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**ABSTRACT**

Chronic ulcers harbor a plethora of microorganisms that are resistant not only to conventional wound care but also to physical debridement, topical therapies and dressings, as well as to multidisciplinary treatment strategies. The presence of biofilms in chronic wounds, present in over 80% of patients with infection, is a significant obstacle to wound closure. Current topical applications are not effective in treating bacterial biofilms in wounds.

To determine if disrupting chronic wound biofilm would be therapeutically efficacious, we studied the use of a novel topical agent for wound management, specifically targeting biofilms. 36 patients with chronic recalcitrant wounds were randomized to a 12-week treatment with a broad spectrum antimicrobial ointment or a biofilm disrupting wound gel. Wound healing rate was assessed by measuring wound size reduction and closure rates.

Wound size decreased significantly with a 71% reduction in wound area for wounds treated with the biofilm disrupting gel, compared to 24% for the control (p < 0.001). Wound closure was attained in more than half of the patients treated with the test product. 53% of these patients achieved closure by 12 weeks, as opposed to 17% for the control (p < 0.01). There were no adverse events related to the biofilm disrupting product while two adverse reactions occurred with the control.

The combination of the novel biofilm disrupting agent with wound debridement, significantly improves wound healing rates by disrupting the biofilm which protects multispecies bacteria within a chronic wound. Given the significant wound size reduction and closure rates observed in these long-term non-healing wounds, and a lack of related serious adverse events, the biofilm disrupting wound gel, in our setting and experience, is a safe and effective treatment for recalcitrant chronic wounds.

**OBJECTIVE**

The present long term clinical study has been done to investigate the efficacy of the biofilm-disrupting wound gel in the treatment of nonhealing, full-thickness chronic wounds to confirm the potential therapeutic effectiveness of this approach; this has been achieved by measuring changes in the healing rate and wound closure when compared with a broad-spectrum, maximum-strength, triple antibiotic ointment over a 3-month time period.

**METHODS**

This was a 12-week to 16-week, 2-site, prospective, randomized, open-label study of patients diagnosed with a recalcitrant chronic wound. This study compared the treatment outcomes of standard debridement with topical application of a biofilm-disrupting wound gel (experimental; BlastX; Next Science, Jacksonville, FL) versus a triple-antibiotic, maximum-strength ointment (control; Neosporin + Pain Relief; Johnson & Johnson, New Brunswick, NJ).

The sample size was calculated to be 15 patients per group by power analysis. Patients were randomized 1:1 to apply either the experimental or control once daily with the prescribed daily wound dressing change. After 1 month, control patients were allowed to cross-over. Wound area measurements were assessed at weeks 0, 2, 4, 8, 12, and 16 using the Silhouette Star camera (ARANZ Medical, Christchurch, New Zealand). The primary endpoint was defined as a percentage reduction in wound area after 12 weeks of experimental treatment compared with the control.

There were 2 defined secondary endpoints for this study. The first secondary endpoint was defined as an improvement in the percentage of patients with closed wounds after 12 weeks of treatment compared with the control. The other secondary endpoint was to determine if there was a difference in the bacterial load and/or biodiversity in the wound when comparing treatments and treatment time. Statistical analyses were performed using Minitab on the intent-to-treat population. Treatment bars that do not fall under the same grouping bar are statistically distinct.

**RESULTS**

The demographics of the two groups were statistically equivalent, with rather old and large wounds (Table 1). The patient population also had a large number of comorbidities (Table 2), but these were not statistically significant factors for wound closure or healing.

Forty-three patients were enrolled in the study with 32 completing all study visits. 22 patients were randomized to the experimental group and 21 to the control group. 12 patients crossed-over.

