‘Super’ silver: the answer to wound infection and biofilm management in venous leg ulcers?

In order for silver to be biocidal it must be in an ionic form. The higher the ionic state (the more electrons missing) the greater the ability of the ionic silver to interfere or react with the normal function of a microorganism’s cell. Most silver dressings generally contain singly ionic silver (Ag^{1+}), making them effective for the management of infected wounds. This article presents the results of a service evaluation in which a new patented silver wound dressing (KerraContact Ag) that uses silver in its most active state (Ag^{3+}) to facilitate fast and effective bacteriocidal activity, was used on patients with venous leg ulceration. Results demonstrate that the dressing both stimulates healing and reduces the signs of infection.

KEY WORDS
- Biofilm
- Infection
- Service evaluation
- Silver oxysalts
- Venous leg ulceration

White (2015) suggests that in conjunction with appropriate compression therapy, when a venous leg ulcer (VLU) is infected, there are four main criteria that a dressing will need to meet. It has to:

- Provide sustained broad spectrum antibacterial action
- Be efficacious against biofilm
- Be efficacious in the presence of exudate
- Be safe.

Along with other topical antimicrobial agents, dressings that contain elemental silver or a silver-releasing compound have been developed for the management of infected wounds. However, their use sparked much debate about their efficacy (Vermeulenet al, 2007; Storm-Versloot et al, 2010) safety and cost-effectiveness (Michaels et al, 2009). A lack of understanding about the mode of action of silver dressings may have led to their inappropriate use; for example, continued use after the infection had cleared or as prophylaxis against infection, thereby increasing local wound dressing costs.

In addition, not all silver dressings are the same; this can make choosing the correct dressing difficult. Silver can either coat the dressing, be incorporated into the structure of the dressing, or both. It is present in dressings in the following forms (International Consensus, 2012):

- Elemental silver such as silver metal, nanocrystalline silver
- An inorganic compound such as silver oxide, silver sulphadiazine (SSD, an antibiotic)
- An organic complex such as silver-zinc allantoinate, silver alginate.

Silver ions bind to the cell membrane and disrupt the cell wall causing it to leak, or they bind to proteins and interfere with energy production, enzyme function and cell replication. They are active against a broad range of bacteria, fungi and viruses including methicillin-resistant *Staphylococcus aureus* (MRSA) and *Vancomycin-resistant Enterococci* (VRE) (International Consensus, 2012).

SILVER OXYSALTS

In order to kill bacteria, silver requires some chemical change; it needs to both lose electrons and be ionic — the fewer the electrons, the more reactive the silver. A silver oxysalt (any salt of an oxyacid) contains silver in its most active state; dressings containing silver oxysalts have three electrons missing (Ag^{3+}), whereas other silver dressings are only missing one (Ag^{1+}) (Spina, 2012).

KerraContact Ag, a ground-breaking, patented silver wound dressing with Ag Oxysalts Technology (Crawford Healthcare) is the first dressing to use silver in its most active state (Lemire et al, 2015a). This facilitates fast and effective bacteriocidal activity (Thomason and Beasley, 2015) and an ability to disrupt biofilms and prevent reformation within 24 hours of application (Thomason and Beasley, 2016).

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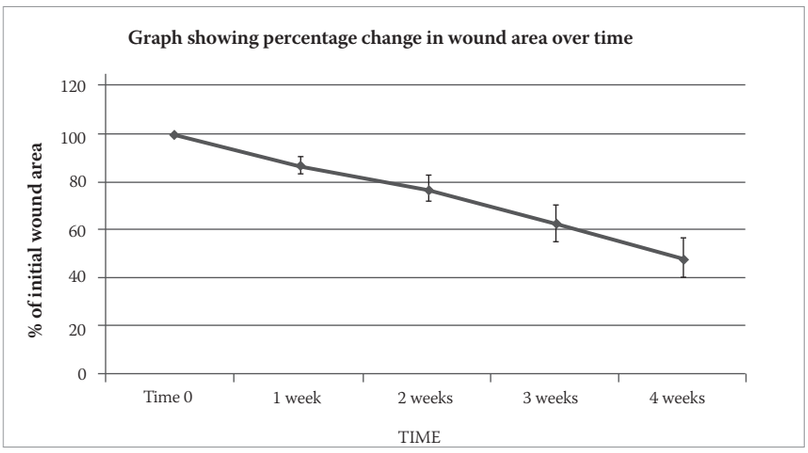

