Silver and Alginates: Role in Wound Healing and Biofilm Control

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Significance: Chronic wounds are known to be a significant issue globally. Of concern in wounds are the numbers and types of residing microorganisms and the ability of the host's immune system to control their proliferation. Wound healing is impeded by colonizing microorganisms growing within the biofilm phenotypic state. In this state microorganisms are recalcitrant to routinely impeded by used antimicrobial interventions.

Recent advances: Silver has been reported to demonstrate efficacy on planktonic microorganisms both within the *in vitro* and *in vivo* environments. However, when silver is incorporated into a wound dressing, its antimicrobial efficacy on biofilms within the *in vivo* environment remains contentious.

Critical Issues: Unequivocal evidence of the efficacy of silver, and wound dressings containing silver, on biofilms in clinical situations is lacking. This is principally due to the deficiency of definite biofilm definitions, markers, and evidence in the chronic wound environment.

Future Direction: Research studies demonstrating antimicrobial efficacy on *in vitro* biofilms can be used to generate data and information appropriate for extrapolation and applicability to the *in vivo* environment. It is very important that inventors of antimicrobial wound dressings ensure efficacy against both planktonic and sessile microorganisms, within the *in vitro* and *in vivo* environments.

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SCOPE AND SIGNIFICANCE

CHRONIC WOUNDS ARE KNOWN to be a significant issue globally. Of particular concern in these wounds are the numbers and types of residing microorganisms and the ability of the host's immune system to control their proliferation. The colonizing microorganisms growing within the biofilm phenotypic state constitute the greatest barriers to healing. Within the biofilm state microorganisms are inherently recalcitrant to routinely used antimicrobial interventions. Consequently, the use of wound dressings containing silver for the treatment of at risk or infected chronic wounds must demonstrate efficacy against

microorganisms in both the planktonic and biofilm phenotypic states.

This brief article aims to provide an overview of the scientific evidence supporting the use of silver, alginate, and silver alginate wound dressings highlighting antimicrobial efficacy on biofilms within the *in vitro* and *in vivo* environment.

TRANSLATIONAL RELEVANCE

The formation of a chronic wound is caused by multiple factors. In the case of diabetic foot ulcers this includes underlying peripheral vascular diseases, diabetes, and prolonged pressure, which combined, can lead

to the ulceration of a wound.¹ The risk of these wounds becoming infected is high due to the presence and prevalence of endogenous and exogenous microorganisms.² Consequently, it is important that appropriate antimicrobials like silver are applied to at risk or infected wounds. However, the delivery vehicle or platform is also important to ensure that the sustainability and efficacy of the antimicrobial is maintained.

CLINICAL RELEVANCE

A wide range of non-antimicrobial wound dressings are commercially available for use in the management of noninfected chronic wounds. The overall aim of these wound dressings are to support and help promote wound healing through the generation and maintenance of a moist environment. Alginate wound dressings, as an example, have been found to be effective primary dressings and appropriate for use in the management of exudating wounds and are associated with positive clinical outcomes.³ Antimicrobials, in particular silver, are incorporated into wound dressings, including alginates, for use in the treatment of “at risk” or infected chronic wounds. Silver is used to both reduce the dressing and wound microbial bioburden.

BACKGROUND

Chronic wounds include pressure, venous, and diabetic ulcers. The costs associated with the management of chronic wounds represent a significant financial outlay to the healthcare provider. These direct and indirect costs are set to increase further due to an ageing population and associated susceptibility to infection and disease. It has been estimated that an annual U.S. expenditure of \$25 billion is associated to the management and treatment of chronic wounds.⁴

Irreversibly adhered and colonizing microorganisms have a significant role to play in the nonhealing of chronic wounds.⁵ Colonizing microorganisms specifically are known to promote a continuous inflammatory state in the wound leading to damage of the localized tissue. The result is interference of the “normal” wound healing process.⁶