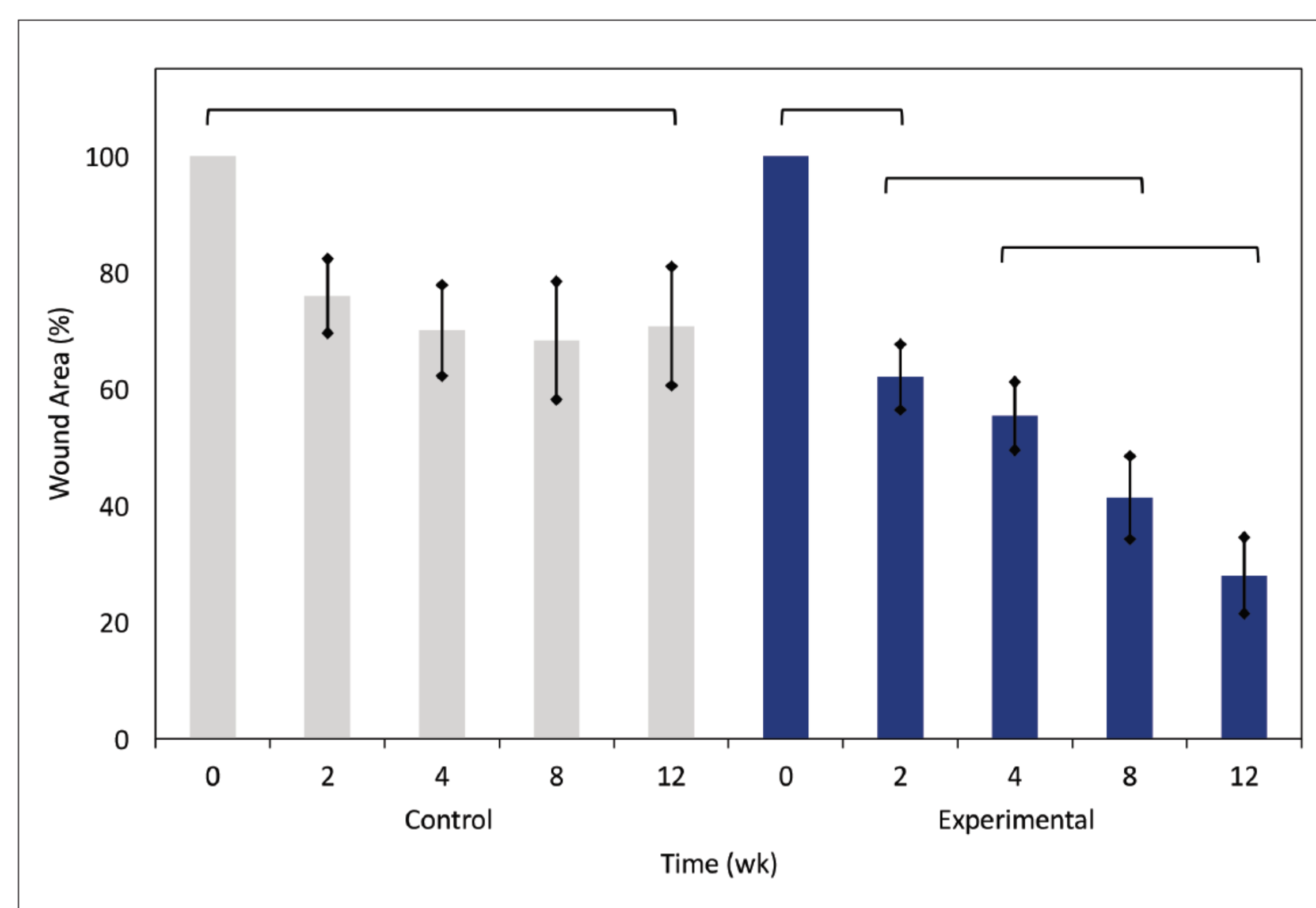
The average wound area reduction (Figure 1) was much greater for the experimental group compared to the control (72% vs. 15% at 12 weeks, p < 0.05). Similarly, the wound closure rate (Figure 2) was much greater for the experimental group compared to the control (52% vs. 17% at 12 weeks, p < 0.01).

