The management of wounds using Silvercel hydroalginate

Many factors result in delayed wound healing, one of which is infection. A variety of wound dressings with antimicrobial properties are now available. Practitioners need to select an antimicrobial dressing most appropriate for the wound being treated, while considering factors such as exudate management and maintenance of a moist wound healing environment. Silvercel, a new hydroalginate dressing with silver (Johnson & Johnson Wound Management, Ascot) appears to offer enhanced moisture management through hydroalginate technology along with the antibacterial potency of silver. This article looks at the role of silver and Silvercel in wound management.

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KEY WORDS
Silvercel
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Antimicrobial
Moist wound healing
Exudate management

Normal wound healing in adults follows an ordered progression of events, which ultimately results in wound closure. In some cases, however, wound closure may not occur. There are many reasons why a wound will fail to heal, including both local (e.g. the presence of a foreign body or infection) and systemic (e.g. malnutrition or diabetes) factors. In a slow-healing or non-healing wound, it is important for the practitioner to consider all underlying pathologies and to treat them appropriately. While it is recognised (Kingsley, 2002) that no single dressing can provide all the answers to the problems and requirements of a wound throughout its life, effective treatments can be prescribed for wounds that become infected or critically colonised with micro-organisms.

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Micro-organisms are very likely to be present in all wounds but will vary in both type and quantity. Non-healing chronic wounds, e.g. leg ulcers and pressure ulcers are usually colonised with a number of species, many of which can be potential pathogens (Scanlon and Dowsett, 2002). When the microflora of the wound become imbalanced, the normal wound healing process is interrupted, resulting in a non-healing and deteriorating wound, which can ultimately lead to systemic infection if left untreated. Unfortunately, with increasing resistance, the treatment of infected wounds with antibiotics is becoming more and more problematic. It is possible, however, to reduce the wound bioburden to avoid systemic infection by the use of topical antibacterial agents such as silver and iodine (White et al, 2001).

Background to the medicinal use of silver

Silver is a broad-spectrum antimicrobial for controlling a wide range of bacterial, fungal, and viral pathogens (White, 2001) and has a long history of use. In a historical overview, White (2001) noted how it has been used medicinally since the 19th century for conditions such as eye infections, burns and postoperative sepsis, but how interest in it declined with the advent of antibiotics, penicillin and sulphonamides. Interest in the antibacterial properties of silver was renewed in the 1960s, and today, it is being used again, mainly in the management of burns. Silver is also being increasingly used as an antimicrobial in medical devices such as wound dressings, catheters, stents, and external fixation pins.

The first wound dressing containing silver, available since 1989 in the UK and across Europe, was Actisorb Plus (now known as Actisorb Silver 220; Johnson & Johnson Wound Management, Ascot), an activated charcoal cloth with silver.

Since that time there have been numerous new silver dressings launched on the market of Europe and North America. These vary in their structure and composition, and, in the chemical nature of the silver source; elemental (metallic) or compound (silver salt). This article will concentrate on the very newest of these dressings — Silvercel (Johnson & Johnson Wound Management, Ascot).

Silver in wound management

Two forms of silver are used in topical wound dressings: compound (silver salts) and elemental (metallic). Both forms of silver release silver ions into the wound, and this is what provides the antimicrobial effect.

The mechanism by which this is acheived differs for each form. Silver compound, on exposure to water (as found in wound fluid), rapidly dissociates giving rise to silver ions ▸▸

Figure 1. Silvercel hydroalginate dressing with silver.

Table 1.
Silvercel hydroalginate with silver: size availability

Size	Number of dressings per box
5x5cm	10
11x11cm	10
10x20cm	5
2.5x30.5 cm	5

(Ag^+). Elemental silver, on the other hand, is virtually insoluble, and needs to form an intermediate stage. This is usually silver oxide (AgO) that is formed on exposure to air or water (as present in the wound fluid). It is the silver oxide that then dissociates into silver ions.

White (2001) in a review of the use of silver in wound management noted that for silver-containing dressings to be effective it is important that the solubility of silver is low (i.e. that it does not solubilize into the wound quickly but does so slowly over a period of days thereby providing sustained release and prolonged antimicrobial activity). He suggested that this slow release ensures there is no bolus dosing that could give rise to transient high silver levels in tissue, blood or urine, which could increase the risk of systemic toxicity.

