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# Pre-Clinical and Clinical Evaluation of a New Silver Antimicrobial Chronic Wound Dressing

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## Introduction

Microbial bioburden in the wound environment can significantly interfere with the rate and quality of wound healing.<sup>1</sup> This is problematic since modern wound management embraces the use of moist wound healing protocols which also optimizes conditions for the proliferation of microorganisms. SilvaSorb Silver Antimicrobial Wound Dressing was developed to combine a broad spectrum sustained release antimicrobial into an absorbent hydrophilic moist wound contact matrix. New wound care products from this technology are intended for use in the control of wound microbial bioburden in the acute and chronic wound environments.

## Pre-Clinical Evaluation

Silver has long been recognized for its broad spectrum activity against bacteria, viruses and fungi.<sup>2</sup> The widespread clinical use has been hampered by the instability of ionic silver, particularly in a moist environment. This new wound dressing is composed of a synthetic polyacrylate hydrophilic matrix that contains 25% moisture for donation and plasticity which contributes to its flexibility, elasticity and absorbency (Table A). Stable, sustained release antimicrobial activity is imparted in this material by the use of chemistry that tricks silver into remaining in a non-ionic state until release is stimulated by wound moisture (Figure 1). Discoloration and staining associated with silver is suppressed by a mechanism that actively protects silver ions from light energy (Figure 2). Ionic silver released from the matrix migrates into the surrounding substrate where it may inactivate or kill microorganisms (Table B). The rate of silver release is controlled to sustain an antimicrobial level of activity throughout the typical wear time for the dressing (Figure 3). This new hydrophilic silver antimicrobial dressing is biocompatible for both intact and broken tissues (Table C). The silver antimicrobial matrix was shown to cause a significant decrease in total microbial bioburden of intact skin on human volunteers (Figure 4).

## Summary

A new silver containing material designed to release antimicrobial activity intended for use in wound care has been evaluated for laboratory and clinical performances. The silver formulation is photo-stable so that it resists discoloration due to light and to irradiation during sterilization. Although the material possesses broad spectrum sustained release of antimicrobial activity, it is non-toxic for tissue culture cells and is non-irritating and non-sensitizing according to accepted test procedures. This material rapidly decreases the bioburden of exposed skin. The bioburden in 10 out of 11 wounds were reduced following the use of this product. Products produced from this silver containing matrix may be indicated in wounds that are at risk of becoming infected.

## Clinical and Efficacy Evaluation

SilvaSorb was evaluated on a variety of wounds of 21 consenting patients (Table D) without encountering adverse reactions associated with the silver containing matrix. The microbial bioburden of the wound and surrounding intact skin of 11 of the patients was assessed before and then 24-48h after use of the silver antimicrobial wound dressing (Figure 5).

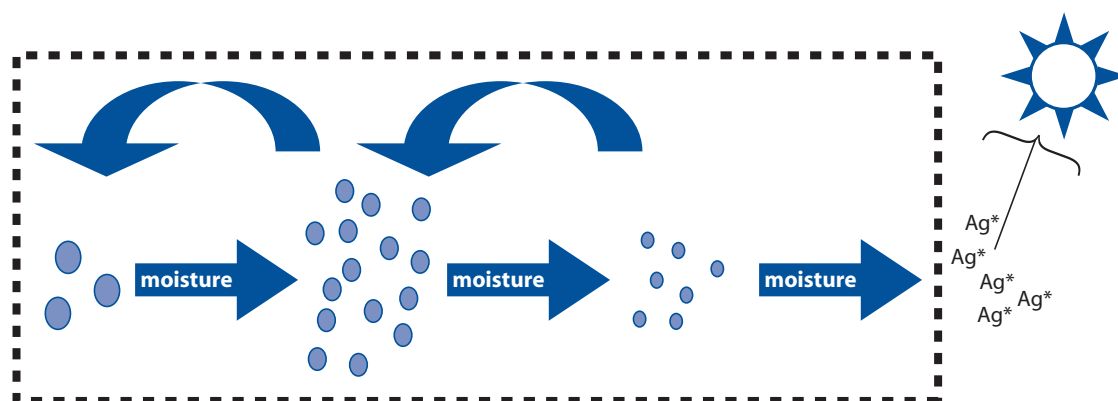
**Table A. Physical properties of SilvaSorb Antimicrobial Dressing.**

