A new innovation in treating infected wounds and disrupting biofilms

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This article is based on a symposium held at the Wounds UK conference in Harrogate on 10 November 2015. The symposium explored infection and biofilm management, and presented the scientific and clinical rationale for KerraContact™ Ag, a wound dressing containing silver-based technology from Crawford Healthcare, that effectively treats infected wounds and disrupts biofilms.

We know that wound bioburden results in poor wound healing, and delayed healing leaves a wound more susceptible to infection. As such, Professor Richard White opened the symposium with the reminder that we must concede infections are often present in wounds and that they must be managed appropriately.

Where infection manifests as biofilm, bacteria are encased in an extracellular matrix and the host becomes more than 1,000 times more resistant to antimicrobial treatment. A biofilm is a complex microbial community of bacteria and fungi; microorganisms synthesise and secrete a protective matrix that attaches the biofilm firmly to a surface (Stoodley et al, 2002). The biofilm barrier protects the microorganisms from external threats (Phillips et al, 2010).

In order to combat this, fast-acting antimicrobials with broad-spectrum activity against bacteria at low toxicity levels, and efficacy against biofilms and in the presence of exudate (from watery serous through to haemopurulent) are needed. Evidence for the potency of silver as an antimicrobial has existed since the 17th century; it is known to offer improved outcomes when released and converted to ionic silver. Ionic silver is essential for effective antimicrobial activity, with dressings generally containing singularly ionic (Ag^{1+}) or metallic silver (Ag^{0}).

The symposium explored the scientific and clinical rationale for use of an innovative new silver dressing that utilises Ag^{3+}, KerraContact Ag. Helen Thomason presented results from studies conducted *in vitro* and *in vivo*, followed by Alison Beasley, who offered clinical insights into infection identification and management, and presented two patient case studies where KerraContact Ag has been used successfully.

SCIENTIFIC RATIONALE FOR KERRACONTACT AG

KerraContact Ag is an antimicrobial dressing that utilises Ag Oxysalts technology, which is formulated in higher oxidative states (Ag^{2+} and Ag^{3+}) than singularly ionic silver (Ag^{1+}), resulting in a more powerful antimicrobial. Data from a number of studies investigating Ag Oxysalts technology have shown:

- Broad-spectrum efficacy when tested against aerobic, anaerobic and multi-resistant bacteria and fungi *in vitro* (Data on File [1])
- Efficacy *in vitro* (Data on File [2]) and *in vivo* (Data on File [3]) against established biofilms in lower concentrations than are required with Ag^{1+}
- That KerraContact Ag is safe, as it does not inhibit healing; in fact, it promotes healing independent of infection (*in vivo* model) (Thomason et al, 2014).

For this symposium, Helen presented the findings of *in vivo* and *in vitro* studies that tested aerobic gram-positive and gram-negative bacteria; results demonstrated KerraContact Ag's potent antimicrobial activity and ability to promote wound healing.

Ag Oxysalts rapidly killed gram-negative and gram-positive bacteria (*Figure 1*), with at least a 5-log reduction within 30 minutes. Since lower quantities of silver were required for antimicrobial action compared with existing dressings, as shown in *Figure 2* (Data on File [4]), KerraContact Ag was shown to be effective at treating wound infection.

Ag Oxysalts also inhibited biofilm formation (*Figure 3*) and rapidly kills established biofilms (*Figure 4*) at a low concentration of silver. Indeed, Ag Oxysalts (Ag^{2+} and Ag^{3+}) was seen to be more effective at inhibiting biofilm

formation (with similar results obtained for both *P. aeruginosa* and *S. aureus)* and at disrupting established biofilms than Ag $^{1+}$.

Results from this study also demonstrated that using KerraContact Ag does not inhibit the normal healing of wounds independent of infection. A series of scratch wound assays showed no adverse effects on fibroblast wound proliferation and promotion of keratinocyte wound closure (*Figure 5*).