**Table 1: Study Demographics**

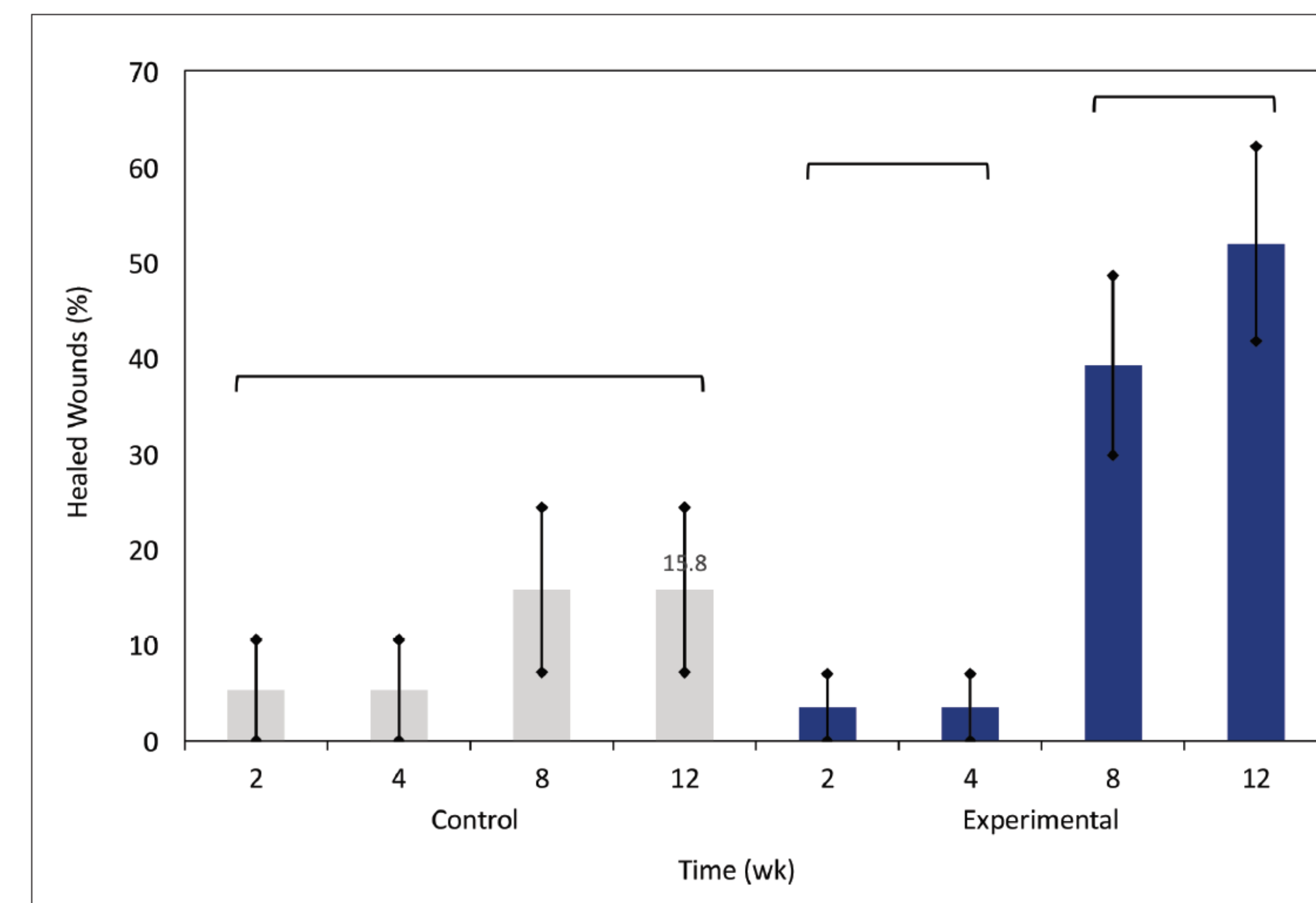
	CONTROL	EXPERIMENTAL
No. of Patients	21	34
Male (%)	82	63
Female (%)	18	37
Age (y ± SD)	61 ± 14	60 ± 13
Wound age (mos ± SD)	17 ± 21	22 ± 47
Wound size (most ± SD)	12 ± 17	9 ± 22

**Table 2: Study Comorbidities**

CONDITION	PREVALENCE
Diabetes mellitus	60%
Peripheral arterial disease	40%
Hypertension	35%
Obesity	26%