Absorbency	6 times weight
Elasticity	>2 times dimension
Adherence	Negligible
Microbial penetration	Occlusive
Moisture vapor transmission rate	2245g/m <sup>2</sup> /24h
Moisture Donation (dry substrate)	10% weight

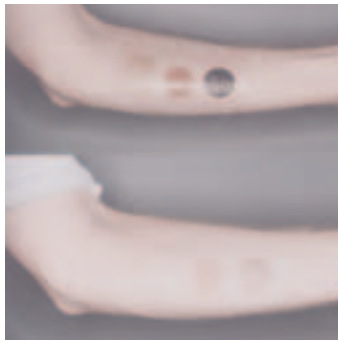
**Table B. Antimicrobial Activity of SilvaSorb Silver Dressing**

Inhibition Zone (measured in mm <sup>o</sup> )		
	SilvaSorb Silver	Control Dressing
Gram Positive		
<i>Staph. aureus</i>	19	<5
<i>Staph. aureus</i> (coagulase -)	28	<5
<i>Staph. aureus</i> (MRSA)	16	<5
Group A <i>Streptococcus</i>	23	<5
<i>B. subtilis</i> (spore former)	15	<5
<i>Listeria monocytogenes</i>	18	<5
Gram Negative		
<i>Ps. aeruginosa</i>	21	<5
<i>E. coli</i>	20	<5
<i>Proteus mirabilis</i>	16	<5
<i>Enterobacter fecalis</i>	20	<5
<i>Enterobacter cloacae</i>	9	<5
<i>Kleb. pneumoniae</i>	20	<5
Fungi		
<i>Candida albicans</i>	13	<5
<i>Candida parapsilosis</i>	20	<5
<i>T. rubrum</i>	15	<5
<i>M. gypseum</i>	9	<5

**Table B.** Diluted fresh overnight cultures of the various microorganisms were uniformly spread over the surfaces of TSA (SAB for fungi) plates. Circles, 5 mm in diameter cut from either the SilvaSorb matrix or plain matrix, were placed onto the surface before incubation at 37°C for 24–48 h before measurement of zones of inhibition.



*Figure 1. Mechanism of stabilization/release. The silver in the matrix is in the form of a silver complex until exposure to skin or wound fluid which activates the release of antimicrobial silver. The amount of silver released is controlled by a suppression mechanism that causes the reformation of the stabilized silver complex. These mechanisms regulate sustained release and protect against photo-conversion of ionic silver from light and irradiation.*



Product Stability - Skin Staining

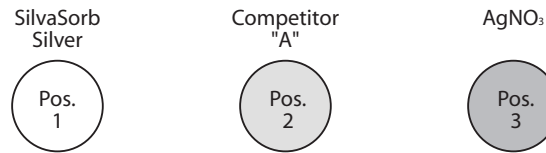


Figure 2. Light stability and skin staining characteristics of silver containing wound care products. Ionic silver ( $Ag^+$ ) is reduced to a black precipitate ( $Ag^0$ ) by light energy. The formulation of the SilvaSorb Antimicrobial Dressing contains chemistry that suppresses the light reaction of silver. This figure shows the skin staining from three silver containing dressings.

Table C. Biocompatibility Evaluation of SilvaSorb Antimicrobial Dressing

Evaluation	Protocol	Result
Toxicity Testing	Elution Assay (AAMI/ISO 10993)	Pass
Toxicity Testing	Agar Overlay (AAMI/ISO 10993)	Pass
Irritation Test	Skin Test (Human)	Non-irritating
Skin Sensitization Potential	LLNA test (Animal)	Non-sensitizing

**Table C.** Toxicity testing was carried out on the mouse derived L-929 fibroblast continuous cell line which measured cell cytotoxicity mediated by extraction fluid or direct contact with matrix with cultured cells. Skin sensitization was evaluated by the Local Lymph Node Assay that evaluates the induction of inflammatory reaction in tissues surrounding a site exposed to silver matrix.

