DEVELOPMENT OF A NOVEL PEROXIDE BASED ANTIMICROBIAL HYDROCOLLOID FOR WOUND DRESSINGS AND FOR OSTOMY APPLICATIONS

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Wound Healing Society Meeting 2016, Atlanta   Poster P.IRD06

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Abstract

We describe a novel hydrocolloid dressing that integrates an antimicrobial based on peroxide to provide durable antimicrobial protection for the product with the excellent wound healing characteristics of a hydrocolloid. This product has recently been cleared for sale by FDA (K151186), both for prescription (Rx) and retail (OTC, or Over the Counter) sale. It is based on a proven pressure sensitive adhesive formulation of hydrocolloid with a history of safe and effective use in wound healing and in ostomy applications, combined with a superabsorbent that contains hydrogen peroxide. This combination forms a hydrocolloid useful for both ostomy and wound healing of low to moderately exudative wounds, including pressure ulcers, diabetic ulcers, etc.

This hydrocolloid features >99.99% kill against common wound pathogens including MRSA, Acinetobacter Baumanii and E. Coli in order to protect vulnerable patient populations and caregivers and help prevent transmission of pathogens.

As part of the development and clearance process, the hydrocolloids were tested in a porcine model of full and partial thickness wounds to assess rate of wound healing against control materials that include nonstick pads, conventional hydrocolloids and a silver dressing. The peroxide containing hydrocolloid showed excellent wound healing with less apparent scar tissue compared to silver dressing. The hydrocolloid products (both with and without peroxide) also demonstrated significant improvements in wound area, especially in days 7 through 14 for full thickness wounds, compared to non-adherent dressing and silver based controls.

Methods: The ability of the peroxide containing hydrocolloids to inhibit the growth and development of wound pathogens was studied. Methicillin Resistant *Staphylococcus aureus* (MRSA, ATCC# BAA-44), *Acinetobacter baumannii* (AB, ATCC# 19606), *E. coli* (EC, ATCC# 8739) and *Staphylococcus Epidermidis* (SE, ATCC# 12228), were tested using ASTM 2180 "Standard Test Method for Determining the Activity of Incorporated Antimicrobial Agent in Polymeric or Hydrophobic Materials". As per FDA requirement, the bacterial inoculum in all cases was at a concentration of 10^6 cfu/ml, and the required level of performance to allow performance claims against an organism is a minimum of 4 log kill measured against the inoculum concentration. Samples were tested both in as-prepared state, as well as after a 5-day exposure to simulated wound fluid to assess end-of-life performance. Further organisms were assessed as noted, including by independent researchers at Texas Tech University.

