Mölnlycke®

Exufiber® and Exufiber® Ag+

Next generation gelling fibre dressings: A review of the scientific and clinical evidence

Wounds International

Published by
Wounds International
A division of Omniamed Communications Ltd
108 Cannon Street
London EC4N 6EU, UK
Tel: +44 (0)20 3735 8244
Email: info@omniamed.com
www.woundsinternational.com

Suggested citation
Gefen A, Timmons J, Carlsson E et al (2021) *Exufiber® and Exufiber® Ag+: A review of the scientific and clinical evidence.* Wounds International, London. Available to download from www.woundsinternational.com

Supported by an educational grant from **Mölnlycke Health Care.**

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FOREWORD

THE IMPORTANCE OF EFFECTIVE EXUDATE MANAGEMENT

Even during these unprecedented COVID-19 times, traumatic, surgical and chronic wounds continue to require routine care, but now there is the added concern of COVID-19 infections, work stress and the hectic schedules of clinicians who are understaffed. The latter factors indicate that, in the current reality, safe and effective wound treatment is even more critical than before. A primary aspect in such effective treatments is the management of exudate.

Exudate is a normal part of wound healing, but it can cause problems when in the wrong amount, in the wrong place or when of the wrong composition (World Union of Wound Healing Societies [WUWHS], 2019). Specifically, the wound bed must be mildly moist to allow transport of nutrients, signaling molecules and immunological factors, as well as for proliferation and migration of the epithelial cells that initiate repair. Excess exudate delays wound healing because it typically contains high concentrations of inflammatory molecules. While exudate release from the wound bed is due to a normal inflammatory response, aimed to increase the local vascular permeability so that immune cells can migrate to the wound, exudate accumulation, known as pooling, is undesirable (Gefen, 2019; Lustig et al, 2021). Excessive exudate is known to disturb healing and may cause cell and tissue damage, for example, by creating a conducive environment for pathogen growth or by wetting periwound skin, which results in maceration. Under the present pandemic circumstances, if a patient has COVID-19, the virus may be present in the exudate, and so pooling of exudate may increase the risk of exposure to COVID-19 for healthcare professionals (Gefen and Ousey, 2020; Zhou et al, 2020). Lastly, pooling of wound exudate may also create unpleasant odours, the intensity of which is typically associated with the bacterial load in the wound (Ousey et al, 2017).

For all these important reasons, wound exudate should be effectively absorbed and retained in dressings, even when mechanical forces are applied to the dressing and wound, such as in a non-offloaded wound, or when the dressing rubs against clothing, bedsheets, devices, the bedframe or wheelchair (Lustig et al, 2021). Regardless of whether the dressing is subjected to forces or not, or whether the dressing is new and dry or used and nearly saturated, the dressing should continue to allow the wound bed to remain warm and moist, but never wet, throughout the period of clinical use. Tissue temperatures at and near the wound bed should be kept at near-normal values. Secondary dressings should further be impermeable to external fluids and pathogens, while still allowing wound–environment gas exchange.

Prevention of exudate pooling and its negative impact on healing requires high absorption and retention of the dressing (including when subjected to mechanical forces), as well as intimate and continuous contact between the absorptive dressing surface and the wound bed. In treatment protocols where primary and secondary dressings are used, effective transfer of exudate from the wound bed to the primary dressing and from the primary to the secondary dressing is a must (Lustig et al, 2021). Fibre dressings are typically used in the management of cavity wounds; these dressings should effectively transfer exudate away from the wound bed to a suitable absorbent secondary dressing.

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INTRODUCTION
THE CHALLENGES OF HIGHLY EXUDING AND CAVITY WOUNDS

CHALLENGES OF CHRONIC WOUNDS

A World Union of World Healing Societies (WUWHS) consensus document highlights the negative impact of chronic wounds on a patient's overall wellbeing. The document discusses the views of patients with chronic wounds and found that they are treated differently from other patients with chronic conditions, and that wounds are not viewed as serious conditions (WUWHS, 2020).

Often viewed as a 'hidden epidemic', chronic wounds can have a significant impact on local and national health care budgets (Guest et al, 2020). A recent audit of the wound care burden within the UK estimated that the cost of treating wounds was approximately £8.3 billion per annum, of which £2.7 billion and £5.6 billion were associated with managing healed and unhealed wounds, respectively (30% of all wounds in the study did not heal in the study year) (Guest et al, 2020).

Chronic wound types include, but are not limited to, venous leg ulcers (VLUs; Figure 1), diabetic foot ulcers (DFUs) and pressure ulcers/injuries (PUs or PIs). Although these three wound types are very different with respect to causation and underlying pathology, they often present with similar features which create a range of challenges for the clinicians involved in caring for them. Chronic wounds are often associated with a continuous inflammatory process, as a result of uncontrolled cellular and molecular activity, which is likely to lead to delayed or stalled healing.