Briefly, following a trauma and a subsequent breach to the skin surface microbial contamination of the wound will occur within seconds. At this point in the “microbial lifecycle of a wound” the microorganisms will reside within a reversible adherent transient state and easily detach from the newly formed wound.⁷ Transient microbes are microorganisms that are able to colo-

nize the skin or wound surface, but they can be easily removed by routine cleansing. They are not generally considered to multiply within a wound, or on the skin, but are able to survive in a more “quiescent” state. On occasions the transient microbes can sporadically proliferate on a surface. They are often acquired during direct contact with patients or contaminated environmental surfaces. Large numbers of transient microbes have the ability to persist for long periods of time within the wound.⁷

As microbial numbers in the wound increase the host initiates an inflammatory response, the primary aim being to reduce microbial numbers. At this state the wound is clinically referred to as being *colonized* and therefore *at risk* of becoming infected. As microbial numbers increase the wound is clinically referred to as being *critically colonized*. The term *critical colonization* implies that at a given microbial bioburden of 10^5 colony forming units per gram of wound tissue or mL of exudate delayed healing is reported.⁸ While this is a routinely used “subjective” clinical concept it does not take into consideration wound etiology, the type of microbial species and genera present, interactions of microbes, or their relative virulence potential and evidence of a biofilm.^{8,9} Indeed, synergy between resident wound microorganisms, microbial virulence, and numbers play a significant factor in contributing to poor wound healing rates.¹⁰ It is only recently that *critical colonization* is being referred to as “*biofilm infected*.” While a more clinically and microbiological relevant term,³ further evidence to substantiate this is warranted.

Biofilms can be defined as “communities of microorganisms attached to a surface or each other, encased within an extracellular polymeric substance.”⁸ In the wound biofilm, the microbial cells phenotypically differ from their free-living or planktonic counterparts. In particular, microbial cells within the biofilm exhibit a much higher tolerance to both the hosts immune defences and antimicrobial agents.^{11,12} Consequently, topical antimicrobials need to be “*fit for purpose*” in view of the mounting evidence regarding biofilms and their role in chronic infections and delayed healing.

DISCUSSION OF FINDINGS AND RELEVANT LITERATURE

Clinical problem

The usage of topical antimicrobials is, without doubt, significant and fundamental for those wounds at risk of becoming infected or locally infected. However, they should not be used indiscriminately.

If antimicrobials are used effectively and appropriately a patient's risk to bacteremia, septicemia, and sepsis is also significantly reduced.

Wound dressings impregnated with silver are used widely and are now considered a mainstay in wound management. They are significant to the treatment of acute and chronic wounds that are infected or at risk of becoming infected.¹³ Silver alginate wound dressings in particular are known to have benefits in wound care, with a recent article highlighting bioavailability of ionic silver for long periods of time.¹⁴ If a wound dressing is to be considered for use over an extended wear time it is important to clarify the ability of the dressing to maintain and sustain levels of ionic silver within it. Bradford *et al.*¹⁴ demonstrated this capacity with a silver-impregnated dressing composed of ionic silver, carboxymethyl cellulose (CMC), and alginate; the study highlighted a sustained antimicrobial effect against a range of planktonic microorganisms over a 21-day test period. Such a sustained release of silver may help to minimize nursing time, thus cutting down healthcare costs, and it can also minimize patient discomfort commonly observed during dressing changes.¹⁵ Furthermore, ionic silver made available in silver-containing alginate wound dressings is known to exhibit activity against a broad spectrum of microorganisms.¹⁶ The incorporation of silver ions into alginate dressings suitably combines the highly absorbent characteristic of alginate with the antimicrobial efficacy of silver; alginate dressings are particularly beneficial in the management of highly exuding wounds.¹⁵ However, the extent of activity of silver will vary in different *in vitro* and *in vivo* environments and depend on the bioavailability of its ionic form. Ionic silver is known to be affected by its interaction with complex organic molecules found in the wound bed.¹⁶ Interestingly, both animal and human studies have demonstrated the capacity of silver to aid healing by accelerating reepithelialization.¹⁷