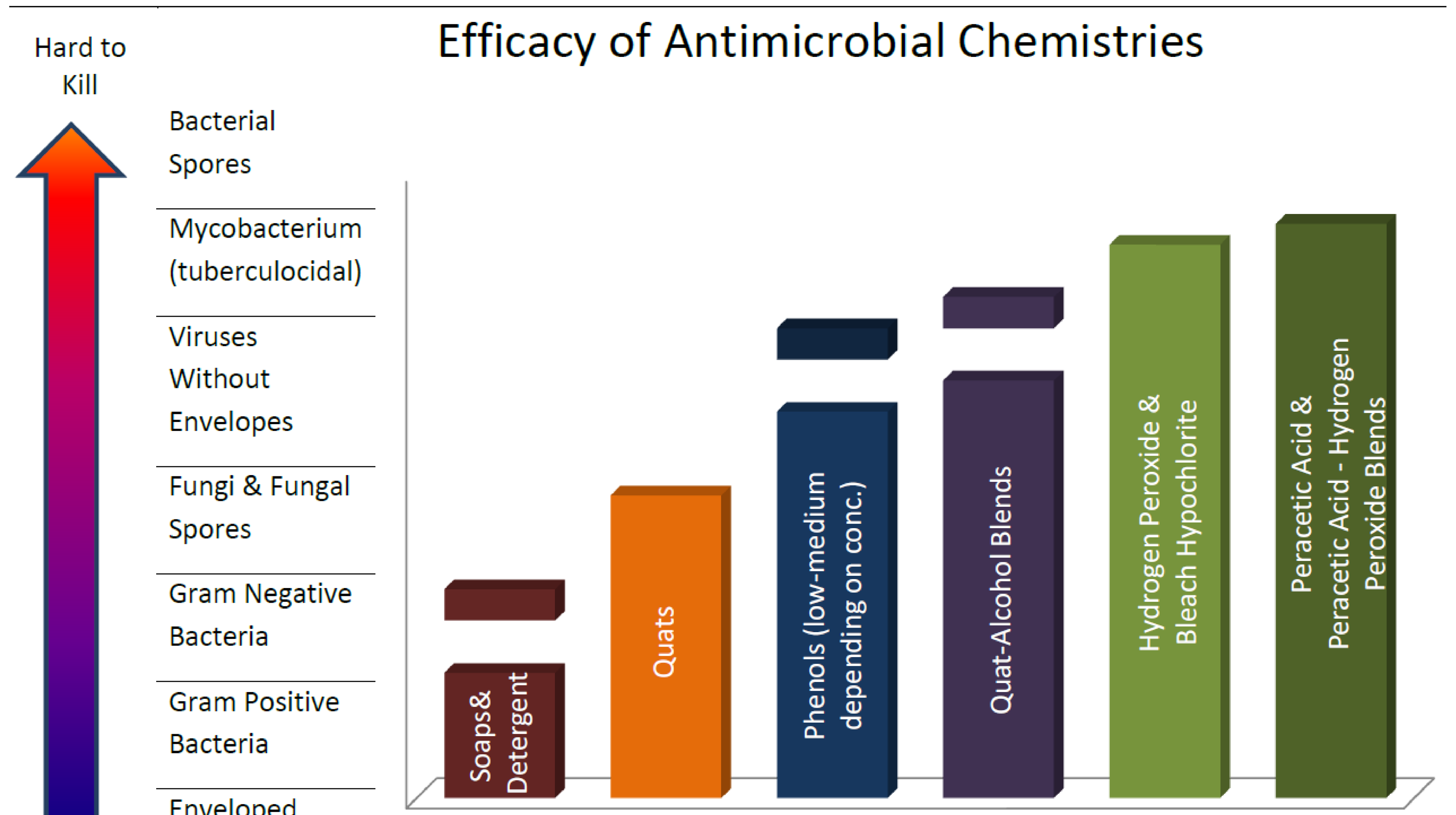


Figure 1 (above) : Hydrogen peroxide is known to have a very broad range of antimicrobial activity. The diagram indicates the range of activity for various antimicrobial chemistries, as adapted for information for surface disinfection research.

Antimicrobial Activity Based on Hydrogen Peroxide

Hydrogen Peroxide, H_2O_2, is an antimicrobial and disinfecting agent that is well known to caregivers and consumers alike. Antimicrobial activity is based on oxidative degradation of cellular components. This mechanism assures that bacterial species do not have the opportunity to develop resistance, thus making peroxide extremely safe for use both in acute situations (wound care) and long term (ostomy applications).

Figure 2, images of hydrocolloids containing peroxide. As packaged and on skin

Wound Healing in Porcine Model

Summary: A wound healing study was executed at the University of Miami Miller School of Medicine by Steve Davis and his research group, to assess how Stay Fresh hydrocolloids containing hydrogen peroxide performed in wound closure of both partial thickness and full thickness wounds. The full thickness wound study is detailed here as the longer time period permits better observations on wound healing. The conclusions in the wound healing study were that the hydrocolloid dressings with hydrogen peroxide did not inhibit wound closure as compared to non-adherent gauze and silver control dressings.

Methods: Full thickness wounds were made, as shown in the sequence of Images in **Figure 3**, by 20mm biopsy punch on paravertebral and thoracic area on female pigs (35-40kg). Wounds were separated by at least 15mm (see layout in **Figure 3**), and were covered with the various dressings. The silver dressing was wet with sterile water to activate. All dressings were covered and secured by self adherent elastic bandages.

