Silver-containing foam dressings — does silver content matter?


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Ionic silver is an antimicrobial agent included in wound dressings to prevent and manage local wound infection. As silver content varies considerably between dressings, an *in vitro* study was conducted to investigate the antimicrobial activity of a variety of silver-containing foam dressings. The results showed considerable variation in the ability of the different silver-containing foam dressings to control wound pathogens. Dressing structure, rather than silver content, was found to be a significant factor in the observed differences in antimicrobial performance between the foam dressings.

Disclosure
Sarah Welsby and Philip G. Bowler are employees at ConvaTec, a Medtech company. Trademarks belong to their respective owners.

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Polyurethane foam dressings are used in the management of a wide variety of acute and chronic wounds, and are considered to be soft and comfortable for patients (Atkin et al, 2015; Nicolson et al, 2018). Many foam dressings also contain a soft adhesive layer, such as silicone, to ensure minimal tissue trauma and pain on removal (Woo et al, 2009; Atkin et al, 2015).

Variations exist in the construction, composition and exudate management capabilities of different foam dressings (Atkin et al, 2015). Effective exudate management is essential to enable moist wound healing while avoiding maceration of periwound skin (Cutting and White, 2002). As wounds have irregular topography with variable depth and cavities, conformability of the dressing to the wound surface is also important to eliminate voids where fluid and micro-organisms can collect and form a nidus for infection. However, the ability of foam dressings to conform to a wound surface has previously been challenged (Bowler et al, 2010).

Wound infection is known to result in wound complications and delayed healing, and as spreading infection can lead to devastating clinical consequences, it is vital that microbial bioburden is controlled (European Wound Management Association, 2005; Haesler et al, 2019). Ionic silver is an antimicrobial agent with broad spectrum activity and is included in a variety of foam dressings to prevent and manage local wound infection (Karlsmark et al, 2003; Vermeulen et al, 2007). Silver content varies considerably between dressings, and there is perception that this could impact the antimicrobial activity of a dressing. However, previous studies have demonstrated that dressing conformability, and the availability of silver from the dressing at the wound surface play a more critical role than silver content or form *per se* in the optimum function of silver-containing dressings (Bowler et al, 2010; Walker et al, 2011).

The aim of this *in vitro* study was to investigate the impact of dressing structure and silver content on the antimicrobial activity of a variety of polyurethane foam dressings with and without additional materials, i.e. Hydrofiber® (ConvaTec).

Methods

Test dressings

The silver-containing foam test dressings are listed in *Table 1* and photographs of the wound contact layer of each dressing are shown in *Figure 1*.

Determination of silver content in test dressings

The silver content per unit area of all samples was determined by inductively coupled plasma-mass spectrometry (ICP-MS, Agilent 7700x) by measuring the 107Ag-isotope compared to a Rhodium internal standard (103Rh) in an ammoniacal analytical solution. The analytical solution for dressings B, C and D was prepared by physically removing the silicone adhesive from

Table 1. Test dressings.

Test dressing	Brand name	Manufacturer	Dressing Size	Pad Size
A	AQUACEL™ Ag Foam Adhesive	ConvaTec	21 cm x 21 cm	17 cm x 17 cm
B	Allevyn™ Ag Gentle Border	Smith & Nephew	17.5 cm x 17.5 cm	14 cm x 14 cm
C	Biatain® Silicone Ag	Coloplast	17.5 cm x 17.5 cm	13 cm x 13 cm
D	Mepilex® Border Ag	Molnlycke	17 cm x 20 cm	13 cm x 16 cm

Table 1. Silver content of test dressings.

Test dressing	Mean silver content (mg/cm^2)	Standard deviation
A	0.11	<0.01
B	0.66	0.01
C	0.54	0.01
D	1.25	0.10

Dressing A (AQUACEL™ Ag Foam Adhesive); Dressing B (Allevyn™ Ag Gentle Border); Dressing C (Biatain® Silicone Ag) and Dressing D (Mepilex® Border Ag).

Figure 1. Photographs of wound contact layers in the test dressings. Wound contact layer in dressing A is absorbent Hydrofiber®; wound contact layer in dressings B, C and D is perforated silicone adhesive.

the foam and discarding it, accurately cutting a 2x2 cm sample of the remaining dressing (*n*=3), adding 10 mL of 12.8M nitric acid, subjecting this to closed-vessel microwave-digestion (CEM MARS6) for 20 minutes at 210°C, neutralising with 25 mL of concentrated ammonia solution, diluting volumetrically to 500 mL with deionised water and finally, and filtering through a 0.45 µm pore size nylon syringe filter. Due to its cellulosic content and gelling nature, dressing A was not suitable for treatment with nitric acid/microwave digestion. Therefore, dressing A was prepared by accurately cutting a 3x3 cm sample of the dressing, adding 10 mL of a 1 in 40 v/v aqueous dilution of cellulase (Sigma C2605), incubating at 60°C for 45 to 60 minutes, cooling, adding 15 mL of concentrated ammonia solution before finally diluting volumetrically to 500 mL with deionised water. In order to keep the dilution volume and concentration of extractant solution constant, adjustments in surface area of dressings sampled were necessary.