Silver chemistry and antimicrobial efficacy

The antimicrobial efficacy of silver for the treatment of infected wounds has been known for over 200 years. Despite this it was not until the latter half of the 1900s that the effectiveness of silver became more apparent and acceptable as a treatment method for infected wounds. Initially its usage was specifically focused for application in the treatment of burns as silver nitrate (0.5%) solution, in conjunction with a gauze dressing, or a silver sulfadiazine cream. Later the use of different silver combinations for the treatment of chronic wounds gained traction.

Many *in vitro* studies have been carried out, which have demonstrated the antimicrobial efficacy of ionic silver and its broad spectrum of activity against microorganisms. In these situations it has been reported that even at low concentrations ($5 \mu\text{g/mL}^{-1}$) ionic silver (Ag^+) is highly efficacious on microorganisms¹⁸ with its efficacy reported to be species-specific.¹⁹

Within the *in vivo* environments it is well documented that numerous compounds and chemicals can affect the bioavailability and therefore effectiveness of Ag^+ . In biologically diverse environments factors such as chloride ions, proteins, phosphates, and lipids in particular are known to effect antimicrobial efficacy.²⁰ The type of bacterial culture broth can have an effect on silver antimicrobial activity *in vitro* while the *in vivo* wound environment contains sera, blood, and tissue fluid, which can all affect silver bioavailability.²⁰ Furthermore, the distribution of silver within the wound dressing, its chemical and physical form, and the affinity of the dressing for moisture are additional factors that will affect antimicrobial performance. Despite this, there are a large number of case studies, reports, and clinical trials demonstrating the antimicrobial efficacy of silver *in vivo*.

Silver has been shown to be effective against a range of device-associated infections. For example, an early study by Spadaro *et al.*²¹ highlighted the efficacy of percutaneous silver wire implants against *Staphylococcus aureus* in rats. The use of silver-coated catheters has also been reported; prevention of urinary tract infection using a silver-coated urinary catheter was demonstrated by Akiyama and Okamoto,²² while Goldschmidt *et al.*²³ highlighted the effectiveness of silver-coated central venous catheters in the prevention of catheter-related infections in oncological patients. Some success was also noted in an early study by Webster *et al.*²⁴ who employed the use of surgical debridement and daily application of electrically activated silver dressings in the management of chronic osteomyelitis.

The mode of action of ionic silver is fundamental to its performance, with its principal mode of action being denaturation of proteins.²⁵ The denaturation of proteins is achieved by silver attaching onto different functional groups including thiol, sulfhydryl, imidazole, and carboxyl groups, leading to protein unfolding and breakdown.^{26,27} Furthermore, silver has been shown to bind to deoxyribose nucleic acid, reduce enzymatic activity and therefore metabolic processes, and affect microbial respiration by inducing the production of destructive reactive oxygen species.

Efficacy of silver on biofilms

Silver has been shown to be very effective in reducing biofilms in and on medical devices.²⁸ However, as with all antimicrobials, at low levels silver has been shown to have a reduced efficacy on biofilms.²⁹ Interestingly, Silvestry-Rodriguez *et al.*²⁹ found that silver at levels of 100 mg/L were ineffective on biofilms. However, contrary to this at the genomic level silver, at low concentrations, has been shown to prevent the formation of biofilms.³⁰ A further study by Chen *et al.*³¹ demonstrated the anti-biofilm effectiveness of silver ions, silver nano particles, and silver chloride colloids on *Pseudomonas aeruginosa* and *Serratia proteamaculans* biofilms.