Wound areas were recorded by acetate trace. Biopsies were taken, and assessed blindly for epithelialization %, epithelial thickness, granulation tissue and new blood vessel formation. No wounds from any treatment groups showed signs of swelling or erythema during the study.

The images below in the panels of **Figure 4** show the progression of the wounds in the treatment groups. All wounds are of course identical at inception. By days 5 through 7 the hydrocolloid sample groups show healthy granulation tissue, while the silver dressing and the non-adherent gauze show margins featuring eschar and dry dessicated tissue – each signs of impediments to optimal healing. In days 10 through 14 we visually observe almost complete healing under the hydrocolloids. The non-adherent gauze controls appear to retain regions that are non epithelialized with eschar. The silver dressings appear to feature black eschar consistent with silver deposits. Overall the analytical measures confirm observations that the hydrocolloids appeared to have slightly faster wound healing as measured by area than did the control and silver groups (p values <0.005 for comparison at 10 days vs. both control groups).

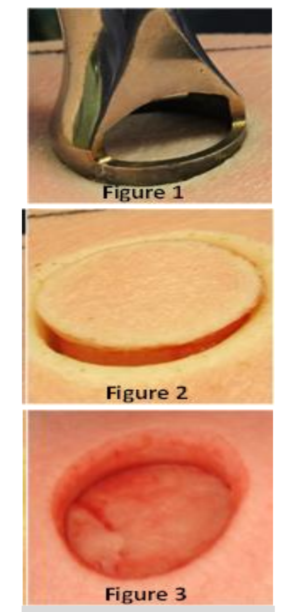
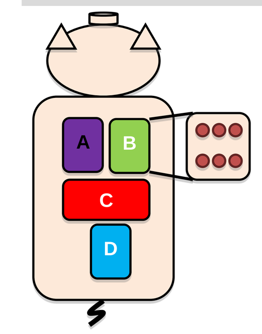
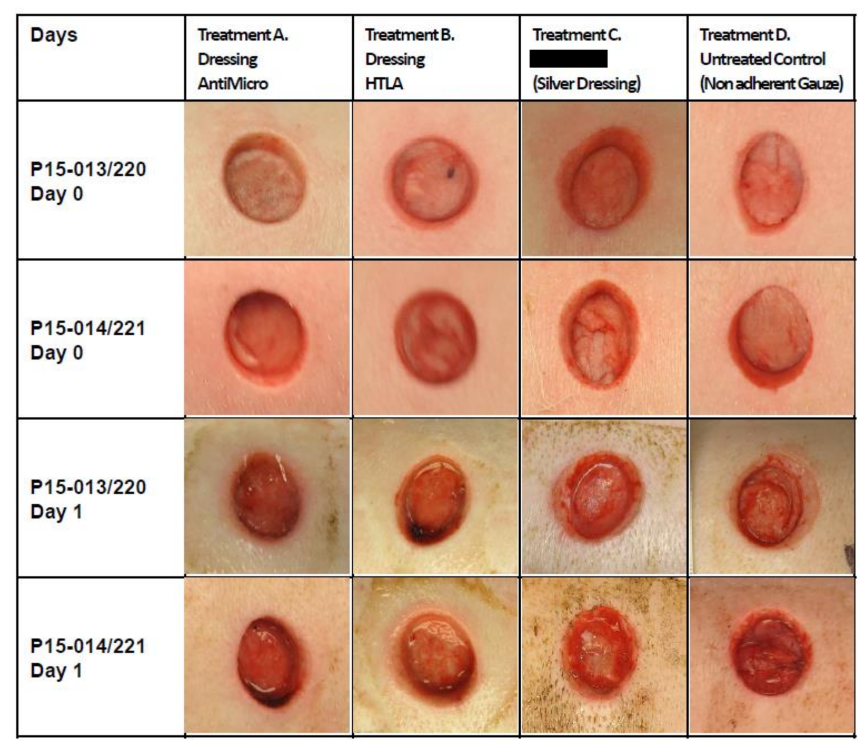
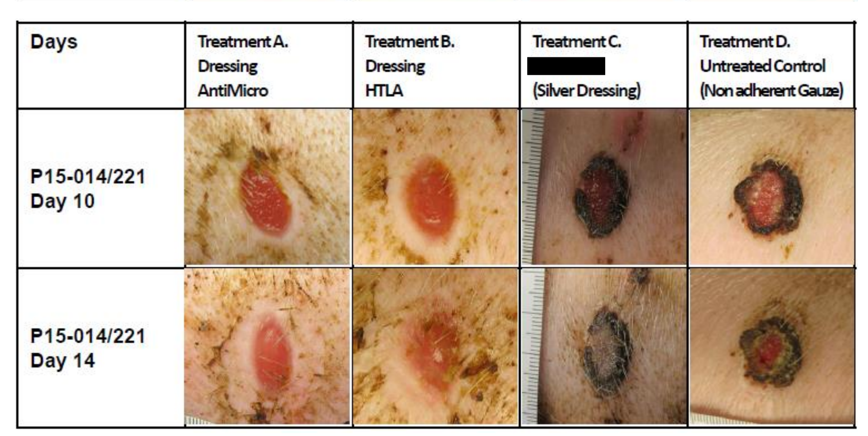