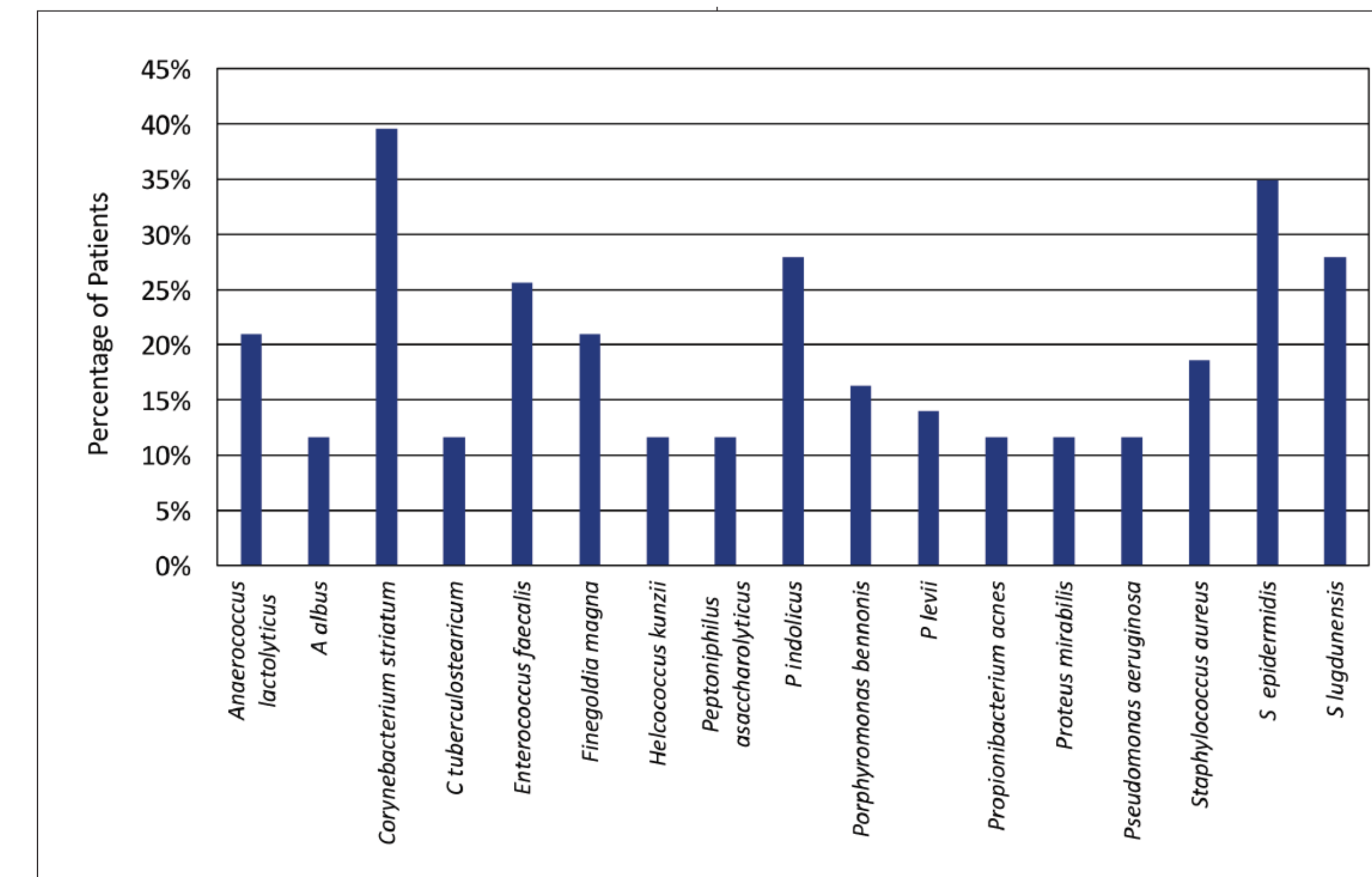
**Figure 1:** Comparison of normalized wound area reduction over time. Bars depict one-standard error from the mean; grouping bars depict groups that are equivalent. Treatment bars that do not fall under the same grouping bar are statistically distinct (P < .05)



**Figure 2:** Comparison of percentage of healed wounds over time. Bars depict one-standard error from the mean; grouping bars depict groups that are equivalent. Treatment bars that do not fall under the same grouping bar are statistically distinct (P < .05)

**RESULTS (continued)**

The next-gen sequencing detected 90 bacteria and 4 fungi, with only 5% of patients having fungi present. Of the 90 bacteria, only 17 were found in at least 10% of patients (Figure 3). The mean number of bacteria in the wounds was 2.9 species. There was no statistically significant relationship between the bacteria present in the wound or number of bacterial species present and wound healing or healing rates. An ANOVA of the bacterial load also was not statistically significant for wound closure or wound healing.



**Figure 3:** Histogram of the most frequently found bacteria in the study wounds. Bacterial species were detected in at least 10% of the patients' wounds.

**DISCUSSION**

This study confirms that topical applications of a biofilm-disrupting wound gel, in conjunction with debridements, produce clinically significant wound size reductions and wound closure versus a broad-spectrum topical antibiotic treatment control. In this study, median wound area reduction was 72% with daily use of the experimental product for 12 weeks versus 24% with the control. Chronic wound closure occurred in 52% of patients with the use of the experimental product versus 17% closure with the control.

This study confirms that topical applications of a biofilm-disrupting wound gel in conjunction with debridements produce clinically significant wound size reductions and wound closure versus a broad-spectrum topical antibiotic treatment control. In this study, median wound area reduction was 72% with daily use of the experimental product for 12 weeks versus 24% with the control. Chronic wound closure occurred in 52% of patients with the use of the experimental product versus 17% closure with the control.

Another important aspect for the practitioner is the patient's tolerance to wound care treatment. The use of the experimental agent did not result in any product-related pain, redness, swelling, burning/stinging, or other adverse reactions in the 34 patients in this study.

**CONCLUSIONS**

In summary, the results of this study confirm that the use of a biofilm disrupting agent combined with debridement is more effective than the experimental antibiotic ointment combined with debridement or prior failed wound treatments. This reinforces previous results<sup>8</sup> obtained when combining this product with other ointments and debridement or with debridement alone.

As the experimental agent specifically targets the biofilm by degrading the EPS, the results seen provide further confirmation that biofilm bacteria significantly contribute to the delay or arrest in the healing of chronic wounds. Given the significant wound healing and closure rates observed in these long-term, nonhealing wounds, as well as the lack of related serious adverse events, using the biofilm-disrupting wound gel appears to be safe and effective for the management of chronic wounds.

**FUNDING**

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