



# SilvaSorb Targeted Antimicrobial Activity

A technical document explaining the methodology and benefits of a targeted release of antimicrobial silver

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## SILVER IS A POWERFUL ANTIMICROBIAL AGENT

Several manufacturers have incorporated silver into their products to impart antimicrobial barrier function to wound dressings. Although silver is most often recognized in its precious metallic form, it does exist in other oxidation states. Interestingly, not all are antimicrobial. Only ionic silver ( $Ag^+$ ) possesses this unique property.<sup>(1, 2)</sup> This requires that the reservoir technology used to deliver silver from wound dressings be capable of liberating the ionic form of silver ( $Ag^+$ ) when the dressing contacts moisture. Several strategies have been successfully developed to meet this requirement. Generally they fall into two broad categories of technologies. One approach has been the use of metallic silver. This relatively stable reservoir is particularly well suited for polyethylene and nylon substrates that can tolerate the metal coating process. The metallic silver dissolves when in contact with wound fluid to release ionic silver. The transition of metallic silver to ionic silver is an oxidation process and is governed by surface properties of the metal deposition used in forming the product. Metal coating technology is the approach used in Silverlon™ and Acticoat™ branded products.

**Table 1. Reservoirs used by various silver antimicrobial wound care products.**

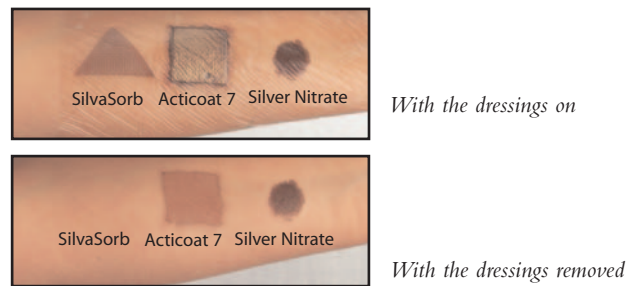
Silver Reservoir	Product	Distributor
<b>Metallic Silver</b>	Silverlon™	Argentum
	Acticoat™	Smith & Nephew
<b>Silver Salt</b>	SilvaSorb™	Medline.
	Aquacel Ag™	Convatec
	Arglaes®	Medline
	Contreet™	Coloplast
	Actisorb™	Johnson & Johnson

The other approach uses silver salts as the reservoir. Certain silver salts are crystalline structures similar to table salt. The particulate form of a salt protects the silver from reactivity with dressing components, and to some degree, from light inactivation. The silver in silver salts is already in the ionic ( $Ag^+$ ) state within the reservoir so it does not need to undergo an oxidation state transition when the dressing is placed on the wound.<sup>(3)</sup> Moisture dissolves the salt to liberate ionic silver. The typical salts are Silver Chloride (SilvaSorb™ and Aquacel™ Ag), Silver Ammonium complex of Contreet™, Silver Calcium Phosphate (Arglaes™) and Silver Carbon (ActiSorb™).

## SILVASORB'S TARGETED CONCENTRATION MINIMIZES NEGATIVE SIDE EFFECTS

The release of ionic silver from either reservoir system occurs by contact with moisture. In the wound environment, the moisture is derived either from wound exudate fluid, transpired moisture from intact skin, or some external source such as topical application. Much has been said recently about the silver delivery capabilities of various products. One manufacturer of metal coated dressings has claimed that high levels of silver are necessary to effect bactericidal activity to pathogens such as MRSA and VRE that are often associ-

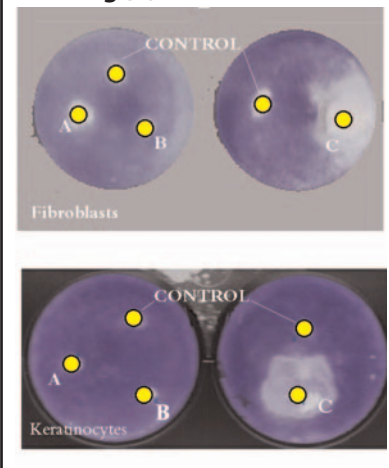
**Figure 1. Skin staining following contact with silver containing wound products.**



ated with wound bioburden. Interestingly, the release from metallic coated products is 1 to 2 orders of magnitude greater than all other silver containing dressings, which may suggest a problem with the controlled release mechanism of metal coated wound dressings.