Figure 3, porcine wound healing model: wound creation (above panels) and layout (below)







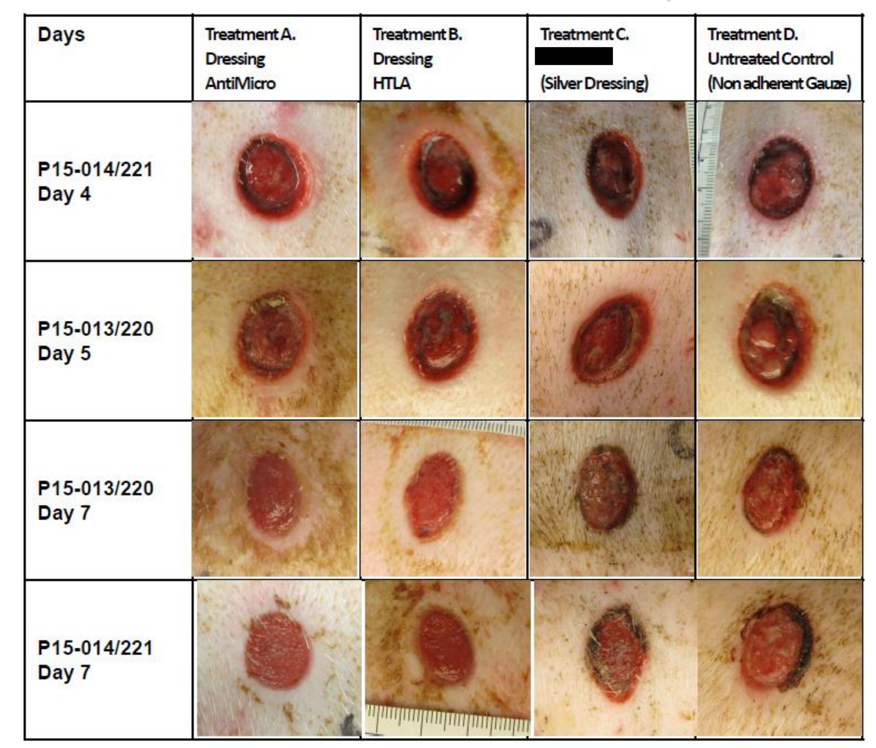


Figure 4 (3 panels above). Wound images from each time point and sample group. These are the images of the actual wounds in the porcine model from inception to experiment conclusion. At inception all are identical. The full thickness wounds are tracked over the course of 14 days as noted. Analytical measurement data from wounds and from biopsies is presented in charts at right (cited as Figures 17, 18, 21 and 24 from final report on wound study).

