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Effects of a Self-Assembling Peptide on Full-Thickness Wound Healing in a Porcine Model

Alexander Higa, Joel Gil, Michael Solis, Colin Simms and Stephen C. Davis
Dr. Phillip Frost Department of Dermatology and Cutaneous Surgery, University of Miami Miller School of Medicine, Miami, Florida

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Abstract

Reduction of blood loss from patients is one of the most important considerations during surgical procedures, especially during emergency events.[1-2] A new composition that provides improved surgical hemostasis while not impeding the wound healing process could greatly reduce patient's recovery time and improved overall patient outcomes.[3] A self-assembling peptide hemostat (SAPH*) is in development to control bleeding during surgical procedures while enhancing wound healing.[4] The purpose of this preliminary study was to examine the effect of SAPH on full thickness wound healing in a porcine model.[5] Porcine skin is morphologically and biochemically most similar to humans, and it is ideal to evaluate wound healing therapies.[6] Thirty-two (32) full-thickness wounds were created using a 10mm punch biopsy. Twelve (12) wounds were randomly assigned to one of two treatment groups: SAPH or Saline control. Eight (8) wounds were assigned to a commercial skin substitute (SS)^. Wounds were treated immediately after they were created. All treated wounds were covered with a polyurethane dressing. Histological assessment was performed blind by a dermatopathologist on days 4, 6, 8 and 11. On Day 8 and 11, the percent of re-epithelialization was highest in wounds that had been treated with SAPH when compared to those treated with SS and Saline control. In addition, wounds treated with SAPH had higher granulation scores and lower inflammatory scores than the other two treatment groups (Day 8). This study indicates that SAPH may enhance healing of full thickness wounds. Further studies are warranted to substantiate these conclusions.

Introduction

Major injuries resulting in excessive bleeding which cannot be addressed by a tourniquet or invasive surgeries, require procedures that will inevitably lead to a large loss of blood.[7-8] Hence, the prevention of excessive hemorrhage is urgently needed. One of the major dermatology complications during cutaneous surgery is postoperative bleeding.[9] This issue can be far more challenging if the patient is taking an anticoagulant, such as warfarin. A modality that provides surgical hemostasis agnostic to patient's anticoagulation status and enhances the wound healing is desirable. This study examines the wound healing effects of an easy to apply hemostatic device in comparison to the skin substitute using a full thickness wound healing porcine model.

References

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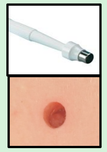
Materials and Methods

1. Experimental Animals:

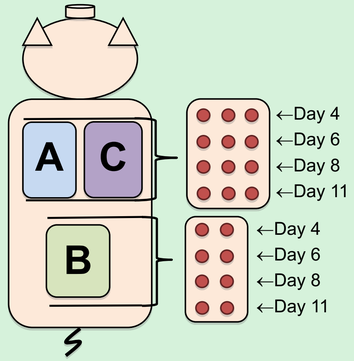
Swine were used as our experimental animal due to the morphological, physiological, and biochemical similarities between porcine skin and human skin.[6]

2. Wounding Technique:

Thirty two (32) full thickness wounds were created on the paravertebral area using a 10 mm punch biopsy. Wounds were treated within 20 minutes after wound creation.



3. Experimental Design:



Treatment Groups

A. SAPH*
B. Skin Substitute alone^
C. Saline

*AC5® Advanced Wound System (USA); AC5® Topical Hemostat (Europe), Arch Therapeutics, Inc. Framingham, MA. ^Integra® Bilayer Wound Matrix (Integra LifeSciences Corp. Plainsboro, NJ)

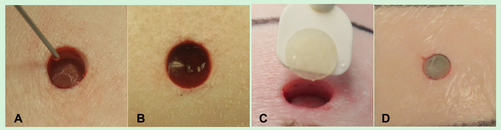
4. Treatment Regimen:

A. Treatment groups received 50µl of either SAPH or Saline control directly on the wound bed.

B. The solution would settle within the wound orifice, leaving no residue from either treatment groups on the surface.

C. For Skin Substitute, a precut 10mm circular graft was placed on the wound bed using sterile spatulas and forceps.

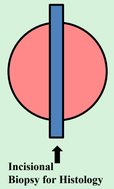
D. Upon completion of each treatment modality, each wound and surrounding healthy tissue was covered with a polyurethane dressing.