Okkyoung *et al.*³² investigated the efficacy of silver ions on bacterial growth using silver colloids and nanoparticles. It was reported that nanoparticles demonstrated the greatest efficacy on microbial growth. However, Bjarnsholt *et al.*³³ evaluated the efficacy of silver on *P. aeruginosa* biofilms and found that the concentration of silver in currently available wound dressings was much too low for treatment of chronic biofilm wounds. Conversely, this study was an *in vitro* study involving one specific bacteria. In contrast, Chaw *et al.*³⁴ reported that very low levels of ionic silver (50 ppb) were able to destabilize the biofilm matrix of *Staphylococcus epidermidis*. Other studies on the effects of silver on biofilms have been carried out highlighting positive anti-biofilm capabilities of ionic silver specifically when used in combination with specific platforms, actives, and chassis. For example, in the patents by Percival *et al.*^{35,36} it was found that combining silver in fibrous materials, hydrogels, and other agents such as surfactants, EDTA, and polyphosphates significantly enhanced the antimicrobial and antibiofilm ability of silver.³⁷ Further to this, Kostenko *et al.*³⁸ found that wound dressings with hydrophobic base material impregnated with silver had sustained antibiofilm activity. This sustained antibiofilm effect was evident for at least 7 days and independent of the microbial strain utilized. Furthermore, Ammons *et al.*³⁹ found that combining lactoferrin and xylitol in a hydrogel in conjunction with a silver wound dressing demonstrated good efficacy on biofilms.

In vitro and *in vivo* efficacy of alginate and silver alginate dressings on planktonic microbes and biofilms

Wiegand *et al.*⁴⁰ evaluated three alginate based wound dressings, an alginate alone, an alginate containing ionic silver, and an alginate containing

nanocrystalline silver on factors known to affect wound healing. All wound dressings were tested for biocompatibility, antimicrobial activity, and effects on elastase, matrix metalloproteinase 2 (MMP2), tumor necrosis factor- α , interleukin-8, and free radical formation. The alginate alone was found to bind much of the elastase, and also reduce the pro-inflammatory cytokines and inhibit the formation of free radicals. Additionally, the dressing was reported to demonstrate some antibacterial activity. The silver alginate was found to demonstrate an increased antimicrobial effect and increased binding of elastase, MMP2, and cytokines. Furthermore, it was shown to have an enhanced antioxidant capacity when compared with the nonsilver-containing alginate. Silver, however, was reported to have a negative effect on human HaCaT keratinocytes in terms of cell viability and cell proliferation. Further to this, Bradford *et al.*¹⁴ conducted a study to determine the spectrum of activity and efficacy of a silver alginate dressing on planktonic microorganisms, by employing the use of a 21-day repeat-challenge log reduction study. The silver alginate wound dressing exhibited a microbiocidal effect for up to 21 days. The silver alginate dressing appeared to demonstrate a superior antimicrobial efficacy particularly against *P. aeruginosa* and *Candida albicans* when compared with other dressings.

A later study by Percival *et al.*⁴¹ investigated the antimicrobial efficacy of a silver alginate dressing against 115 wound isolates that had been routinely isolated from patients at West Virginia University Hospital, Morgantown, USA. The study provided evidence on the broad antimicrobial activity of a silver alginate dressing on wound isolates grown in the nonbiofilm and biofilm state. The authors considered such a finding to be clinically relevant as both the nonbiofilm and biofilm phenotypic states of microorganisms are evident in wounds and therefore significant to delayed healing. Further to this work, Thomas *et al.*⁴² investigated the antimicrobial effectiveness of a silver alginate dressing on 40 microorganisms isolated from patients attending three burn centers in the United States. The study demonstrated the broad spectrum antimicrobial activity of a silver alginate dressing on a wide range of burn isolates, including antibiotic-resistant bacteria. The study also highlighted the importance of pH and its potential effects on antimicrobial performance and microbial susceptibility.