Figures 17, 18, 21 and 24 (charts right). Wound Healing Analytical Data.
Figure 17. All wounds are fully epithelialized by day 14.
Figure 18. Epithelial thickness changes with wound maturity through the process of keratinocyte proliferation, then differentiation, and epidermal maturation. Epidermis initially becomes thicker, then at later stage of healing becomes thinner. Epithelial thickness measurements for the hydrocolloid groups indicate more advanced healing compared to both control and silver samples.
Figure 21. Granulation tissue formation is largely equivalent for hydrocolloids (with or without peroxide) and control, with the silver dressing treatments showing some delay in formation of granulation tissue. This metric measures percent of wound bed filled with new tissue, and was equivalent by end point for all groups.
Figure 24. Wound contraction measures wound area over time, with the hydrocolloid groups showing significantly faster reduction in wound area compared to silver and control groups.

Antibacterial Efficacy

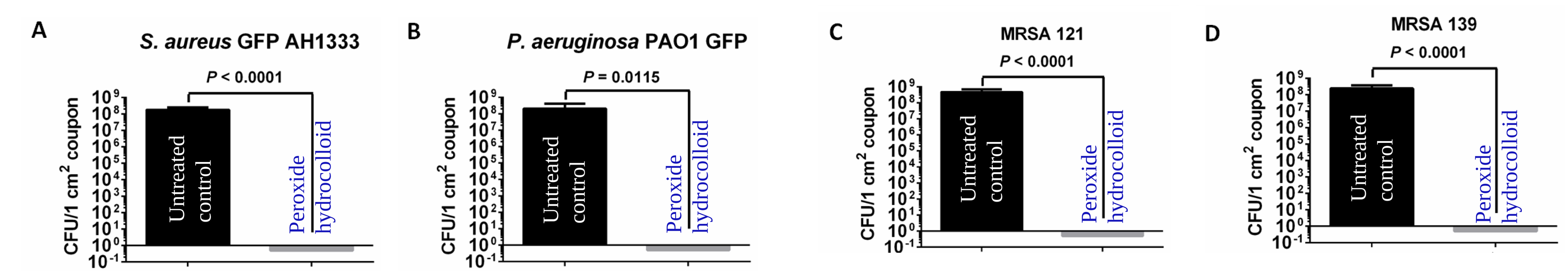
Hydrocolloids were tested by ASTM 2180 (data on **Table 1**). The data presented is directly from FDA clearance K151186.

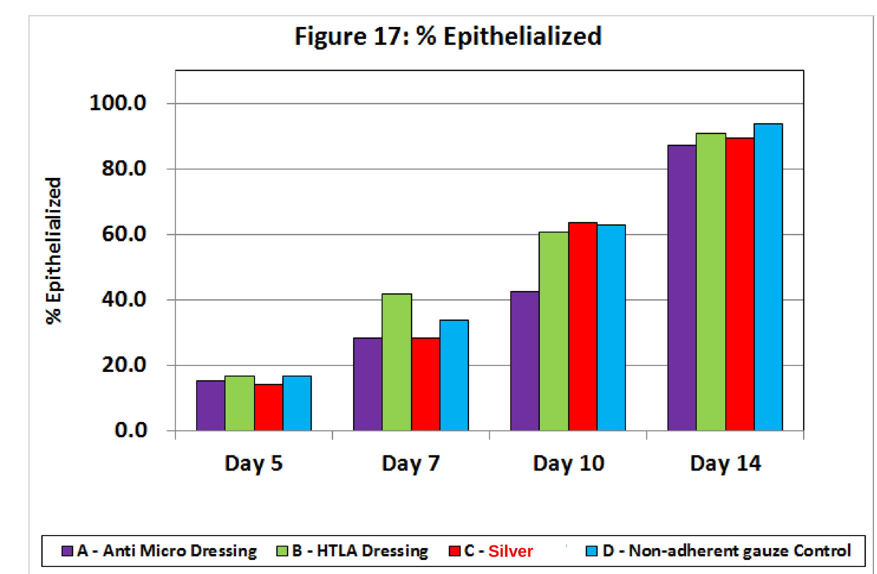
Direct inoculation assays were conducted using Colony Forming Unit (CFU) Assays at Texas Tech University (work from groups of Ted Reid and Phat Tran) on species including clinical isolates of MRSA (species identified per ATCC#).

