

Chronic wound healing using a novel bioengineered collagen-honey sheet in an urban hospital wound care center setting

AUTHORS

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ABSTRACT

Summary: A novel bioengineered collagen-honey (BCH) sheet has been shown to achieve improved wound closure rates in both chronic and acute wounds when compared to standard of care (SOC). The goal of this retrospective evaluation was to assess chronic wound closure rates of SOC compared to the BCH sheet (APIS[®], SweetBio, Inc. Memphis, TN) in an urban hospital wound care center setting (Regional One Health, Memphis, TN). **Methods:** 47 chronic wounds in 43 patients were treated with SOC or a novel BCH sheet. Weekly visits and product reapplications were recommended per instructions for use. The primary endpoint was time to closure. Investigations occurred for wounds that did not close to determine a justification. **Results:** 20 wounds were treated with SOC which varied in usage of multiple products/therapies and 27 wounds were treated with the BCH sheet. The average initial wound size was comparable between SOC (2.1 cm²) and BCH (1.6 cm²) treated groups. In both groups, most of the wounds that were treated did not close. For the wounds that did close, the average time to closure was 2x faster in the BCH treated group (7.4 weeks) compared to the SOC group (14.8 weeks).

Conclusions: The results and observations from this evaluation support the BCH sheet's ability to improve average wound closure rates from 14.8 weeks (SOC) to 7.4 weeks in patients who maintained compliance with regular visits.

KEYWORDS

diabetic foot ulcer, lower extremity, wound healing, collagen, manuka honey, health disparities

Introduction

Wounds, regardless of location, are complex and require a multifaceted approach for healing.¹ Yet, current products have restricted ability. Manuka honey is one of few materials capable of this advanced approach as it is antibacterial, deregulates harmful matrix metalloproteinases (MMPs), and upregulates pro-regenerative growth factors.^{2,3} However, it is unusable for advanced treatments in its messy, short term and topical form. Collagen and its derivatives are also attractive materials in wound care as they can buffer harmful high levels of MMPs by acting as a sacrificial substrate.^{4,5} However, additional materials/compounds (such as silver) must be incorporated to pursue a more comprehensive approach for healing. APIS® (SweetBio, Inc., Memphis, TN) is a novel, FDA-cleared, and CMS-covered wound care product that uniquely synthesizes a collagen derivative (gelatin), Manuka honey, and hydroxyapatite (a naturally occurring inorganic mineral) into a solid sheet for the management of wounds (Figure 1). In earlier clinical evaluations, this absorbable, bioengineered collagen-honey (BCH) sheet has been shown to close chronic and acute wounds in an average of 4-6 weeks.^{6,7} Published *in vitro* data demonstrated that the BCH sheet comprehensively reduced bacterial load, decreased MMP-9, and triggered the release of growth factors, which are contributors to instill balance to the microenvironment and progress wounds towards healing.^{8,9} This 43-patient IRB approved retrospective clinical evaluation (#21-07962-XM) was performed to assess chronic wound closure rates of the BCH sheet versus standard of care (SOC) in an urban hospital wound care center setting (Regional One Health, Memphis, TN) where >20% of their patients are uninsured and do not get the consistent comprehensive care they need outside of the center. A secondary area of interest was patient compliance to help provide insights into external factors impacting wound healing.

Methods and Materials

Patients were required to be at least 18 years of age, be ambulatory, have adequate circulation, have type 1 or 2 diabetes, and have a 9cm² or less wound surface area. All wounds should be non-healing, have no clinical signs of infection, and diabetic foot ulcers (DFUs) should be a Wagner Grade 1 or 2. For all patients, wounds were cleaned, debrided, measured, and photographed prior to any product application. If any product was used, it was covered with a secondary dressing and secured in place via compression wrapping. Patients were instructed to offload and not change dressings until the next visit in one week. Patient demographics, wound type/duration/size, number of visits, number of products used, time to closure (complete re-epithelialization), and reason for stopping treatment (if wound did not close) were documented.