Further studies reporting on the efficacy of a silver alginate wound dressing have been documented recently. Hooper *et al.*⁴³ compared the antimicrobial activity of a silver alginate dressing

with a silver-free control dressing using a combination of *in vitro* culture and imaging techniques. The opportunistic pathogens examined included *C. albicans*, *Escherichia coli*, *P. aeruginosa*, *S. aureus*, β -hemolytic *Streptococcus*, and anaerobic bacteria. Antimicrobial efficacy of the dressings was assessed using $\log_{10}$ reduction and 13-day corrected zone of inhibition (CZOI) time course assays. Confocal laser scanning microscopy was used to visualize the relative proportions of live/dead microorganisms sequestered into the dressings over 24 h and estimate the comparative speed of kill. The silver alginate dressing demonstrated significantly greater $\log_{10}$ reductions and CZOIs for all microorganisms compared with the control, indicating the antimicrobial effect of ionic silver. Antimicrobial activity was evident against all test organisms for up to 5 days and, in some cases, up to 12 days following an on-going microbial challenge. Imaging bacteria sequestered in the silver-free dressing showed that each microbial species aggregated in the dressing and remained viable for more than 20 h. Growth was not observed inside the dressing, indicating a possible microbiostatic effect of the alginate fibers (AFs). In comparison, microorganisms in the silver alginate dressing were seen to lose viability at a considerably greater rate. After 16 h of contact with the silver alginate dressing, >90% of cells of all bacteria and yeast were no longer viable. Collectively, the data highlighted the rapid speed of kill and antimicrobial suitability of a silver alginate dressing on wound isolates and highlighted its overwhelming ability to manage a microbial wound bioburden in the management of infected wounds.

The efficacy of silver dressings and antibiotics on methicillin-resistant *S. aureus* (MRSA) and methicillin-sensitive *S. aureus* (MSSA) isolated from burn patients has also been reported.⁴⁴ In this study the objectives were to investigate whether MRSA demonstrated an increased tolerance to silver wound dressings compared with MSSA and to evaluate the effects of bacterial phenotypic states of MRSA and MSSA, and pH, on the activity of silver wound dressings and two antibiotics, ampicillin and clindamycin. Twenty MRSA and 10 MSSA isolates from burns patients in South Africa were evaluated for their susceptibility to a silver alginate and a silver carboxy methyl cellulose wound dressing, employing a CZOI assay, conducted on Mueller Hinton agar (MHA) and a poloxamer-based biofilm model. When exposed to the two silver dressings all thirty *S. aureus* demonstrated susceptibility. Possible enhanced antimicrobial efficacy of the silver dressings occurred

when pH was lowered to 5.5, compared to a pH of 7.0. When all *S. aureus* isolates were grown in the biofilm phenotypic state and exposed to both silver dressings and antibiotics, enhanced tolerance was noted. Overall, susceptibility to silver was higher for MRSA when compared to MSSA. This study demonstrated that the effect of pH and bacterial phenotypic state must be considered when the antimicrobial activity of silver wound dressings are being investigated. It is evident from the data generated that both pH and the bacterial phenotypic state are factors that induce changes that affect both antimicrobial performance and bacterial susceptibility.

Corum *et al.*⁴⁵ compared the antimicrobial efficacy of a silver alginate to a silver CMC dressing on burn isolates grown in the biofilm phenotypic state. The purpose of this study was to (1) evaluate the efficacy of a silver alginate dressing on burn isolates grown within the nonbiofilm and biofilm phenotypic states and (2) compare the antimicrobial efficacy of a silver alginate and a silver carboxymethyl cellulose dressing in preventing the growth of burn wound isolates grown in the biofilm phenotypic state. The antimicrobial activity of both silver dressings was evaluated using a CZOI assay, conducted on MHA. For antimicrobial efficacy testing on microorganisms in the biofilm phenotypic state poloxamer, known to induce a biofilm phenotypic state, was applied to Mueller Hinton Broth. Thirty-one Gram-negative isolates were evaluated and 58% were found to have reduced sensitivity to silver when grown as a biofilm, compared with growth in the nonbiofilm phenotypic state. Similarly, 64% of the Gram-positive bacteria when grown as a biofilm, were found to have reduced sensitivity to silver when compared to sensitivity in the nonbiofilm state. When a comparison of antimicrobial activity was made between a silver alginate and a silver CMC silver dressing on Gram-negative isolates grown in the biofilm phenotypic state both dressings demonstrated equivalent activity. However, antimicrobial efficacy varied and was dependant on the different strains of bacteria being tested. The findings in this research were considered to have clinical significance particularly for those wounds known to "house" biofilms with a high percentage of Gram-positive bacteria.