In the *in vivo* wound model, the wound was visually much smaller after three days with KerraContact Ag and histological analysis revealed a smaller wound area when compared with control (Thomason et al, 2014). Results at seven days were consistent with these findings, with the wound fully epithelialised. Importantly, with KerraContact Ag the wound barrier had fully reformed and epithelialisation was advanced, whereas in the control it had not reformed fully, leaving the wound at risk of re-infection. In addition, KerraContact Ag reduced infiltration of both neutrophils and macrophages at 3 days and 7 days.

CLINICAL RATIONALE FOR KERRACONTACT AG

Alison Beasley, Head of Specialist Teams at Oxleas NHS Foundation Trust, went on to discuss the process of working with patients to recognise and effectively treat clinical infection, presenting the clinical rationale for using KerraContact Ag in two specific patients.

Recognition of infection must start with understanding the difference between localised and spreading infection, then appropriate treatment must be instigated. Classic signs of pain, heat, swelling, redness and loss of function may not always be present in chronic wounds, and other signs of nfection may be identified: new or altered pain, delayed healing, friable tissue, periwound oedema, bleeding, odour, discolouration, purulent exudate, induration, pocketing, or bridging may be present (World Union of Wound Healing Societies, 2008).

When choosing the right antimicrobial dressing, the patient's preference and sensitivities are important first and foremost. The clinician must also consider exudate levels, the position of the wound and how the dressing will be secured, the frequency of dressing change (taking into account whether the patient is community or ward based), the wound bed status, how much expertise is available in the environment of care, and the availability of and familiarity with the dressing, including who will be applying it.

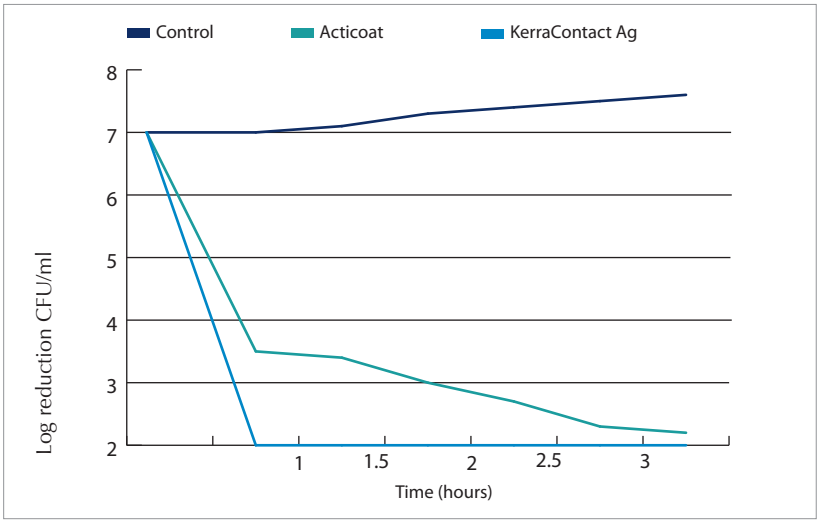

Figure 1. KerraContact Ag rapidly kills bacteria (results from MSSA)

