Quantitative Analysis of Collagens in DermACELL®, Apligraf®, and Dermagraft®

Objective

Quantify the presence of human collagens type I, III, and IV in Dermacell, Apligraf, and Dermagraft.

Background

Dermacell is a technologically advanced Acellular Dermal Matrix (ADM) that is used to treat diabetic foot ulcers and chronic non-healing wounds. Dermacell is created from donated human tissue, and it goes through a validated and patented process called Matracell®, which renders the Dermacell graft acellular without compromising the biomechanical or desired biochemical properties of the graft. This process is gentle, yet robust enough to ensure the native scaffold, vascular channels, growth factors, and proteins are preserved to assist in the healing of the wound.

Apligraf is a unique, advanced treatment for healing that is created from cells found in healthy human skin. Apligraf contains two types of cells – an outer layer of protective skin cells, and an inner layer of cells contained within collagen. Both types of cells contain substances similar to those found in human skin. It is used to heal ulcers such as diabetic foot and venous leg ulcers that are not healing after 3-4 weeks, despite treatment with conventional therapies.

Dermagraft is a cryopreserved human fibroblast-derived dermal substitute. It is composed of fibroblasts, extracellular matrix, and a bioabsorbable scaffold. Dermagraft is manufactured from human fibroblast cells derived from donated newborn foreskin tissue. Dermagraft is indicated for use in the treatment of full-thickness diabetic foot ulcers greater than six weeks duration, which extend through the dermis but without tendon, muscle, joint capsule, or bone exposure.

Methodology

Samples of Dermacell, 2 mm thick (LifeNet Health, Virginia Beach, VA), Apligraf (Organogenesis, Canton, MA), Dermagraft (Advanced BioHealing, La Jolla, CA), and human dermis (2 mm thick) were cut into small pieces and extracted in 0.5M acetic acid with 924U/mL pepsin (Sigma-Aldrich, St. Louis, MO). Samples were placed on a shaker for 24 hours at room temperature. Samples were then centrifuged at 2390g for three minutes to remove large cellular debris followed by 10,000g for 10 minutes. The supernatants were recovered and stored at -80°C. The samples were assayed for human type I collagen by an ELISA kit from Cosmo Bio USA (Carlsbad, CA) human type IV collagen by ELISA kit from Echelon Biosciences (Salt Lake City, UT), and type III collagen by indirect ELISA with a anti-type III collagen monoclonal antibody (MAB3392) from EMD Millipore (Billerica, MA). All results represent the average of two samples.

Conclusion

The results of this study indicate that Dermacell provides dramatically more human Type I, III and IV collagens to the healing wound than either Apligraf or Dermagraft and possesses a collagen profile characteristic of healthy human skin. Dermacell provides structural integrity to damaged skin by supplying human ECM that chronic wounds (such as diabetic wounds) lack and are unable to properly synthesize.

Findings

Dermacell Processing

Dermacell shows no significant reduction in human Type I, III, or IV collagens compared to non-processed human dermis.
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**Collagen Quantification**

Dermacell provides more than 15 times as much human Type I collagen, 500 times as much human Type III collagen and 20 times as much human Type IV collagen to a covered wound than either Apligraf or Dermagraft (Figure 1).

**Collagen Ratios**

Dermacell not only provides a larger quantity of all three tested human collagen types, it also provides the relative quantities of human Type I and III collagens that resemble healthy human dermis. (Figure 2)

**Discussion**

The extracellular matrix of skin performs multiple functions during wound healing including structural support for cells, direct cell signaling, and controlled growth factor binding/release. Collagens are the most abundant extracellular...
molecules in human skin accounting for more than 70 to 80% of the dry weight.

Dermacell provides more human type I, III, and IV collagens than either Apligraf or Dermagraft and is the only product that provides a full profile of human collagens resembling healthy human dermis.

Collagens are substrates for many of the proteases known to inhibit wound healing in chronic wound environments. Dermacell provides abundant human collagen that chronic wounds (such as diabetic wounds) are unable to properly synthesize yet are required to create structural integrity for new skin and a scaffold for cellular infiltration.

When healthy human skin is damaged, the structural components of the ECM are broken down and internalized. It has been demonstrated that collagen cleavage products can act as signaling molecules (matrikines) and are capable of encouraging vital wound repair processes. The collagen cleavage products tumstatin, pentastatin and endostatin are known promoters of cell proliferation and angiogenesis.

What is DermACELL?

- Dermacell is biocompatible decellularized human dermal allograft with an intact acellular framework.
- Dermacell retains native ECM components, matrikines, growth factors, and cytokines while providing a scaffold for recipient cell proliferation and migration for wound repair.
- Dermacell is an effective natural barrier to help control infection and assist in the promotion of granulation tissue and epithelialization for wound repair.

References

1. www.apligraf.com
2. www.dermagraft.com

LifeNet Health helps to save lives, restore health and give hope to thousands of patients each year. We are the world’s most trusted provider of transplant solutions, from organ procurement to new innovations in bio-implant technologies and cellular therapies—a leader in the field of regenerative medicine, while always honoring the donors and healthcare professionals that allow the healing process.