e.g., combination products, Hyalomatrix®)
- **Classification**
 - Based on Origin Layer:
 - Epidermal: EpiDerm®
 - Dermal: OASIS wound Matrix®
 - Dermal-Epidermal: OrCel®
 - Based on Durability:
 - Temporary: Tegaderm®
 - Permanent: Suprathel®
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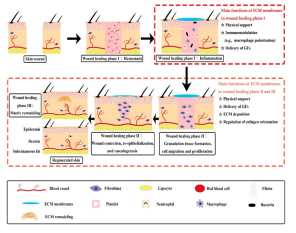


Branichowski, G. et al., 2019. A review of skin engineered skin biosubstitutes suitable for skin reconstruction. Journal of the Royal Society Interface. 2019;16(1):20190248




Mechanism of Action

- Replace or enhance extracellular matrix (ECM)
- Promote angiogenesis and cellular proliferation
- Reduce infection risk, support re-epithelialization

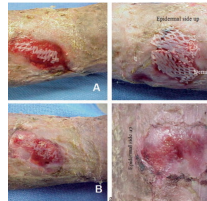


Shi, L.-C., Huang, T.-C., Wu, H.-C., Zheng, S.-H., Huang, Y.-C., Su, S.-H. Membrane Extracellular Matrix-Based Substitutes for Skin Wound-Healing. Pharmaceutics 2020, 12, 1709.



Clinical Evidence

- Improved healing rates:
 - Studies show faster wound closure
 - Reduction in pain and treatment time
- Example: Apligraf® demonstrated significant benefits

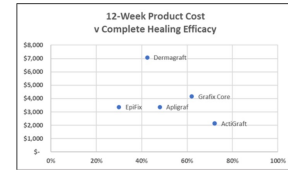


Venck and Knaflitz (2002) Skin substitutes as treatment for chronic venous ulcers and lower extremities. Post. Med. 12:117-120



Cost-Effectiveness

- High initial cost but potential long-term savings
- Reduces healthcare burden by shortening treatment duration
- Cost-effectiveness varies by patient and wound characteristics

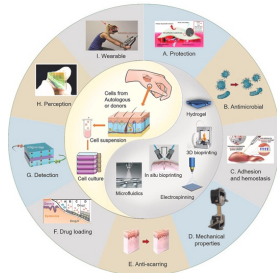


Source: Sabeti (2005). A Comparative Analysis of the Cost Effectiveness of Two Advanced Skin Substitutes in the Treatment of Full-Thickness Leg Ulcers with Diabetic Arterio- Venous Disease. Annals of Internal Medicine. 42:1060-1066



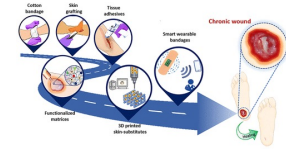
Challenges and Limitations

- Cost
 - High cost limits accessibility for some substitutes
- Durability
 - Fragility of certain substitutes like amnion-derived products
- Cultural Acceptability
 - Issues with products like porcine or fish-derived substitutes
- Rejection and Immunogenicity
 - Potential for rejection in xenografts
- Availability of Data
 - Limited large-scale RCT data comparing substitutes



Future Directions

- 3D Printing
 - Potential to create substitutes with skin appendages (e.g., hair follicles, glands)
- Vascularization
 - Prevascularization using growth factors or 3D printing to improve integration
 - Essential for nutrient and oxygen diffusion in large defects.
- Stem Cells
 - Stem-cell-based substitutes for reduced scarring and accelerated healing
 - Challenges: immunogenicity and processing optimization



Conclusion

- Summary of Benefits
 - Skin substitutes are valuable tools for managing venous leg ulcers
 - They enhance healing, reduce recurrence rates, and improve patient quality of life
- Current Challenges
 - High costs and limited data remain barriers to broader adoption
 - Advances in technology (e.g., 3D printing, stem cells) offer hope for overcoming these limitations
- Closing Statement
 - Continued research and innovation are essential to make these life-changing therapies accessible to all patients in need.

Conclusion