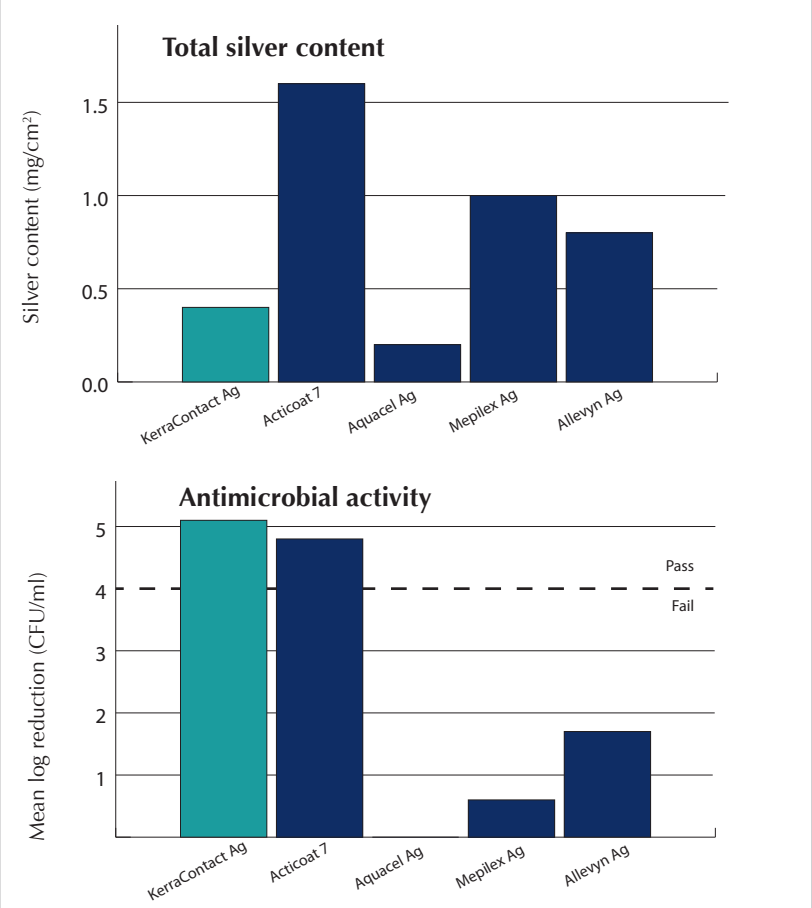

Figure 2. KerraContact Ag demonstrates superior antimicrobial activity at low concentrations of silver (results for *P. aeruginosa)*

Declaration of interest
This symposium was sponsored by Crawford Healthcare

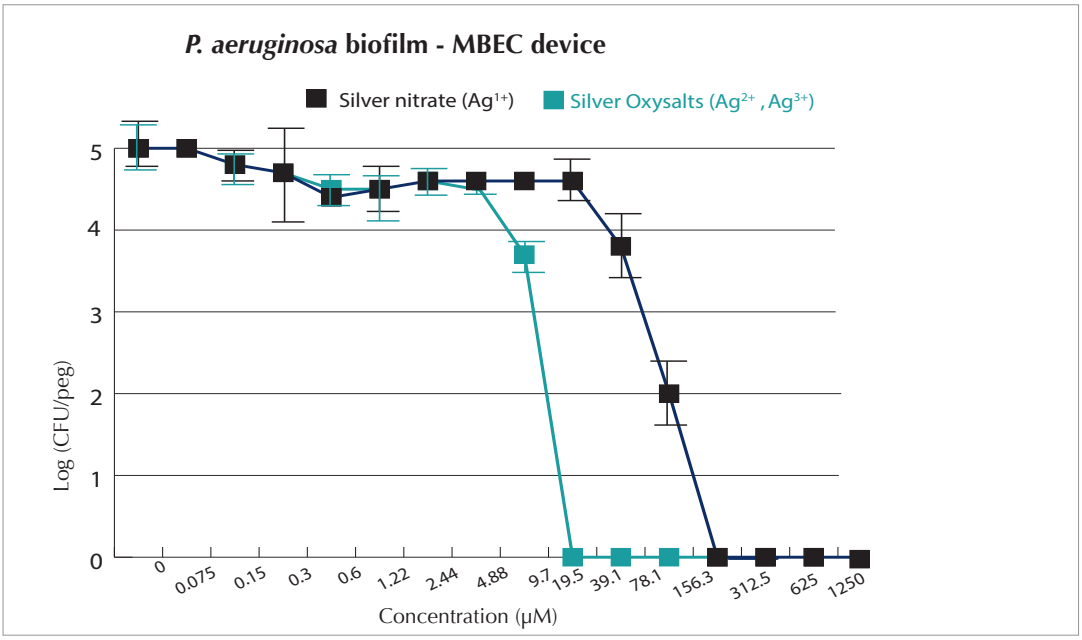

Figure 3. Silver Oxysalts inhibits biofilm formation (results for *P. aeruginosa)* (Adapted from Lemire et al, 2015)