Simulated shallow wound model

The antimicrobial activity of the four silver-containing foam dressings was investigated against two common wound pathogens using an *in vitro* simulated shallow wound model (Bowler et al, 2010). The model was prepared using gauze squares to create a graduated indentation (7.5cm x 7.5cm x 2–3 mm depth) with an irregular surface in the centre of an agar plate (245 mm x 245 mm). Pin holes were created in the lid of each agar plate to allow ventilation during incubation.

Suspensions of each challenge organism, *Staphylococcus aureus* NCIMB 9518 and *Pseudomonas (P.) aeruginosa* NCIMB 8626, were aseptically added to Tryptone Soy Broth and incubated for 4 hours on a roller mixer at 35±3˚C to allow bacteria to achieve log phase growth. Following incubation, each bacterial suspension was diluted in 0.85% saline to obtain a final working concentration of approximately 5x102 CFU/mL. 8 mL of challenge suspension (i.e. approximately 4,000 bacterial cells) was inoculated into the centre of the simulated shallow wound agar plate.

Test dressings were aseptically and centrally applied to the inoculated simulated shallow wound agar plates such that the dressing pad covered the simulated wound area (*n*=3 for each challenge organism per test dressing). Inoculated simulated shallow wound agar plates without dressings were prepared as negative controls to confirm the extent of bacterial growth in the absence of dressings (*n*=1 for each challenge organism). Agar plates were then incubated at 35 °C (±3 °C) for 48 hours prior to removal of each test dressing. A 48-hour incubation period was chosen to enable bacteria to grow sufficiently, followed by a further 24-hour re-incubation period without the dressing in place.

Following dressing removal, agar plates were then re-incubated for an additional 24 hours to enable observation of any remaining viable

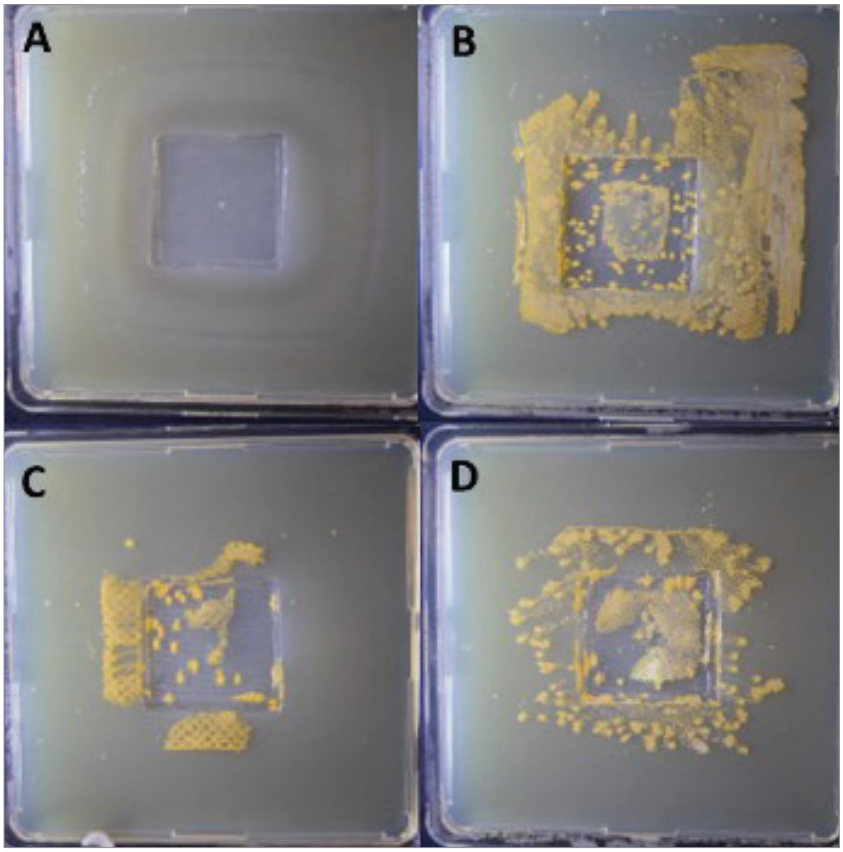


Figure 2. Examples of Staphylococcus aureus growth beneath dressings A, B, C and D.