Healthcare practitioners are rightly concerned about using products that are linked with a risk of toxicity, however, the toxicity attributed to silver is usually associated with the silver carrier (used to deliver or stabilise the silver) rather than the silver ions, e.g. nitrate from silver nitrate or sulphadiazine from the silver sulphadiazine creams (Demling and DeSanti, 2001). These effects are therefore not regarded as being applicable to modern wound dressings (Cutting, 2001).

The recent development of a number of wound dressings that contain metallic silver and provide a sustained release of low but effective levels of ionic silver can be seen as a way of reducing the risk of silver toxicity. Cutting (2001) also observed that most negative reports on elemental silver were published before 1940 and suggested that the bad press associated with the use of silver relates to the use of silver nitrate solution which may cause staining and a burning sensation on the skin.

The systemic absorption of deposits of silver which can result in a cosmetic problem of skin discolouration (which can be permanent), is known as argyria. It arises due to the deposition of minute granules of silver or silver sulphide in the dermis around the basement membrane and sweat ducts (at least 10g of silver needs to be absorbed to observe argyria). It is usually associated with prolonged non-medical environmental exposure to silver metal. There is no current evidence that modern silver wound dressings result in detectable systemic absorption of silver through chronic wounds. One case of argyria has been reported in a patient treated with a modern nanocrystalline silver dressing for 30% TBSA burns of the legs and abdomen (Lansdown and Williams, 2004). There have been no reports of argyria or other toxic responses with silver hydroalginate in clinical use.

As for the development of silver resistance, it is recognised (Lansdown, 2002) that most, if not all, of the sustained silver ion release products are effective against methicillin and vancomycin resistant strains and that no resistant strains have been encountered. While the potential for development of resistance to silver exists, it has been suggested that this is low. Bacteria have been exposed to silver for four billion years with no widespread resistance to date, whereas widespread resistance to antibiotics has developed within the last 60 years (Percival and Bowler, 2005).

Proposed mechanism of action of silver

The antimicrobial effects of silver ions have been attributed to four different mechanisms (Thurman and Gerba, 1989):

- Interference with bacterial electron transfer
- Binding to bacterial DNA and spores thus increasing the stability of the double helix and impairing cell replication
- Binding to the bacterial cell membrane causing structural and receptor function damage

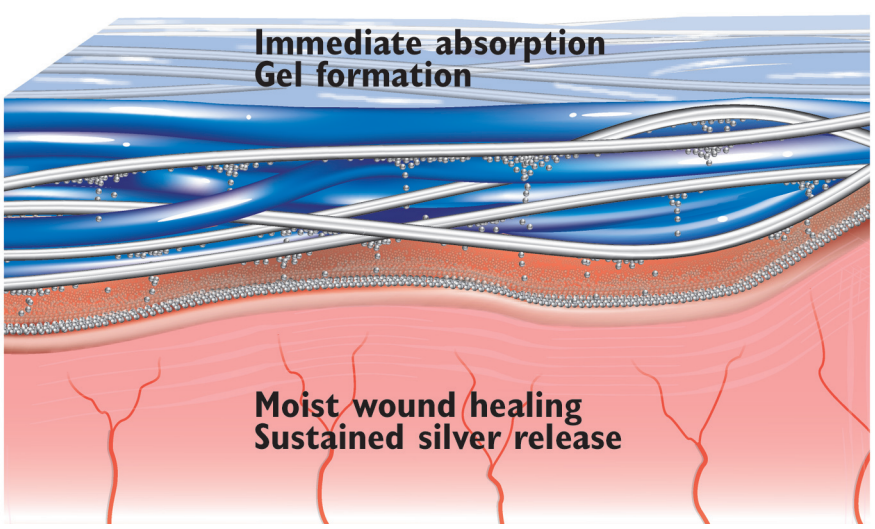

Figure 2. The mode of action of Silvercel.

- Formation of insoluble, metabolically ineffective compounds with bacterial anions, sulphydryl groups as in methionine and thiolated nucleotides, histidine and enzymes.