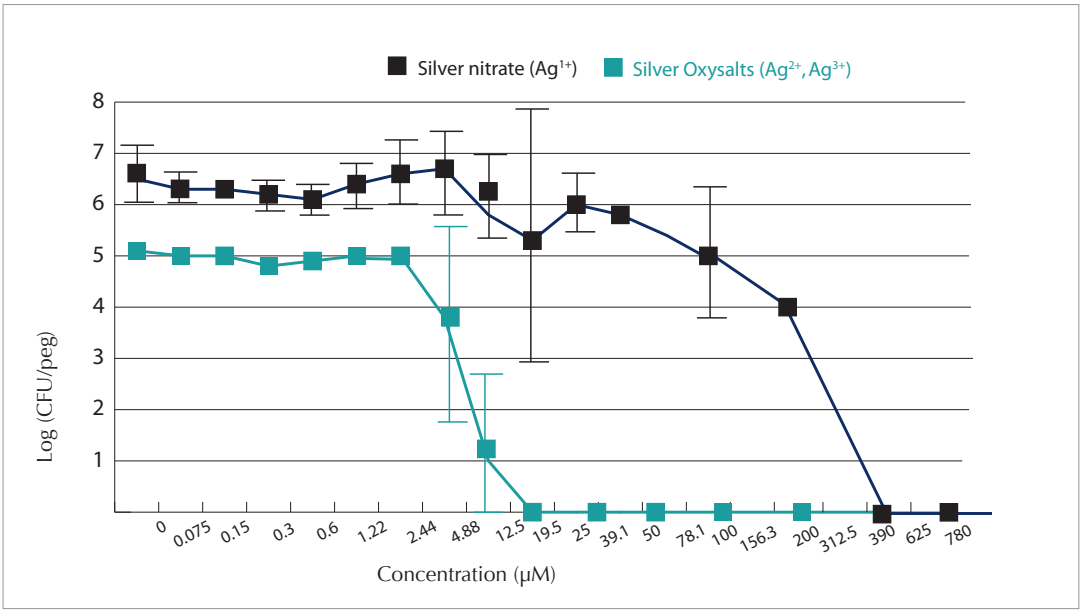

Figure 4. Silver Oxysalts kills established biofilms (results *for P. aeruginosa)*

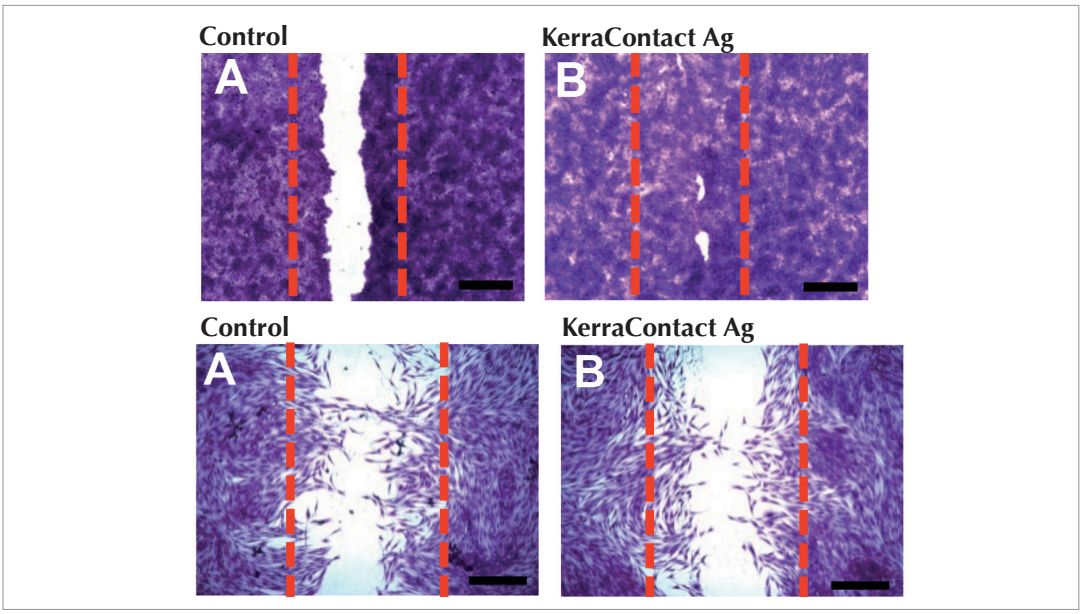

Figure 5. Scratch wound assays: fibroblast (top) and keratinocyte (bottom) wound closure with control (A) versus KerraContact Ag (B)

CASE STUDIES

With this in mind, Alison presented two case studies where KerraContact Ag has been used successfully. These case studies focus on why KerraContact Ag was considered the most suitable dressing, based on the patients' individual preferences and the needs dictated by their wounds.