Figure 1. Graph showing % change in mean wound area over time

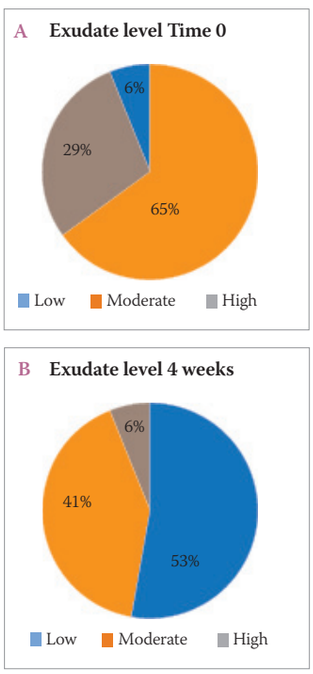

Figure 2. Exudate levels at baseline (Time 0) (a) and at week 4 (b)

This article reports on the efficacy of this new product, in the management of venous leg ulcers.

STUDY

The main aim of this study was to evaluate the ability of KerraContact Ag dressing to reduce the clinical signs of infection in venous leg ulcers.

This four-week clinically-based evaluation involved 15 patients (7 male and 8 female) with a total of 17 wounds (two patients had two wounds) who had consented to participate in the study. Ethics committee approval was not required as this was a service evaluation. Wound surface area ranged from 1 cm^2–20 cm^2. The mean age of participants was 73 years (range 39–92 years of age); all had an ankle brachial pressure index (ABPI) >0.7 and were able to ambulate in their home environment or clinic with or without mobility aids. All patients were on compression bandaging regimens both prior to and during the study.

It is recognised that a diagnosis of infection is made by assessing and identifying the clinical signs and symptoms of infection (World Union of Wound Healing Societies, 2008). Accordingly, these were considered as inclusion criteria.

A clinical diagnosis of infection or suspicion of infection was judged by the presence of at least two of the following criteria:

- Increased exudation (increase in exudate level over the past 7 days)
- Purulence
- Odour
- Pain caused by wound (using VAS scale)
- Friable dull granulation tissue
- Erythema >1–2 cm from wound margin (World Union of Wound Healing Societies, 2008).

Wounds were assessed and photographed once per week and all relevant data recorded. The wound was photographed together with patient identifier and ruler to assess changes in wound dimensions over time. KerraContact Ag was applied as per manufacturer's instructions.

Data were collected assessing the following:

- Wound size/area
- Level and type of wound exudate
- Level of odour
- Type of pain and pain level on application, wearing and removal of dressing
- Integrity of peri-wound skin
- Appearance of dressing on removal (to ascertain that it has remained intact upon removal)
- Wear time of dressing (KerraContact Ag remains active for seven days after application, thus ensuring maximum time in compression)
- Wound pH.

RESULTS

Wound size

Figure 1 shows the reduction in mean wound area as a percentage of initial wound area at time 0 to week 4. At week four, the mean percentage had reduced to 48.4% of the original size (+/- SEM 8.14), a 52% reduction in area.

Level and type of wound exudate

The data in *Figures 2a* and *2b* show the exudate levels at week 0 (baseline) and week 4 respectively. At time 0 only 6% of the wounds were classed as having a low exudate level, whereas the remaining 94% were classed as having moderate to high exudate. After 4 weeks, only 6% of wounds were classed as having a high exudate level and 53% were classed as having low exudate levels.

At week 0, no wounds had serous exudate, 5.88% had haemoserous exudate and 94.1%, had purulent exudate. At week 4, these percentages were 82.4%, 0% and 17.7% respectively, indicating a reduction in infection.

Odour

At the study start, 18% of the wounds had significant odour, 76% had some odour and 6% had no odour. At study completion, 82% of wounds had no odour and 18% had some. There was a reduction of 93% of participants who initially presented with odour. Odour is cited as a socially isolating aspect of wound management and can have a negative effect on the patients wellbeing (Gethin et al, 2004).

Pain

Of the 17 wounds, only three were described as pain free. Participants described their pain as burning, stabbing, aching, continuous, intermittent or itching, or any combination of these at week 0.