Silvercel

Silvercel hydroalginate with silver is a new product from Johnson and Johnson Wound Management, Ascot. It is indicated for use in the management of all moderate to heavily exuding partial- and full-thickness chronic wounds. The dressing consists of a sterile, non-woven pad composed of high G (guluronic acid) calcium alginate, carboxymethylcellulose (CMC), and silver-coated fibres (*Figure 1*). It combines the moisture management properties of the alginate and CMC with the broad-spectrum antimicrobial action of silver ions. Silvercel is available in both pad and rope format in a variety of sizes (*Table 1*) and is available for use in both hospital and community settings in the UK, as well as in other European countries and the US.

Hydroalginate technology

Hydroalginate is a highly-absorbent material that maintains an optimal moist wound healing environment in exuding wounds. Its unique composition is a mixture of high G calcium alginate and CMC. The hydroalginate material increases its tensile strength when in contact with wound exudate, facilitating dressing removal from exuding wounds.

Mode of action

The absorbency of Silvercel is attributed to the hydroalginate component of the dressing, which also maintains a moist wound healing environment.

Table 2. Absorbency of dressings: SMTL method TM101 based on BP1993 monograph for alginate dressings

Dressing	Absorbency g of fluid/100cm^2
Hydroalginate	22.9
Hydrofibre	16.3
Alginate	22.7

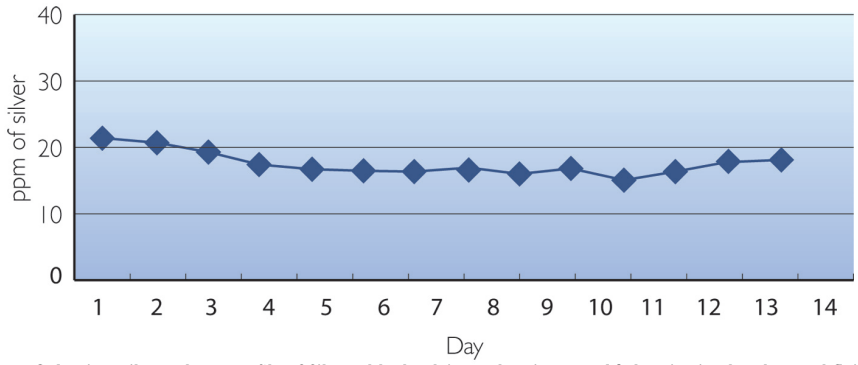

Figure 3. In-vitro silver release profile of Silvercel hydroalginate dressing over 14 days in simulated wound fluid.

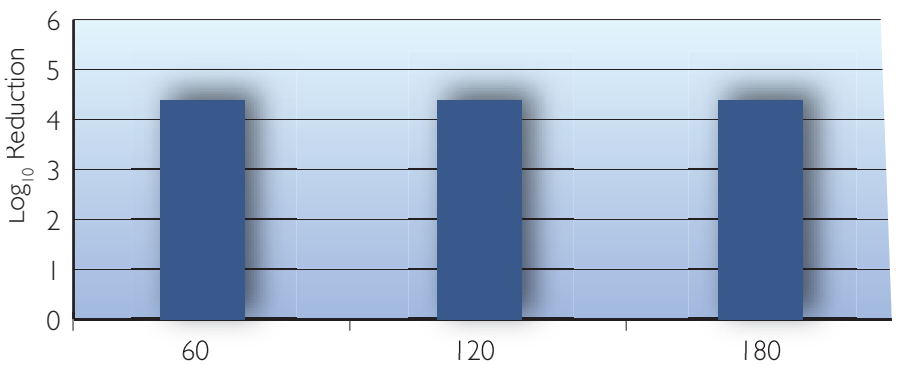

Figure 4. Silvercel dressing Log_{10} reduction *Pseudomonas aerugenosa* post-14 day challenge in simulated wound bed.

The silver fibres kill a broad spectrum of microorganisms associated with bacterial colonisation and infection of wounds. Silvercel uses elemental silver, which releases ions in a sustained and controlled manner, allowing access to all wound areas, including into cavities (*Figure 2*).

Absorption and gelling properties

Alginates have found their use in a wide variety of acute and chronic wounds (especially wet), since their introduction into wound care practice.