Case Study 1

Patient 1 is a 28-year-old with sickle cell disease, who works as an accountant. He was referred following an unsuccessful skin graft over his ulcer, which had healed to a point following debridement and compression, but had then stalled (*Figure 6*). His wound had previously been treated with various antimicrobials; topical negative pressure; increasing levels of compression and synthetic haemoglobin.

It was important to the patient that he only received weekly dressing changes and could continue working. He wanted no additional interventions, his treatment to be discrete and pain-free on removal, and to eliminate the odour from his wound.

KerraContact Ag was chosen because it works for seven days, is unobtrusive and easily removed. It was anticipated that KerraContact Ag would continue to encourage the wound to heal after disrupting the biofilm. It was also expected to deal with the wound's malodour as it treated the wound infection.

At week 1, there was an increased level of granulation tissue and the wound was smaller in size (*Figure 7*). At the time of the symposium, the wound had moved into the healing phase, with a substantial change in its size and shape (*Figure 8*).

Case Study 2

Patient 2 is a very active 89-year-old lady who is able to dress her ulcers herself. Five years ago she suffered a spider bite and has since had several chronic venous leg ulcers. The ulcers repeatedly begin to heal then break down.

No antimicrobials had been effective on this particular wound, with little change seen over a period of months despite being treated appropriately with compression (*Figure 9*). The patient wanted to reduce malodour and encourage wound healing. She wanted to wear proper shoes, so did not want any bandages, and looked forward to being able to go on a holiday without having to receive nursing care.

KerraContact Ag was chosen due to its seven-day antimicrobial effectiveness, which was expected to reduce the wound's exudate and odour.

At week 1, there was a noticeable difference in the wound, with less redness and more epithelial