Claims such as this are difficult to reconcile against the overwhelming body of evidence that has shown that silver is extremely active against microorganisms at concentrations at 1 ppm or less.<sup>(1, 4, 5)</sup> The term “oligodynamic” has been conferred to silver due to its antimicrobial effect at extremely low concentrations.<sup>(4)</sup> Silver is highly reactive and may cause problems when used in amounts greater than that needed for effectiveness. Tissue repair requires proliferation and matrix protein production by a variety of cell types in

**Figure 2. Fibroblasts (top panel) and Keratinocytes (lower panel) exposed to control matrix, Silver Salt reservoir matrices (A, B) and Metallic Silver coated wound dressing (C).**



order to achieve wound closure. These cells are acutely sensitive to the chemistry of their environment, particularly agents that impede cellular function. Excess amounts of heavy metals, even silver, may impart undesirable action in the wound bed. This may present as staining to the wound and surrounding skin (see figure 1).

Figures 2 (fibroblasts) and 3 (keratinocytes) illustrate the effects various wound care products have on proliferating tissue cells in vitro. Product samples were placed on seeded tissue cultures until cultures grew to confluence. The layers of viable cells were then stained (dark area) to reveal the density of growth. These illustrations show that cell density was unaffected around the control (no silver), and wound products that use silver salts (A and B) as the reservoir (SilvaSorb). By contrast, a large zone devoid of proliferating and adherent cells was observed around the product that uses metallic silver (C) as a reservoir. Fibroblasts and keratinocytes are important cells that must function in the wound environment so care must be taken to minimize interference with their growth.

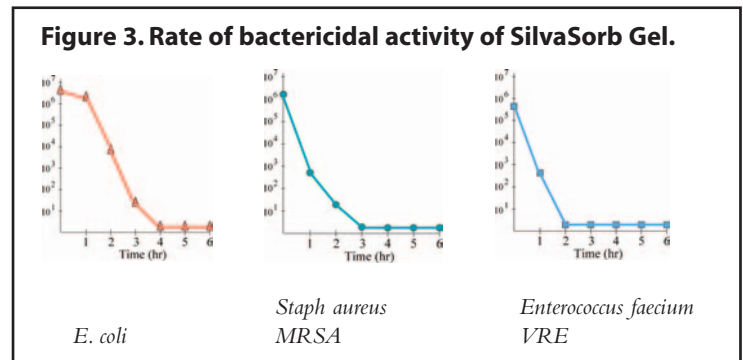
### SILVASORB'S TARGETED RELEASE FOR EXTENDED BACTERICIDAL EFFECT

Silver salt sustained release of silver aids in maintaining a constant level of ionic silver in the contact area. The level of ionic silver is controlled by the presence of chloride ion in wound fluid. Chloride ions will react with silver ions to form a silver chloride salt ( $\text{AgCl}_{(n)}$ ). Silver chloride, as a reservoir, is uniquely compatible with the mechanism that controls the free silver ion concentration at 1-2 ppm regardless of the presence of bacteria.<sup>(5)</sup> This is the reservoir system that is used in SilvaSorb™. Recently a manufacturer of metal coated dressings claimed that the control of bioburden is dependent upon higher levels of silver. The effectiveness of SilvaSorb (Sheet, Cavity and Gel) has consistently been shown to be effective against a wide range of microorganisms. In an *in vitro* study of bacteriostatic vs bactericidal testing, SilvaSorb sheet and SilvaSorb gel were placed upon culture plates inoculated with a variety of common medically important organisms. After initial incubation the plates were

observed for inhibition of microbial growth. After scoring, samples were taken from under the SilvaSorb for subculture to fresh media to determine if viable organisms were present. The results in Table 2 illustrate that all 23 strains of microorganisms were killed by SilvaSorb. It was further revealed that no viable organisms could be recovered from the contact area. These results confirm that SilvaSorb is bactericidal for these organisms.