Alginic acid is a hydrophilic, high molecular weight polymeric acid that is derived from seaweed and is readily formed into fibres. Alginate is a polymer composed of a mixture of two monomer units in varying proportions. These are:

- Alpha-L-guluronic acid (G type)
- Beta-D-mannuronic acid (M type).

Alginate that consists largely of G-type monomer units is referred to as high G alginate. Silvercel dressing utilises high G calcium alginate (JJWM, 2003).

High G fibres are not as absorbent as high M, and do not form a gel, but they retain their structure more and do not break down and gel in the presence of sodium ions. When in contact with wound fluid, there is an exchange of sodium ions from the wound fluid with calcium ions on the high-G calcium alginate. In order to increase the exudate handling properties of Silvercel, CMC has been incorporated which gives the dressing increased absorbency, similar to a high M alginate (JJWM, 2003). The absorbency properties of the hydroalginate have been tested in-vitro and have been shown to be superior to a hydrofibre dressing (*Table 2*) (SMTL[Surgical Materials Testing Laboratory]/JJWM, 2003).

The alginate and CMC combination also provide a certain level of gelling of the hydroalginate fibres, designed to maximise the conformability of the dressing to the wound contours and to ease dressing removal.

Silvercel is indicated for use on all moderate to heavily exuding

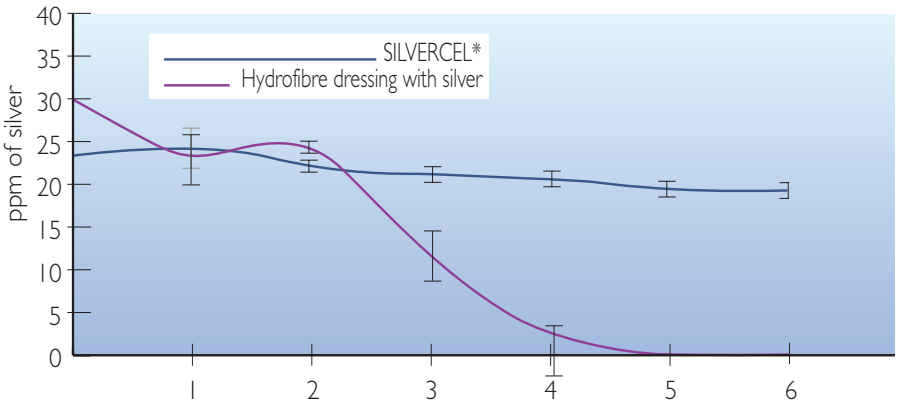

Figure 5. In vitro silver release in simulated wound fluid.

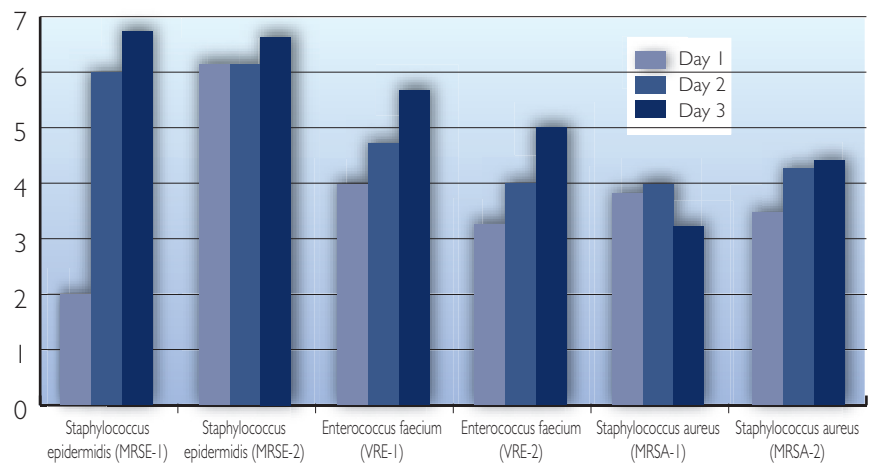

Figure 6. Average zone of inhibition around Silvercel hydroalginate dressing, in mm.

chronic wounds. As wound conditions improve and exudate levels decrease, it may be preferable to switch to a more appropriate dressing.