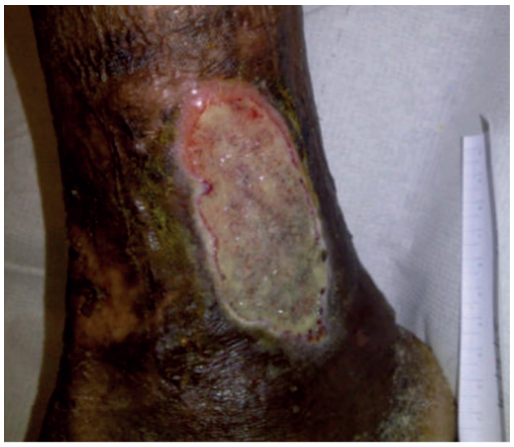

Figure 6. Patient 1: wound prior to treatment

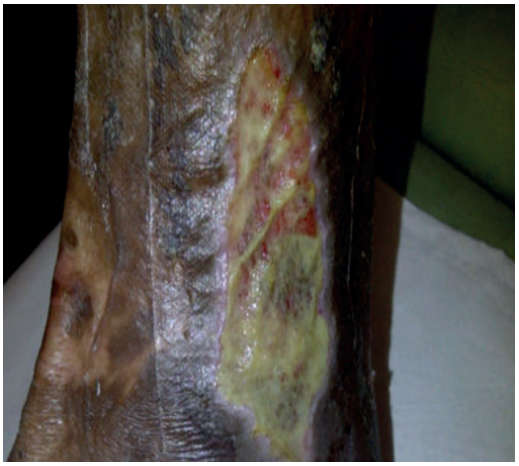

Figure 7. Patient 1: week 1 review

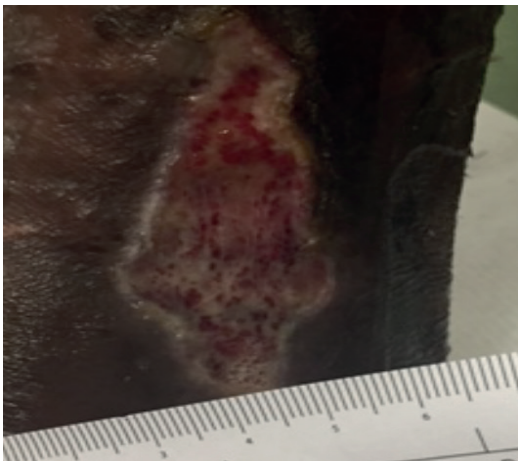

Figure 8. Patient 1: to date

tissue (*Figure 10*). At week 2, the dressing seemed to be working very effectively (*Figure 11*). After four weeks of treatment, there were no further signs of infection, exudate levels had decreased, and the wound had decreased in size, thus allowing the patient to go on holiday without any need for nursing care.

CONCLUSION

The presence of wound bioburden often leads to poor wound healing, and delayed healing leaves a wound more susceptible to infection. It is important to be able to quickly recognise the signs and symptoms of wound infection, since their impact on patients' quality of life and on healthcare resources can be great, potentially leading to hospital admissions and complications such as amputation. There is a need to identify effective topical antimicrobials to treat infections and, in turn, reduce the need for antibiotics.

KerraContact Ag is a cost- and clinically-effective antimicrobial treatment, which prevents and disrupts biofilms effectively; works in a short time-frame, with action demonstrated within 30 minutes [1] and sustained across seven days (Data on File [5]); and promotes healing independent of infection (Thomason, 2014). KerraContact Ag should be considered for its safety and efficacy in appropriate patients with infection and suspected biofilm. A clear plan should be put in place that takes into account the patient's preferences and ensures they know what their treatment might achieve. Once antimicrobials have worked, it is then important to move to a new dressing, always evaluating and documenting the progress of the wound, and taking appropriate action. WUK

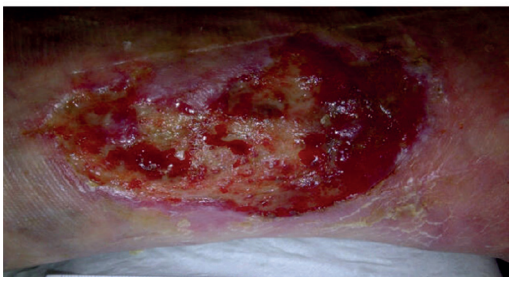

Figure 9. Patient 2: wound prior to treatment

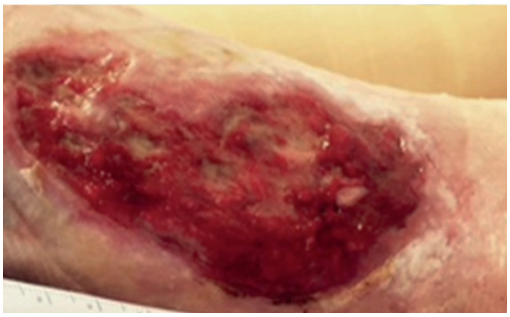

Figure 10. Patient 2: week 1 review

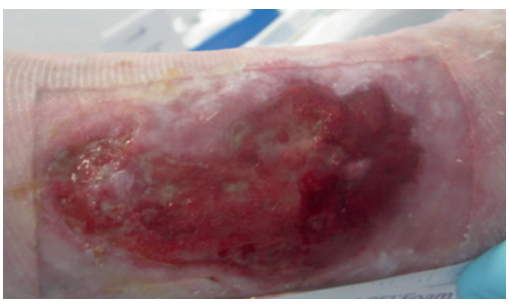

Figure 11. Patient 2: week 2 review

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Crawford Healthcare Data on File [1] – Log Reduction Report

Crawford Healthcare Data on File [2] - Final Report Crawford 005 V1.3

Crawford Healthcare Data on File [3] - Evaluation of a Silver Oxysalts treatment to reduce Pseudomonas auriginosa biofilms using an in vivo porcine burn wound model

Crawford Healthcare Data on File [4] –PR-0044.3 Effective and cost-efficient

Crawford Healthcare Data on File [5] – Equivalence performance

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Further information

For more information on KerraContact Ag, please visit: www.crawfordpharma.com

This symposium can be viewed at: http://video.molehost2.net/wounds-uk/harrogate-2015/crawford/

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