Using a scale of 1–10, pain was also assessed at the following:

- Upon application of the dressing
- Wearing of the dressing
- Upon removal of the dressing.

Figure 3 shows that pain levels decreased at these time points from week 0 to week 4.

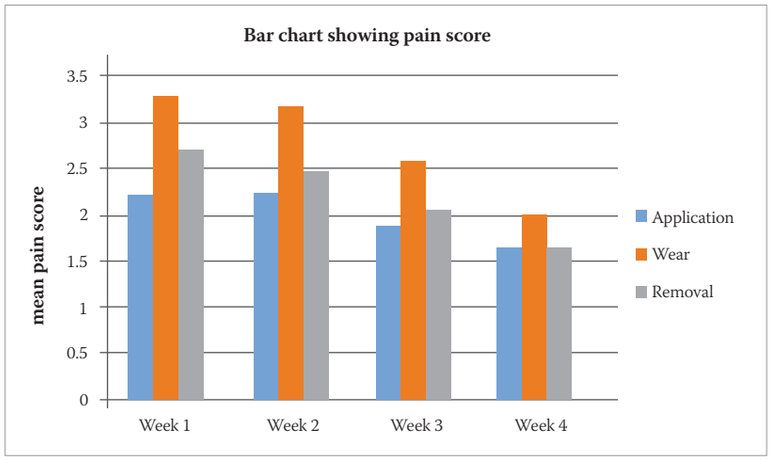

Figure 3. Pain levels from week 0 to week 4

Periwound skin

The following parameters relating to periwound skin condition were assessed: maceration, oedema, and erythema at each assessment point. The results for week 0 and week 4 are shown in *Figures 4a* and *4b*.

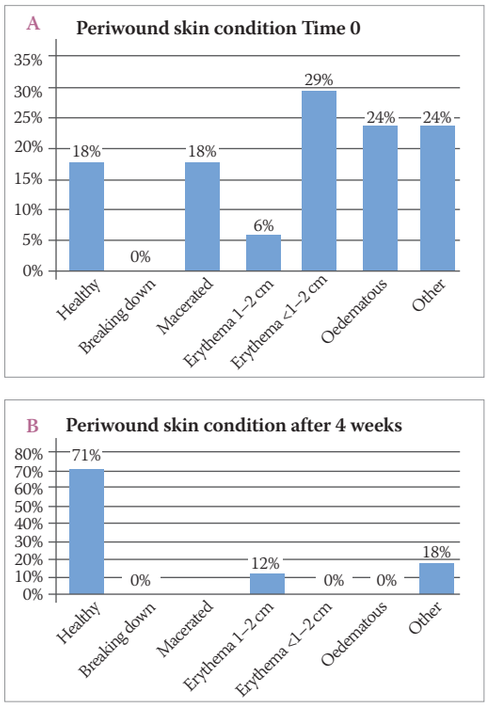

Figure 4. Condition of periwound skin at baseline (time 0) (a) and at week 4 (b)

Appearance of dressing upon removal

The appearance of the dressing on removal was rated by the clinician as:

- Applied
- Partially adhered
- Not in situ
- Desiccated.

The 17 wounds were assessed four times after the initial time zero assessment, giving 68 individual time points to assess the wear time of the dressing. The data shows that the dressing performed well as it remained integral as originally applied. There were a few cases of adherence, although this was resolved soaking the dressing off.

Wear time

The 17 wounds were assessed four times after the initial time zero assessment, giving 68 individual time points to assess the wear time of the dressing. The majority of dressings were changed at 3, 4 and 7 days (*Table 1*).

Wound pH

The pH level of a wound can be a clinical indication to healing (Sharpe, 2009). In this study litmus paper was applied to the wound fluid at dressing changes.

Table 1: Dressing wear time (in days)				
Patient	1 week	2 week	3 week	4 week
1	7	3	5	4
2	3	7	7	7
3 (wound 1)	2	3	3	3
3 (wound 2)	4	7	4	4
4	3	3	3	4
5	4	3	3	7
6	3	7	7	7
7	4	4	4	4
8	4	4	4	4
9	4	4	2	2
10	7	7	4	6
11	3	7	3	7
12	3	4	7	7
13 (wound 1)	7	7	4	4
13 (wound 2)	7	7	4	4
14	7	7	4	7
15	5	7	7	7

A pH of 7 represents neutral; a pH below 7 is acidic representing a higher hydrogen concentration, while a pH value above 7 is termed base or alkaline and represents a lower hydrogen concentration.