Slone *et al.*⁴⁶ investigated whether pH had an effect on the antimicrobial barrier efficacy of a silver alginate wound dressing on wound isolates. Twenty-five bacteria and yeasts that had been routinely isolated from chronic wounds were separately exposed to a silver alginate wound dressing

with the use of a standardized CZOI assay. The silver alginate dressing demonstrated a broad spectrum of antimicrobial barrier activity within the dressing against all wound isolates. However, at a pH of 5.5, compared with a pH of 7, the antimicrobial barrier activity of the silver alginate dressing significantly increased. For all yeasts, the CZOI ranged from 6.25 to 11 mm at a pH of 7. At a pH of 5.5, the CZOI range increased from 8.5 to 12.25 mm. For the Gram-negative isolates, the CZOI ranged from 0.75 to 6.5 mm at a pH 7, compared with a CZOI range of 2.75 to 8 mm at pH 5.5. The CZOI for the Gram-positive isolates, including MRSA, ranged from 3 to 7.75 mm at pH 7 and from 4.5 to 11.75 mm at pH 5.5. For all isolates tested, excluding one strain of *C. albicans* and one vancomycin-resistant *Enterococcus* strain, lowering pH to 5.5 resulted in an improvement in the antimicrobial barrier activity within the silver alginate dressing. Based on these initial *in vitro* findings, it is possible to suggest that there may be benefits to maintaining an infected or recalcitrant wound in a slightly acid (pH 5.5) environment. In particular, doing so may lead to an enhanced antimicrobial barrier effect of silver, a quicker reduction in the wound microbial bioburden, and therefore a reduction in the need for prolonged antimicrobial use. However, more *in vitro* and *in vivo* studies would be warranted to further substantiate these claims.

Khan *et al.*⁴⁷ demonstrated that alginate oligosaccharides (OligoG) can impair the growth of bacteria. This effect has previously been reported to be bacteriostatic and a result of the ability of alginates to chelate cations such as calcium and iron. The authors also reported that OligoG inhibited biofilm formation and caused the disruption of 24-h biofilms. More recently, Powell *et al.*⁴⁸ investigated the mechanical disruptive properties of alginate OligoG on biofilms. The researchers employed the use of atomic force microscopy and rheometry to measure biofilm disruption and concluded that following exposure of the biofilm to OligoG disruption of the biofilm occurred.

A recent clinical study by Beele *et al.*³ reported on the clinical signs and symptoms of wounds at risk of infection, that are critically colonized or biofilm infected. The researchers investigated the antimicrobial-performance of an ionic silver alginate/carboxymethyl cellulose (SACMC) dressing, in comparison with a nonsilver calcium AF dressing, on chronic wounds. Thirty-six patients with wounds, considered clinically to be critically colonized (biofilm infected), were recruited to receive either an SACMC dressing or a nonsilver calcium

AF dressing. The researchers reported that the SACMC group appeared to show a statistically significant improvement to healing over the 4-week study period when compared with AF controls. A further study by Trial *et al.*⁴⁹ compared the efficacy of a silver alginate matrix with a nonsilver alginate dressing in patients with locally infected chronic or acute wounds. This was a prospective, open label and randomized study. Local signs of infection and the bacteriological status for each wound were used to measure the dressing's efficacy. The study concluded that the local signs of infection, tolerance, and usefulness of each dressing were similar. The researchers also reported that the silver alginate matrix dressing did improve the bacteriological status of the wound; however, no reference was made to the efficacy on biofilms.