Table 1 Organism	Log kill as packaged	Log kill after 5 day wound fluid exposure	ATCC#
Pathogenic organisms cited in K151186			
MRSA	>5.03 log kill,	>5.05 log kill,	BAA-44
Staphylococcus epidermidis	>5.36 log kill,	>4.60 log kill,	12228
Acinetobacter baumanii	>5.11 log kill	>5.40 log kill	19606
Escherichia coli	>5.05 log kill	>5.18 log kill,	8739

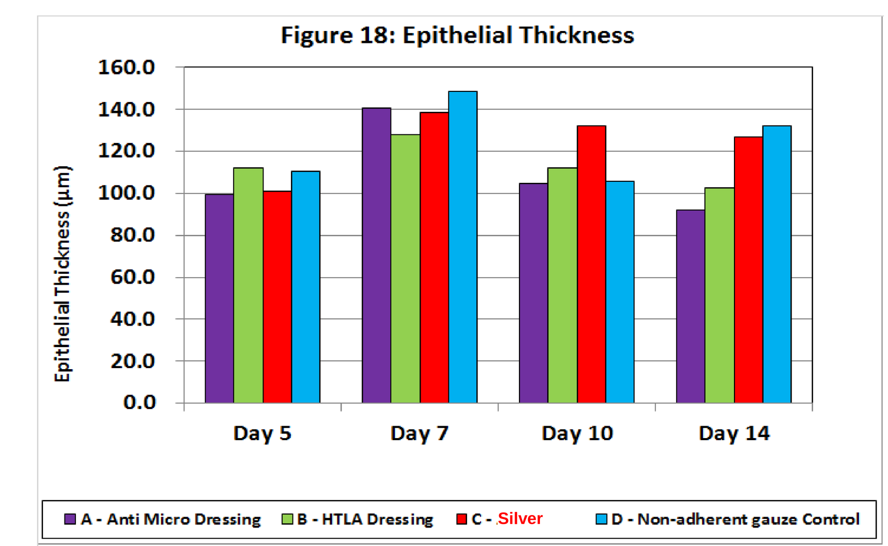
Table 1 (above). Antibacterial efficacy as per FDA clearance K151186.

Images A through D (below) show CFU assays performed at Texas Tech University, on S. aureus, Pseudomonas aeruginosa, and two MRSA strains as described, comparing peroxide containing hydrocolloids against untreated hydrocolloids