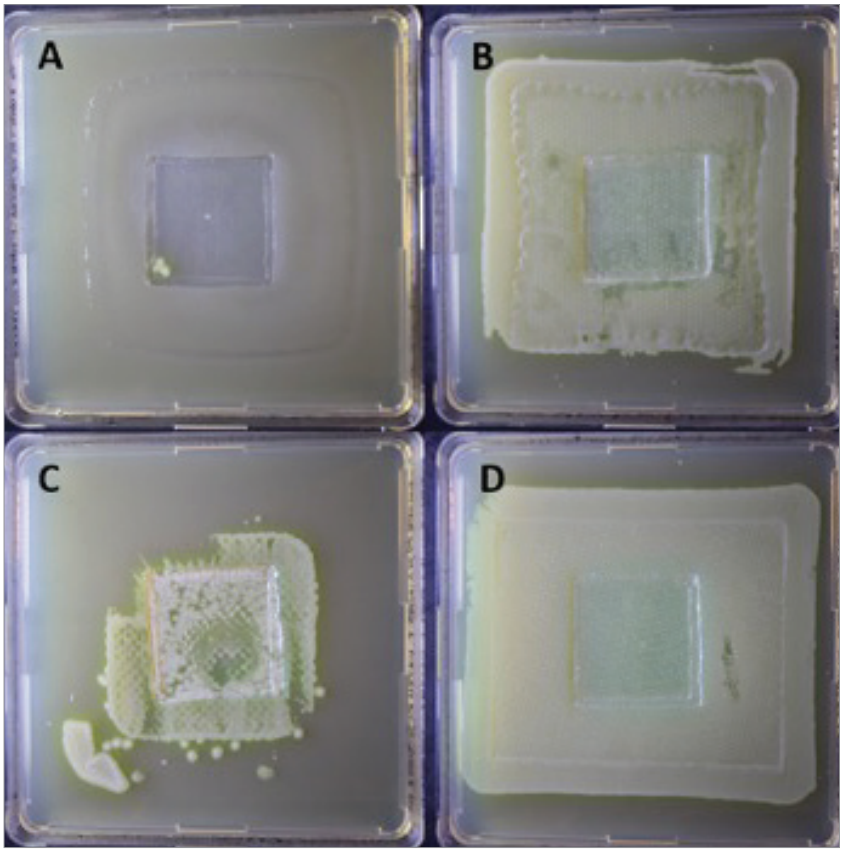


Figure 3. Examples of Pseudomonas aeruginosa growth beneath dressings A, B, C and D.

bacteria. This process was not meant to replicate clinical conditions where a new dressing would be applied. Re-incubation was purely undertaken to allow any remaining viable bacterial cells to form complete colonies, i.e. in the event that bacterial cells had been suppressed without being killed, in which case they would grow following the additional 24-hour incubation. This additional incubation step was also necessary to enable image analysis to be performed and subsequent quantification of extent of bacterial growth.

Photographs were taken using a Canon EOS450D camera and EFS10-22 mm lens, under fixed focus and standardised lighting conditions. Image analysis software (ImageTool for Windows, Version 3.0; The University of Texas Health Science Centre) was used to quantify the relative surface area covered by bacterial colonies within the simulated shallow wound area from these images.

Statistical Analysis

Statistical analyses were performed using a paired two-tailed student t-test to compare the area covered by bacteria under dressings B, C and D against dressing A. The level of significance was set at $P<0.05$.

Results

Silver content in test dressings

The silver content of test dressings A, B, C and D is provided in *Table 2*. The silver content of dressings B, C and D were 6-, 5- and 11-fold greater than in dressing A, respectively.

Simulated shallow wound model

The photographs provided in *Figures 2 and 3* are examples of bacterial growth in the simulated shallow wound area beneath the test dressings (of the three plates for each dressing, the one with the median bacterial growth was selected as the example). The images illustrate that there was negligible growth of *S. aureus* beneath dressing A, which contrasted with the considerable growth beneath test dressings B, C and D *[Figure 2]*. A similar pattern of growth was observed for *P. aeruginosa*, with negligible growth beneath dressing A compared with considerable growth beneath the other three silver-containing foam dressings *[Figure 3]*. For both challenge organisms, bacterial growth was observed to have spread beyond the area of inoculation (i.e. simulated shallow wound area), beneath dressings B, C and D.