Table D. Clinical Applications of SilvaSorb Antimicrobial Dressing

Wound Classification	Number of Patients	Duration of Use Average (Range)	Incidence of Adverse Reactions
Surgical Incision	3	3 weeks (1-6)	0/3
Skin Tear	3	1.2 weeks (1-2)	0/3
Pressure Ulcer	7	12.8 weeks (2-21)	0/7
Diabetic Foot Ulcer	3	10 weeks (1-16)	0/3
Venous Stasis Leg Ulcer	5	4 weeks (<1-8)	1/5 (pain)

**Table D.** Wounds were classified by standard clinical assessment protocols. The duration of use for the patient populations was a measure of the total time silver matrix was used in wound management for the patient. Adverse reaction assessment was made by clinician evaluation and patient perceptions.

Sustained Antimicrobial Levels of SilvaSorb

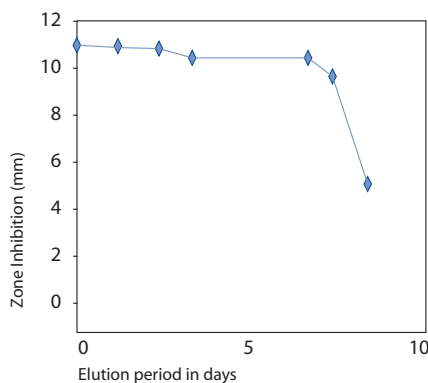


Figure 3. The sustained release of antimicrobial levels of silver was determined by placement of 5mm circles of matrix on the surface of protein containing agar for 1-8 days. The circles were removed and held until day 8 when each was placed on the surface of staph aureus immolated TSA. Zones of inhibition were measured after incubation.

## SilvaSorb Mediated Bioburden Reduction on Intact Skin

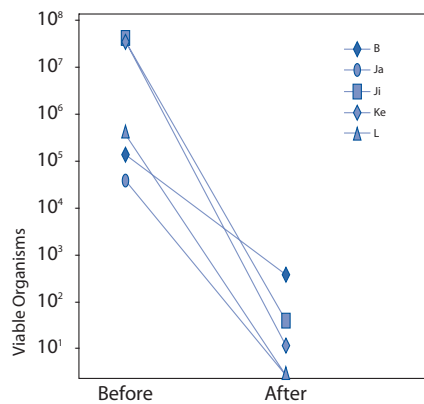


Figure 4. Natural bioburden on the forearms of each of 5 volunteers was challenged by 25 mm circles of either occlusive film or SilvaSorb™ silver matrix secured in place by a thin film cover dressing. After 24 h wear, each site was sampled by exhaustive saline rinse which was then cultured on TSA for total bacterial counts. The results compare the bioburden of the occlusive covered area (Before) with the silver matrix exposed area (After).

## Bioburden Index

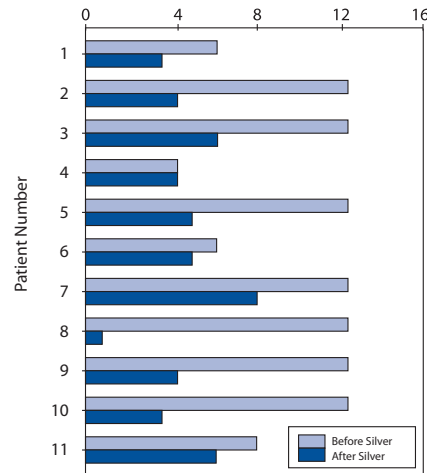


Figure 5. The bioburden in wounds from informed patients were estimated by the semi-quantitative swab method prior to the application of silver containing matrix over the wound bed. The silver matrix was then removed 24-48 h later and the bioburden of the wounds was again estimated. Bioburden Index is a scoring based on the amount of growth on spread areas on culture plates.

## Conclusions

- SilvaSorb Antimicrobial Dressing has broad spectrum antimicrobial activity.
- The release of silver ions is sustained over a typical dressing change interval.
- Matrix is biocompatible with intact and broken skin.
- Its application to skin causes a significant decrease in skin bioburden.
- Decreased bioburden of wound and surrounding intact skin occurs with the silver dressing's use on a variety of wounds.
- No adverse reactions have been associated with the use of this new product.

## References

- <sup>1</sup> Dow, G., Browne, A., and Sibbald, R. *Infection in chronic wounds: Controversies in diagnosis and treatment*. Ostomy Wound Management 45:23, 1999
- <sup>2</sup> Russell, A., and Hugo, W. *Antimicrobial activity and action of silver*. Prog. Med. Chem. 31:351, 1994