### SILVASORB'S TARGETED RELEASE HAS A FAST-ACTING BACTERICIDAL EFFECT

Prolonged contact in the previous study showed SilvaSorb was effective in killing cultured microorganisms, including *E. coli*, *Staph aureus* MRSA, and *Enterococcus faecium* VRE. To test the rate of bactericidal activity, fresh cultures of these strains were placed in contact with SilvaSorb Gel. The numbers of viable organisms in the original inocula were determined as were the survivors at various time points after contact with the SilvaSorb. Figure 3 illustrates that organisms are rapidly killed following contact with the SilvaSorb. In all cases greater than 99.9% of the organisms were killed within 2 hours. Moreover no organisms were recoverable from the assay after 4 hours of contact with SilvaSorb Gel. Similar results have been obtained with all formats of SilvaSorb dressings (data on file).



**Table 2. SilvaSorb activity on common strains of medically important microorganisms.**

Strain	SilvaSorb Sheet		SilvaSorb Gel	
	Bacteriostatic	Bactericidal	Bacteriostatic	Bactericidal
<i>E. coli</i> ToP10F	yes	No growth	Yes	No growth
<i>E. coli</i> 8739	yes	No growth	Yes	No growth
<i>Kleb. pneumoniae</i> 33472	yes	No growth	Yes	No growth
<i>Kleb. pneumoniae</i> 33475	yes	No growth	Yes	No growth
<i>Listeria monocytogenes</i>	yes	No growth	Yes	No growth
<i>Staph aureus</i> 25923	yes	No growth	Yes	No growth
<i>Staph aureus</i> MRSA	yes	No growth	Yes	No growth
<i>Staph sp</i> Coagulase neg	yes	No growth	Yes	No growth
<i>Staph aureus</i> 6538	yes	No growth	Yes	No growth
Group A <i>Streptococci</i>	yes	No growth	Yes	No growth
<i>Proteus mirabilis</i>	ND	No growth	ND	No growth
<i>Ps. aeruginosa</i> 27853	yes	No growth	Yes	No growth
<i>Ps. aeruginosa</i> 9027	yes	No growth	Yes	No growth
<i>Bacillus subtilis</i>	yes	No growth	Yes	No growth
<i>Enterobacter cloacae</i>	yes	No growth	Yes	No growth
<i>Enterococcus faecium</i>	yes	No growth	Yes	No growth
<i>Enter. faecium</i> VRE	yes	No growth	Yes	No growth
<i>Enter. faecium</i> ENFA	yes	No growth	Yes	No growth
<i>Serratia marcescans</i>	yes	No growth	Yes	No growth
<i>Candida albicans</i> 10231	yes	No growth	Yes	No growth
<i>Candida parasilosis</i>	yes	No growth	Yes	No growth
<i>Candida albicans</i>	yes	No growth	Yes	No growth
<i>Aspergillus niger</i> 16404	yes	No growth	Yes	No growth

### CONCLUSION

Silver is a fast acting antimicrobial agent that kills a wide range of pathogens associated with wounds and it has been incorporated into a variety of sophisticated wound care products. The rate of delivery is regulated by the nature of the silver reservoir in the products. Metallic reservoirs have less control on the rate of silver delivery than do silver salt reservoirs. This may explain the reason for tissue staining and abnormal cellular adhesion and proliferation in vitro with these products. SilvaSorb uses a silver salt ( $\text{AgCl}_{(n)}$ ) which maintains a steady state 1-2 ppm of ionic silver in isotonic fluid of the wound environment. The targeted controlled release mechanism of SilvaSorb was developed to provide adequate ionic silver for achieving rapid microbiocidal action without detectable staining or growth inhibiting effects in the wound environment. SilvaSorb is an effective antimicrobial dressing for use on acute and chronic wounds.

### REFERENCES

- <sup>1</sup>Russel AD, Hugo WB. *Prog Med Chem* 31:351-70, 1994.
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- <sup>4</sup>Ravelin J. *Sci Nat* 11:93-102, 1869.
- <sup>5</sup>Von Naegelli V. *Deut. schr. Schweiz. Naturforsch. Ges.* 33:174-182, 1893.