The photographs in *Figure 4* are examples of bacterial growth in the simulated shallow wound in the absence of any test dressing i.e. negative

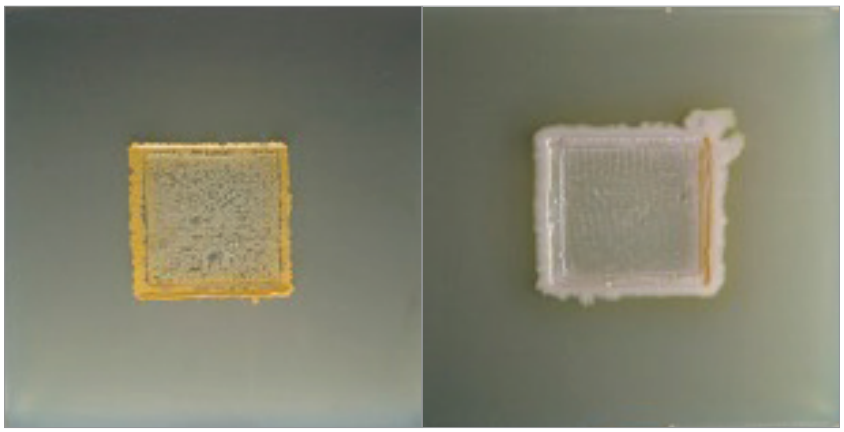
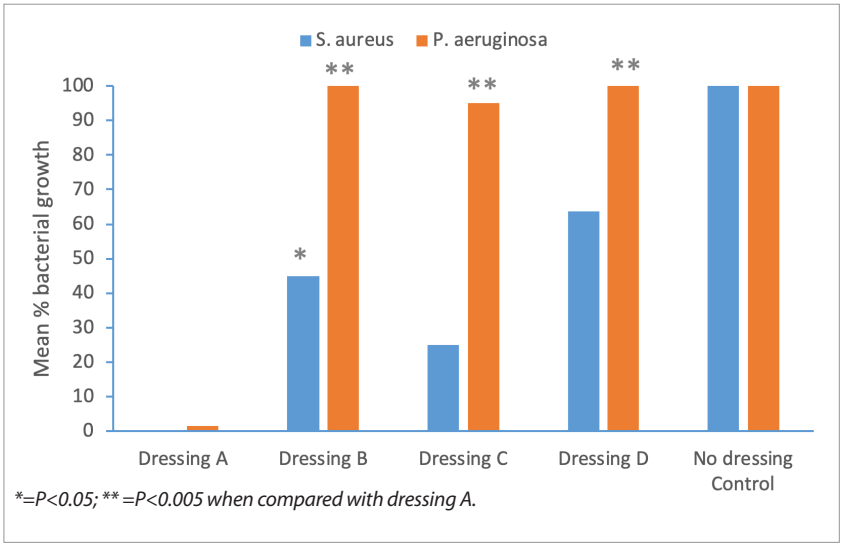


Figure 4. Examples of Staphylococcus aureus *(A) and* Pseudomonas aeruginosa *(B) growth with no dressing (negative controls).*



**=P<0.05; ** =P<0.005 when compared with dressing A.*

Figure 5. Mean percentage (n=3) of the total shallow wound area covered by growth of Staphylococcus aureus *and* Pseudomonas aeruginosa.

controls. Marginal growth of *P. aeruginosa* was observed beyond the area of inoculation due to both the volume of inoculum applied (i.e. to the brim of the simulated wound area), and the motile nature of the bacterium *[Figure 4b]*.

The mean percentage growth (n=3) of S. aureus and *P. aeruginosa* within the shallow wound area beneath the test dressings is shown in *Figure 5*. There was no growth of *S. aureus* beneath dressing A (0.0% of the total simulated shallow wound area), which contrasted with growth beneath dressings B, C and D (44.8%, 25.1% and 63.8% percentage surface area growth, respectively). The difference in extent of growth of *S. aureus* beneath dressing B compared with dressing A was statistically significantly (P<0.05). Growth of *P. aeruginosa* beneath dressing A was on average 1.5% of the simulated shallow wound area, in contrast to 100%, 94.9% and 100% for dressings B, C and D, respectively. The difference in extent of growth of *P. aeruginosa* beneath dressing B, C and D compared with dressing A was statistically significant (P<0.05).