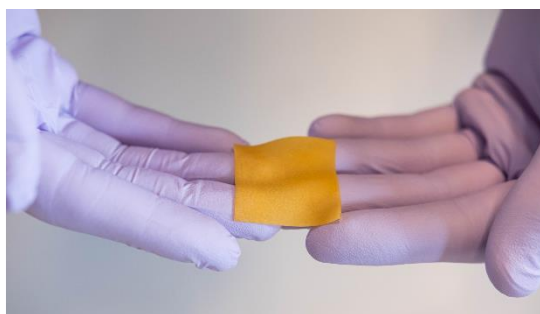


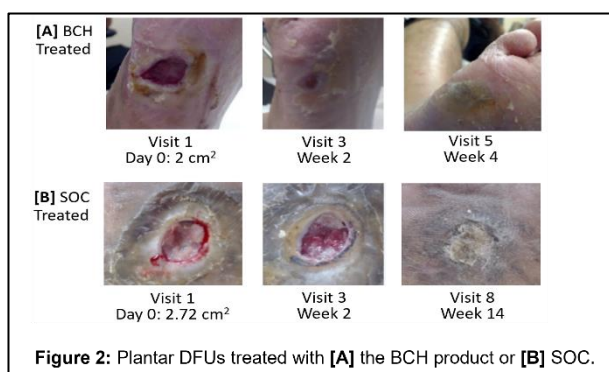
Figure 1: Image of hydrated BCH sheet used in this evaluation.

Results & Discussion

47 wounds were evaluated from 43 patients (several patients presented more than one wound). See Table 1 for a breakdown of patient demographics and wound details. 80% of the wounds were DFUs with the majority located on the plantar surface or the toe. Other wound types included pressure and venous leg ulcers. 20 wounds were treated with SOC which varied in usage of multiple products/therapies such as foams with silver, cadexomer iodine, silver coated high density polyethylene meshes, collagen sheets, mafenide acetate cream, silver nitrate, and hyperbaric oxygen. 27 wounds were treated with the BCH sheet with reapplications recommended per instructions for use. The average initial wound size was comparable between SOC (2.1 cm²) and BCH (1.6 cm²) treated groups. The SOC treated group had a slightly higher percentage of wounds closed (40%) compared to BCH treated wounds (26%). However, the average time to closure for wounds was 2x faster in the BCH treated group (7.4 weeks) compared to the SOC group (14.8 weeks). See Figure 2 for wound closure visualization of each group. In both groups, most of the wounds that were treated did not close. This is consistent with a literature review published in 2018 that demonstrated how real-world and randomized controlled trial data provide convincing evidence that most patients (55–70%) do not heal their wounds, in contrast with a mean publicly reported healing rate of 92%. The 2018 review further stated that it is likely that in the real world with complicated patients (like an urban hospital wound care center), healing rates above 40% are not achievable.¹⁰ To further understand this phenomenon, the authors of this manuscript investigated the reasons wounds did not close. The top results were noncompliance (i.e. missing appointments, not offloading, dietary indiscretion) – 14 patients, comorbidities – 6 patients, reclassification (wound initially treated as Wagner 2 but reclassified to Wagner 3 then treated outside of this study) – 5 patients, and treatment facility location changed – 3 patients.

Demographic	BCH	SOC
Patients, n	23	20
Age (years)		
mean ± SD	62 ± 6	57 ± 4
Gender, n (%)		
Male	15 (65)	13 (65)
Female	8 (35)	7 (35)
Ethnicity, n (%)		
African American	11 (48)	16 (80)
Caucasian	10 (43)	2 (10)
Hispanic	2 (9)	2 (10)
Wounds, n	27	20
Wound size (cm ²)		
mean ± SD	1.6 ± 0.8	2.1 ± 0.8
Wounds closed, n (%)	7 (26)	8 (40)
Weeks to closure		
mean ± SD	7.4 ± 5.8	14.8 ± 5.6
Wounds not closed, n (%)	20 (74)	12 (60)

SD, standard deviation



A notable case to highlight is one patient who had a DFU present for 6+ months on each foot with no progress using SOC. This patient was not the most compliant with offloading as they enjoyed going to the store and playing with their grandkids. In this scenario, the patient served

as their own control. The BCH sheet was used to treat the left foot while SOC was used to treat the right foot. Within 6 weeks, the wound treated with the BCH sheet was closed while the SOC wound remained open. At this time, the BCH sheet was used to treat the right foot and after 2 weeks, the wound on the right foot closed. This case produced similar results in that treatment with the BCH sheet facilitated faster wound closure.

As with any retrospective study, there are limitations to controls. However, the design and number of patients provide enough data to analyze and make sound interpretations.

Conclusions

Previously published clinical evaluations of the BCH sheet have shown average wound closure rates of 4-6 weeks for chronic and acute wounds.^{6,7} This retrospective evaluation challenged the BCH sheet by using it in an urban hospital wound care center where patient compliance and comprehensive care is a significant challenge. The results and observations from this evaluation support the BCH sheet's ability to improve average wound closure rates from 14.8 weeks (SOC) to 7.4 weeks in patients who maintained compliance with regular visits.

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