The pH values were assessed at each time point and show that there was little change in pH value, with most being just above neutral (*Table 2*).

DISCUSSION

The results from this study indicate that KerraContact Ag meets White's (2015) requirements of a dressing to be used for infected leg ulceration.

Considering the indicators used for the identification of infected wounds in this study, the use of KerraContact Ag resulted in:

- 52% mean healing rate after 4 weeks; predictors of healing state that if they reduce in area by 40% in 4 weeks the wound will track to healing (Kimmel, 2013)
- A reduction in moderate to high levels of wound exudate from 94% to 47%
- A 79.5% reduction in purulent exudate from week to week 4
- Decreasing levels of pain at all time-points assessed (upon application, during wear and upon removal). This reduction in pain is indicative of a decrease in infection (Cutting, 2008)
- An improvement in the condition of periwound skin. At week 0, only 18% of wounds were associated with health periwound skin, with 18% macerated, (18%), 29% erythematous >2 cm, and 24% oedematous. At week four, 71% of periwound skin was healthy, and no maceration, erythema nor oedema was noted
- A stable pH level of the wounds; this may be a clinical indication to healing; at all time points in this study, most wounds remained pH neutral or above.

The results support those of other studies. Motta et al's 50-patient multi-centre study, demonstrated a dramatic response within 7 days of dressing application. Of the 50 patients, 45% went on to heal within an average of 2.9 weeks. Clinicians reported improvement in all wound characteristics, particularly an increase in granulation tissue, and decreased inflammation and odour. In 93% of patients, pain level was reduced with no pain at dressing application or removal.

The effect of silver dressings on biofilms

Delayed healing and wound infection are considered often due to biofilm formation (Phillips et al, 2010). Lemire et al (2015a) suggest the current standardised antimicrobial dressing test methods focus on bacteria in their planktonic state and not as biofilms. This is problematic as biofilms are characteristically more tolerant to metal poisoning. Ag Oxysalts and various metal compounds were tested for their antimicrobial and anti-biofilm activity against bacterial strains, and found that a lower level of Ag Oxysalts was required. In another in vitro study with known wound pathogens, Lemire et al (2015b) found that Ag^{2+} and Ag^{3+} ions effectively eradicate organisms growing planktonically or in a mature biofilm state, and prevent biofilm reformation at low concentrations which reduces the risk of toxicity as well as the overall exposure to silver.

Beasley (2015) aimed to assess the effectiveness of KerraContact Ag at treating wound infection, specifically reporting on the reduction in signs and symptoms of infection and any changes in the wound appearance. KerraContact Ag was

used for 7 days. In the first patient, after seven days wear, the dressing was removed and a 60% reduction in thick, green slough was noted, along with a reduction in wound size, and an increase in epithelial tissue. The second patient's wound had a suspected biofilm. After seven days wear, most sloughy tissue had been removed and granulation tissue was present.

Although this study investigated the effect of KerraContact Ag on infection indicators, the data also shows that almost all wounds studied were on a healing trajectory after 4 weeks (Kimmel, 2013). This result suggests that all these wounds would go on to healing.

CONCLUSION

This study has produced positive results demonstrating that KerraContact Ag both stimulates healing, as shown in the wound area reduction data, and reduces the signs of infection, as demonstrated in the other assessments.

The results demonstrate that even when the underlying cause of the venous leg ulcer is being treated with compression therapy, wounds can become infected and the additional intervention of KerraContact Ag can facilitate healing. WUK

Table 2: Wound pH from baseline to week 4

Patient	Week 0	1 week	2 week	3 week	4 week
1	8	8	8	8	8
2	8	8	8	8	8
3 (wound 1)	8	8	8	8	8
3 (wound 2)	8	8	7	8	8
4	8	8	7	8	7
5	8	8	8	8	8
6	8	8	8	8	8
7	8	8	8	8	8
8	8	8	8	8	8
9	8	8	8	8	8
10	7	7	7	8	8
11	8	8	8	8	8
12	8	8	8	8	8
13 (wound 1)	8	8	8	8	8
13 (wound 2)	8	8	8	8	8
14	8	8	8	8	8
15	8	8	8	8	7

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