Discussion

This *in vitro* study showed considerable variation in the ability of different silver-containing foam dressings to control wound pathogens inoculated in a simulated shallow wound directly beneath each dressing. Whereas bacterial growth beneath dressing A was either absent or negligible, growth of both *S. aureus* and *P. aeruginosa* beneath dressings B, C and D, was considerable, with bacterial growth spreading to the agar surface around the simulated shallow wound area under each of these three dressings. These observations are clearly not related to silver content, because the most effective dressing (dressing A) contains the lowest silver content per unit area of the four dressings tested (6x, 5x and 11x lower silver content than dressings B, C and D, respectively). However, the structure of these dressings differs considerably *[Figure 1]*. Dressing A is comprised of a gelling, silver-containing Hydrofiber wound contact layer backed by a secondary foam layer with a silicone adhesive border around the periphery of the Hydrofiber. Foam dressings B, C and D are each comprised of a perforated silicone adhesive wound contact layer, with a silver-containing foam layer behind the silicone adhesive. The silicone adhesive wound contact layer in dressings B, C and D, is likely to have acted as a barrier to the availability of silver from the dressing, hence resulting in negligible antimicrobial effect on the bacterial suspensions inoculated into the simulated shallow wound area.

Since considerable spread of both *S. aureus* and *P. aeruginosa* onto surrounding agar beneath dressings B, C and D was observed, the silicone layer is likely to have facilitated transfer of bacterial suspension between it and the agar surface, resulting in the spreading growth observed. Our observations are consistent with previous studies that have also demonstrated that the adhesive layer in some silver-containing foam dressing acts as a physical barrier preventing direct contact between the silver and the microorganisms (Walker et al, 2011). The reduced availability of silver to the microorganisms could explain the lack of antimicrobial activity observed for dressings B, C and D in this *in vitro* simulated shallow wound model.

In contrast, the silver-containing Hydrofiber in dressing A was in direct contact with the inoculated simulated shallow wound areas, which led to hydration and gelling of the dressing, creating better conformability with the

simulated shallow wound space, and effective antimicrobial activity. Additionally, the locking of bacterial inoculum within the dressing (Newman et al, 2006) prevented lateral movement of the inoculum, preventing spread and growth of bacteria on the surrounding agar.

A limitation of this study is that it was conducted using an *in vitro* model and so it is not known how the observations translate to real-life clinical situations. However, clinical evidence has shown the ability of Dressing A to manage infection and enhance wound healing (Durrant, 2014; Jozsa et al, 2018).

In this *in vitro* study, dressing structure, rather than silver content, was found to be a significant factor in the observed differences in antimicrobial performance between the foam dressings tested. WINT

References

Atkin L, Stephenson J, Bateman SD (2015) Foam dressings: a review of the literature and evaluation of fluid-handling capacity of four leading foam dressings. *Wounds UK* 11(1): 75–81

Bowler P, Jones S, Towers V et al (2010) Dressing conformability and silver-containing wound dressings. *Wounds UK* 6(2): 14–20

Cutting K, White RJ (2002) Avoidance and management of peri-wound maceration of the skin. *Prof Nurse* 18(1): 33, 35–6

Durrants S (2014) *The Burden of Chronic Wounds: Effective use of Topical Antimicrobial Dressings to Manage the Wound Symptoms*. Poster presented at Wounds UK Conference, Harrogate, November 10–12, 2014

European Wound Management Association (2005) *Position Document: Identifying Criteria for Wound Infection*. London: MEP Ltd.

Haesler E, Swanson T, Ousey K, Carville K (2019) Clinical indicators of wound infection and biofilm: reaching international consensus. *J Wound Care* 28(Sup 3b): s4–s12

Jozsa G, Vajda P, Garami A et al (2018) Treatment of partial thickness hand burn injuries in children with combination of silver foam dressing and zinc-hyaluronic gel: case reports. *Medicine (Baltimore)* 97(13): e9991

Karlsmark T, Agerslev RH, Bendz SH et al (2003) Clinical performance of a new silver dressing, Contreet Foam, for chronic exuding venous leg ulcers. *J Wound Care* 12(9): 351–4

Newman GR, Walker M, Hobot JA, Bowler PG (2006) Visualisation of bacterial sequestration and bactericidal activity within hydrating Hydrofiber wound dressings. *Biomaterials* 27(7): 1129–39

Nicolson S, Henry L, Sanderson T (2018) Mepilex® Border Comfort: a new 5-layer bordered foam dressing with Flex technology. *Wounds UK* 14(4): 94–9

Vermeulen H, Van Hattem JM, Storm-Versloot MN, Ubbink DT (2007) Topical silver for treating infected wounds. *Cochrane Database Syst Rev* (1): CD005486

Walker M, Jones S, Parsons D, Booth R et al (2011) Evaluation of low-adherent antimicrobial dressings. *Wounds UK* 7(2): 32–45

Woo KY, Coutts PM, Price P, Harding K et al (2009) A randomized crossover investigation of pain at dressing change comparing 2 foam dressings. *Adv Skin Wound Care* 22(7): 304–10