Another recent study by Woo *et al.*⁵⁰ reported on the use of a silver alginate powder in managing chronic wounds that exhibited clinical signs of critical colonization, or more specifically biofilm infected. The study was a 4-week randomized controlled trial (prospective, open label) with an end point of changes in signs of critical colonization and wound surface area. The conclusion drawn was that the silver alginate powder was deemed effective in the treatment of wounds that had an increased microbial bioburden.

SUMMARY

To date, based on the review of research articles available the efficacy of silver *per se* on biofilms has a mixed outcome. In general, ionic silver at high concentrations demonstrates some efficacy on *in vitro* biofilms. However, little substantiated evidence exists with respect to the *in vivo* environment. This is principally due to the fact that biofilms are poorly diagnosed clinically in the wound. Consequently, there is a significant need for further studies, in both *in vitro* and *in vivo* environments, demonstrating the efficacy of silver impregnated wound dressings, in particular silver alginates and next generation dressings on biofilms. This will ensure that future wound dressings are developed that will fulfill the fundamental basics of antimicrobial interventions and therefore positive clinical outcomes.

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Professor Steven Percival holds a PhD in microbiology and biofilms, a BSc in Applied Biological Sciences, Postgraduate Certificate in Education, diploma in Business Administration, an MSc in Public Health, and an MSc in Medical and Molecular Microbiology. Early in his career, Steven held R&D positions in the Department of Biotechnology, British Textile Technology Group (BTTG) Plc, followed then by 6 years as a senior university lecturer in medical microbiology and Head of the Biofilm Research Group and later the positions of Director of R&D and Chief Scientific Officer at Aseptica, Inc., and senior clinical fellowships at the Centers for Disease Control, Atlanta, and Leeds Teaching Hospitals Trust, Leeds. More recently, Steven held senior management R&D and innovation positions at Bristol Myers Squibb, ConvaTec, Advanced Medical Solutions Plc and held an Honorary Professorship in the medical school at West Virginia University. In 2011, Steven joined Scapa Healthcare Plc as Vice

TAKE-HOME MESSAGES

- The risk of a infection in a chronic wound is significantly heightened by microorganisms growing as a biofilm
- Silver is incorporated into wound dressings, including alginates, for use in the treatment of at risk, often clinically referred to as critical colonized, or infected chronic wounds
- Silver has been reported to demonstrate efficacy on planktonic microorganisms both within the *in vitro* and *in vivo* environments
- Silver has an effect on some biofilms but this effect appears to vary in different environments

President of Global Healthcare R&D and in 2012 was awarded the position of Honorary Professor in Microbiology and Anti-infectives at the University of Liverpool, United Kingdom. He has written over 300 scientific publications and conference proceedings, authored and edited 8 textbooks, and provided over 100 presentations globally. He is an editor of the Journal of Medical Microbiology and associate editor of BMC Microbiology and holds a number of honorary and advisory board roles.

Sara McCarty gained her BSc in Biomedical Sciences in 2008 from the University of Chester, United Kingdom. Since then, Sara has undertaken positions as a research technician and enjoyed gaining experience within the field of dermatology. She is currently completing a PhD in the role of proteases in wound healing at the University of Liverpool, United Kingdom.

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Abbreviations and Acronyms

AF = alginate fiber
 CMC = carboxymethyl cellulose
 CZOI = corrected zone of inhibition
 MHA = Mueller Hinton agar
 MMP = matrix metalloproteinase
 MRSA = methicillin-resistant *Staphylococcus aureus*
 MSSA = methicillin-sensitive *Staphylococcus aureus*
 OligoG = alginate oligosaccharides
 SACMC = alginate/carboxymethyl cellulose