Treatment groups A and B were treated once, while group C wounds were treated 4 times with their respective applications and redressed appropriately.

5. Histology Assessment:

Incisional biopsies were recovered on days 4, 6, 8 and 11, then placed in formalin and stained with hematoxylin and eosin (H&E). One section per block was analyzed. The specimens were evaluated blindly and examined for the following elements to determine a potential treatment response:



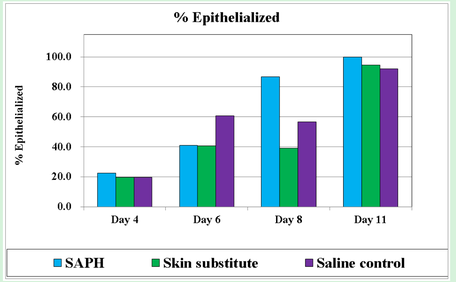
1. **Percent of wound epithelialized (%).** Measurement of the length of the wound surface covered with epithelium was taken.

2. **Epithelial thickness (cell layers µm).** Because epithelial thickness may vary from area to area within the biopsy, the thickness of the epithelium in µm was measured on five points equal distance from each other and averaged.

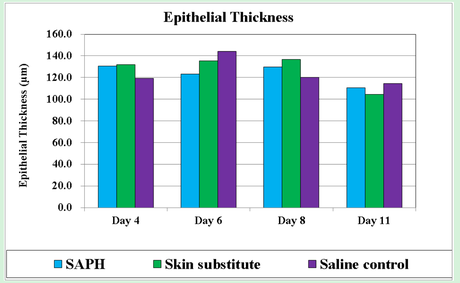
3. **White cell infiltrate.** Measured by the presence of subepithelial mixed leukocytic infiltrates. Mean Score: 1 = absent, 2 = mild, 3 = moderate, 4 = marked, 5 = exuberant.

4. **Granulation Tissue Formation.** The approximate amount of new granulation tissue formation (dermis) was graded as follows: 0: <1%, 0.5: 1-10%, 1: 11-30%, 2: 31-50%, 3: 51-70%, 4: 71-90%, 5: >90%

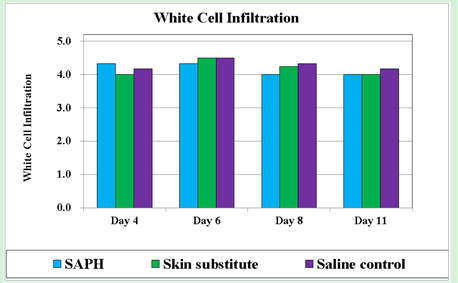
Results



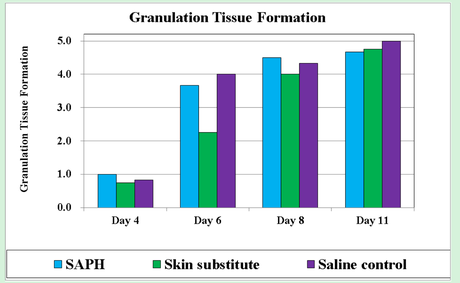
No wounds reached over 23% re-epithelization by day 4. By days 8 and 11, SAPH reached the highest percentage when compared against all other groups.



Saline control reached the highest epithelial thickness measurements on day 4. By day 11, no treatment group exhibited over 120 µm.



White cell infiltration was slightly lower for SAPH when compared against all other wounds on days 6 and 8. By the end of the study, Saline control showed the highest WCI scores.



Skin Substitute reached the lowest granulation tissue formations scores on days 6 and 8. By day 11, all treatment groups had scores of at least 4.7.

Conclusions

• SAPH exhibited an increase in epithelialization and granulation tissue formation on day 8 as compared to all other treatment groups. SAPH was the only treatment application reaching full re-epithelialization by day 11.

• Wounds treated with Skin Substitute had lower granulation tissue formation on day 6 as compared to the other treatment groups.

• SAPH appears to be a promising easy to apply treatment for enhancing wound healing; additional studies are needed to validate these findings.

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Contact Information
Stephen C. Davis / Research Professor
University of Miami, Miller School of Medicine
Dept of Dermatology and Cutaneous Surgery
sdavis@med.miami.edu
Ph: 305.243.4897