Silver release profile

The release of silver ions from the Silvercel hydroalginate dressing is a dynamic process that is triggered by application to an exuding wound with micro-organisms present. An in-vitro comparison of two elemental silver dressings in simulated wound fluid at 37°C demonstrated that silver release stopped when saturation was reached (15–25 ppm) (Addison et al, 2004). Maintaining this level of saturation is a constant process. The silver ions are taken up and used within the wound fluid, promoting further release of silver ions from the dressing to achieve saturation again. It is therefore suggested, that it is the wound environment that controls the release of the silver ions from Silvercel, keeping the release controlled and balanced. There is no depositing of high doses of silver ions from dressings impregnated with elemental silver, such as Silvercel. The silver-coated fibres within the dressing provide a reservoir of silver ions and data (*Figure 3*) confirms that these are released at effective antimicrobial levels, in-vitro, for at least 14 days in simulated wound fluid, with the simulated wound fluid being changed daily (Addison et al, 2004).

At the end of the 14-day study period in this in-vitro test, the samples were tested for their antimicrobial activity against *Pseudomonas aeruginosa* in a Log_{10} reduction test over three hours. The data showed that even after 14 days of silver release in simulated wound fluid (which was changed every 24 hours), the dressing samples demonstrated a 5 Log reduction, i.e. essentially no viable bacteria remained (Addison et al, 2004).

It is suggested that slow-release products are ideal at both decreasing bacterial burden as well as diminishing or eliminating excess exudate (Falanga, 2001) and that silver-impregnated fabrics that continuously release silver ions into the wound have the greatest antibacterial effect (Lansdown, 2002). A further in-vitro study compared the silver release in simulated wound fluid of a silver compound dressing with an elemental silver dressing, Silvercel hydroalginate. Samples of dressings were placed in fresh simulated wound fluid each day over seven days and the silver release was determined by atomic absorption (*Figure 5*) (Addison et al, 2005).

The elemental silver product, Silvercel hydroalginate, provided a continuous sustained in-vitro release of silver ions over the entire test period. The silver compound product, a hydrofibre dressing, showed diminished silver ion release between days 3–4. The elemental silver provides a reservoir of silver ions which is likely to be far greater than the potential wear time of the dressing. For dressings containing silver compounds, the longevity of silver ion release may be more difficult to predict. In vitro with wound fluid changed only once every 24 hours, the silver compound product's silver ion release fell to residual levels before the end of the test period. In a wetter/heavily exuding environment there may be potential for the release to stop even sooner.

Elemental silver dressings typically have much higher levels of silver within the product (8–20%) than dressings containing silver compounds (0.02–1.5%). The actual parts per million (ppm) of silver released from both types of dressings is approximately the same (15–25 ppm) in simulated wound fluid during the first few hours. However, the two products differ in the length of time that they can sustain silver release. As elemental products have a higher percentage of silver within the dressing, not necessarily linked to a higher concentration of silver ions released, the time that they can sustain silver ion release appears to be greatly extended. The silver that is not utilised for silver ion release is removed with the dressing.

Antimicrobial activity

It is generally regarded that silver is a broad spectrum anitmicrobial. In-vitro data on the antimicrobial activity of Silvercel has confirmed this effect against a wide range of microorganisms (>150 human clinical isolates tested), including *Pseudomonas aeruginosa*, *Escherichia coli, Streptococcus pyogenes*, *Staphylococcus aureus, Staphylococcus epidermidis, Klebsiella pneumoniae* and *Candida albicans* (Addison et al, 2005). Testing was conducted using the zone of inhibition test, where a 2.5cm x 2.5cm sample of the dressing is placed on an agar plate pre-inoculated with the microorganism under test. The zones were read after 24 hours incubation, then again at 48 and 72 hours, with the dressing sample being transferred to a new-freshly prepared pre-inoculated agar plate at each timepoint. The zone of inhibition was measured in mm.

These in-vitro tests included assessing the repeat challenge zone of inhibition over a three-day period for antibiotic resistant strains including *Staphylococcus epidermidis* (MRSE), *Staphylococcus aureus* (MRSA), *Enterococcus faecium* (VRE) and *Enterococcus faecalis* (VRE) where Silvercel was shown to have a bactericidal effect on these organisms over a three-day period following repeat challenge (*Figure 6*)(Addison et al, 2005).