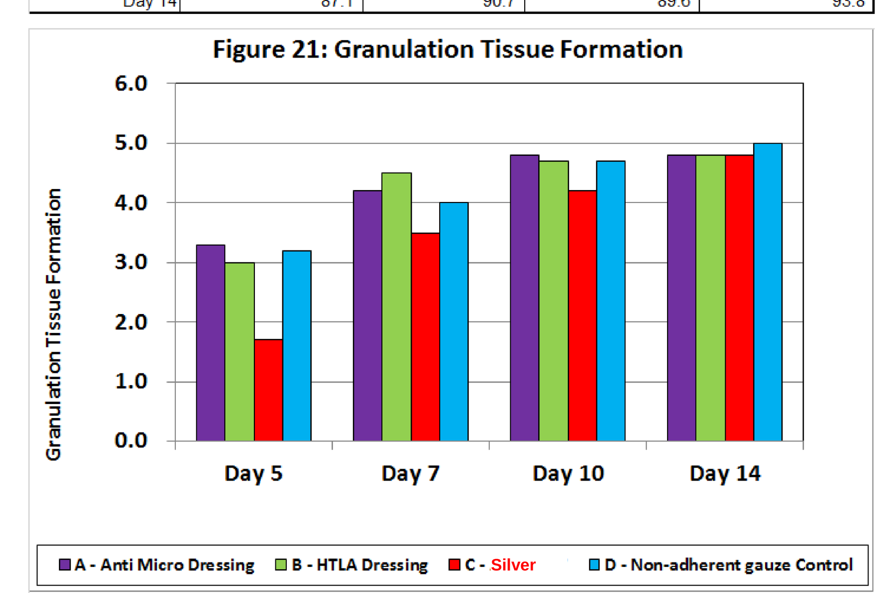




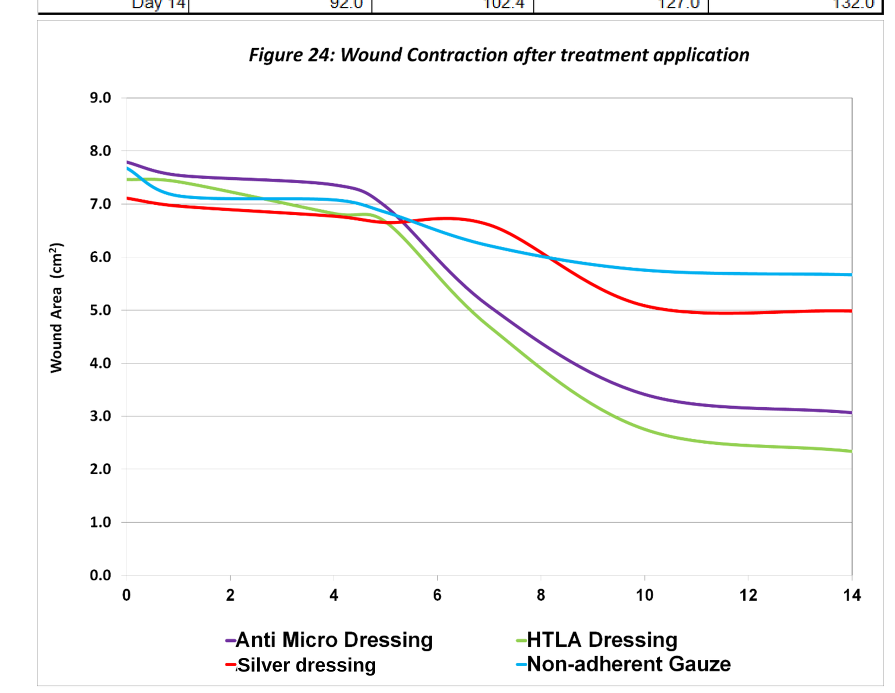
%Epithelialized	A - Anti Micro Dressing	B - HTLA Dressing	C - Silver dressing	D - Non-adherent gauze Control
Day 5	15.2	16.8	14.3	16.8
Day 7	28.3	41.9	28.5	33.9
Day 10	42.6	60.8	63.8	63.0
Day 14	87.1	90.7	89.6	93.8



Epithelial Thickness	A - Anti Micro Dressing	B - HTLA Dressing	C - Silver dressing	D - Non-adherent gauze Control
Day 5	99.2	112.0	100.8	110.4
Day 7	140.8	128.0	138.4	148.8
Day 10	104.8	112.0	132.0	105.6
Day 14	92.0	102.4	127.0	132.0



Granulation Tissue	A - Anti Micro Dressing	B - HTLA Dressing	C - Silver dressing	D - Non-adherent gauze Control
Day 5	3.3	3.0	1.7	3.2
Day 7	4.2	4.5	3.5	4.0
Day 10	4.8	4.7	4.2	4.7
Day 14	4.8	4.8	4.8	5.0



Conclusions: The Hydrogen Peroxide containing hydrocolloids were found to be effective antibacterial dressings. Additionally, a porcine model showed that wounds treated with HP Hydrocolloids healed at least as well as non adherent and silver controls, and reduced area faster than both silver and controls for the wounds in the model.

References – available on request

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