Wet tensile strength

It has been demonstrated (SMTL / JJWM, 2003) that Silvercel hydroalginate dressing has a very high wet tensile strength not usually associated with alginates or hydrofibres. The data shows that the wet tensile strength of Silvercel increases by over 50%, permitting the dressing to be removed easily from the wound (*Figure 7*).

Clinical evidence

A randomised, multi-centre, clinical trial is in progress to assess the impact of Silvercel in the management of chronic wounds with signs of local infection and it is expected that the results will be available during 2005. Initial evidence of the effectiveness of Silvercel in managing critically colonised wounds comes from case reports. Several have been documented to date (JJWM, data on file, Case Studies) and two are described here to provide an insight into its use on a chronic venous leg ulcer and a pressure ulcer over a 28-day period.

Case report 1

A 93-year-old woman with a right venous leg ulcer and also suffering from malnutrition and coronary insufficiency, had Silvercel applied to her leg ulcer over a period of 28 days. She had a previous history of leg ulceration and had also undergone recent orthopaedic surgery after which the current leg ulcer developed. On assessment, the wound measured 4.5 cm x 2.6 cm, was heavily exuding with signs of inflammation and maceration of the surrounding skin. The wound was cleansed with saline solution and redressed using Silvercel 11cm x 11cm dressing under compression bandaging (*Figure 8a*).

By Day 7, a clinical improvement was seen with a decrease in the amount of exudate and commencement of epithelialisation. Wound size had reduced by 42.5% and the dressings were well-tolerated and accepted by the patient. Only seven days later the wound size had reduced by 70% to 3.1cm x 1.1cm, the amount of exudate continued to reduce and epithelialisation to increase. There were signs of inflammation of the wound and surrounding tissue at this timepoint (Day 14), which had all disappeared by Day 28. There was a further reduction in exudate levels. By the end of the evaluation, the wound size had reduced by 83.1% to 2cm x 1cm (*Figure 8b*).

Case report 2

A 93-year old man, with a history of coronary insufficiency and Parkinson's disease, presented with a deep sacral pressure ulcer. The ulcer was Grade 3 and had been present for two months. On assessment, the wound measured 5.5 cm long x 2 cm wide, was necrotic with extensive fibrin deposits, exuding, malodourous and painful. There was erythema, eczema and trophic changes of the surrounding skin (*Figure 9a*). Previous treatment was with a sterile hydrocellular dressing. After initial assessment, the wound was cleansed with saline solution and a Silvercel 11cm x 11cm dressing applied. Hydrating gel and cream were applied to the surrounding skin.

By day 7, there was a significant decrease in exudate, odour and necrosis, with the appearance of some granulation tissue (*Figure 9b*). After a further 14 days (day 21), there was no longer any odour. The necrotic tissue and fibrin deposits had also disappeared, with significant ▸▸

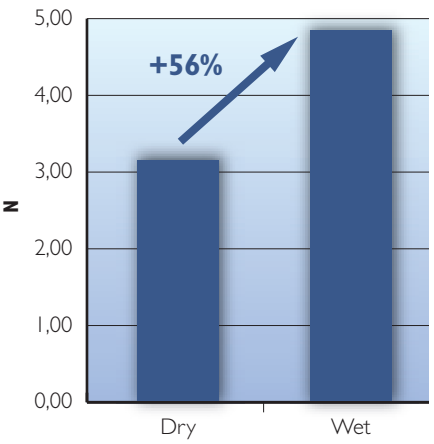

Figure 7. The tensile strength of Silvercel hydroalginate dressing.

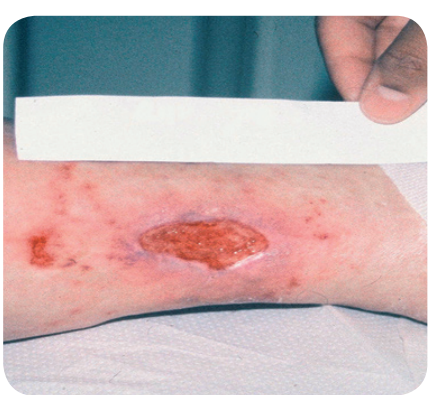

Figure 8a. Venous leg ulcer at presentation.

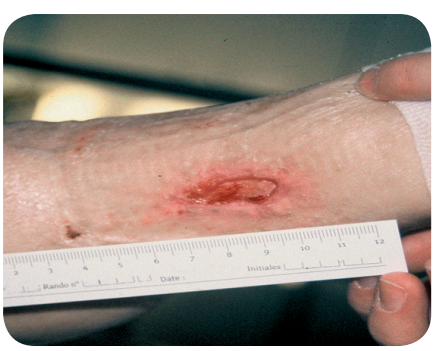

Figure 8b. Venous leg ulcer at day 28 of dressing with Silvercel.

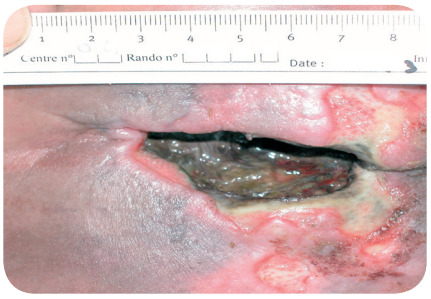

Figure 9a. Grade 3 pressure ulcer at presentation.

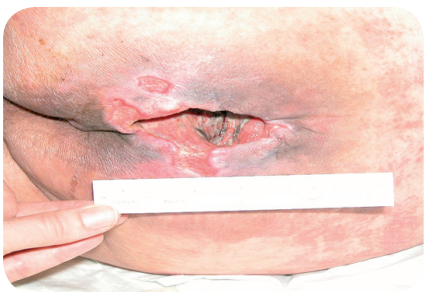

Figure 9b. Grade 3 pressure ulcer at day 7 of dressing with Silvercel.

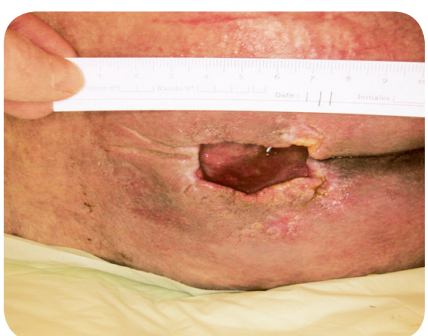

Figure 9c. Grade 3 pressure ulcer at day 28 of dressing with Silvercel.

amounts of new tissue growth and consequent reduction in wound area and depth. The amount of exudate was also regarded as having decreased significantly. By the end of the evaluation (day 28), the wound was assessed as being healthy, with no further signs of infection. Inflammation had decreased and the wound had reduced in size by 52% to measure 4.1cm x 1.3cm (*Figure 9c*). It was noted that the dressing was well-tolerated by the patient and easy to remove and apply.

Conclusions

Increasing resistance to antibiotics has meant that the treatment of infected wounds is becoming more and more problematic. The recent introduction of a number of dressings containing silver into the wound care market is a reflection of the interest in topical antimicrobial agents in reducing wound bioburden, in order to avoid systemic infection. When choosing an antimicrobial dressing, practitioners need to take into consideration other factors such as ability to handle exudate and maintenance of moist wound healing. Clinical evaluation of the hydroalginate silver-releasing dressing is underway in a randomised, multi-centre clinical study. Initial case reports have shown that the hydroalginate technology of Silvercel is beneficial in managing exudate and encouraging moist wound healing and that it may help to promote wound cleansing. Silvercel may become a useful addition to the range of wound care products available. WUK

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Key Points

- Silvercel combines silver and alginate with carboxymethylcellulose to provide the benefits of both exudate handling to encourage moist wound healing and a broad spectrum antimicrobial.
- The wound environment controls the release of the silver ions from Silvercel. keeping the sustained release controlled and balanced at effective levels..
- Silvercel Hydroalginate is effective against a wide range of microorganisms (>150 human clinical isolates tested).
- The tensile strength of Silvercel increases by more than 50% when wet, making it easy to remove from the wound
- Silvercel is intended for use in the management of all moderate to heavily exuding partial- and full-thickness chronic wounds.