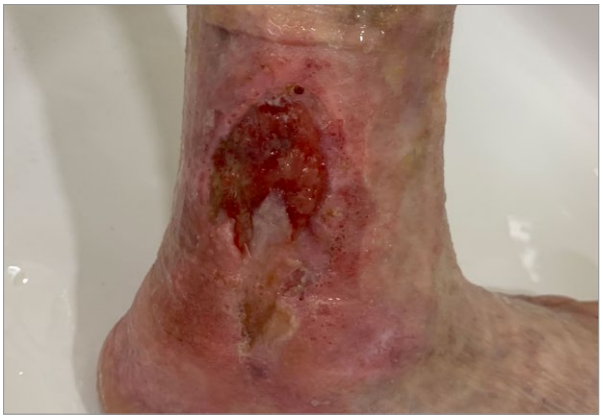


Figure 1 | Three-year-old venous leg ulcer (VLU) with high levels of green/yellow, non-viscous exudate. *Photograph kindly supplied by Paulo Alves, Wounds Research Laboratory, Centre for Interdisciplinary Research in Health (CIIS), Universidade Catolica Portuguesa, Oporto, Portugal*

MANAGING EXCESS WOUND EXUDATE

In normal wound healing, as the inflammatory process progresses, and as the wound is covered with new epithelium, the exudate levels will reduce. However, in many chronic wounds there is a tendency for the wound to remain in the inflammatory phase of healing, which can be due to underlying pathology and changes in the cellular dynamics within the wound (Lazaro et al, 2016). Chronic wound exudate has been shown to contain an excess of proteases, specifically matrix metalloproteinase (MMP)-2 and MMP-9. These MMPs are associated with the dissolution of the extracellular matrix (ECM). Put simply, when these proteases are present at elevated levels, there is a risk to the newly formed granulation tissue. In normal wound healing, proteases play an essential role, with specific proteases produced for precise durations, at distinct locations, and at controlled levels (Power et al, 2017). However, prolonged, elevated levels of proteases or a change in the ratio of MMPs and tissue inhibitors of metalloproteases (TIMPs) cause a shift in the balance between matrix deposition and tissue turnover, thus affecting wound healing.

In this context, MMPs (particularly MMP-2 and MMP-9) and TIMPs are frequently measured components of wound exudate (Power et al, 2017). Therefore, in chronic wounds where exudate levels remain persistently high, there is a risk that exudate containing excessive MMPs will leak onto the surrounding tissue and damage the periwound skin, often referred to as maceration. This can lead to an increase in the size of the wound and cause pain for the patient (Chadwick and McCardle, 2015). If exudate is not managed appropriately, there is a risk that the fluid can leak from the wound dressings onto the patient's clothing and bedding, which may

add to their discomfort and contribute to increased anxiety (Tickle, 2013). Furthermore, wounds with elevated levels of exudate may take longer to heal and this will have a direct impact on healthcare resource utilisation (Wounds UK, 2013). Box 1 highlights some of the issues associated with poorly managed exudate.

Box 1. Description of some of the issues associated with poorly managed exudate (Wounds UK, 2013)

- Frequent dressing change: discomfort, pain, trauma, skin stripping
- Periwound skin damage: maceration, excoriation
- Infection
- Strikethrough (leakage)
- Odour
- Social and psychological effects
- Delayed healing: breakdown of extracellular matrix (ECM)
- Protein loss/fluid and electrolyte imbalance: systemic problems.

The management of wound exudate should include the following steps:

- Accurate wound assessment: this is to ensure that treatment not only helps in managing the wound itself, but also addresses any underlying pathologies that may have an impact on the production of wound exudate. Addressing underlying pathologies, such as the use of compression in patients with venous disease to aid venous return, is essential. In patients with diabetic foot ulceration, there is a need to offload the affected area to assist in the healing process and prevent further localised pressure on the affected area (Chadwick and McCardle, 2015).
- Exudate assessment: exudate should be assessed not only for the quantity, but also for the colour and consistency (WUWHS, 2019).
- Wound bed optimisation: the presence of sloughy and/or necrotic tissue can lead to a prolonged inflammatory response. Regular wound cleansing and debridement are necessary to soften and remove sloughy tissue to help promote granulation tissue and allow wound healing to progress (Wounds UK, 2013).
- Management of the wound bioburden: chronic wounds will often present with elevated levels of bacteria either in planktonic form or as wound biofilm. Wounds that have a significant bacterial load and exhibit signs of infection are likely to produce higher than normal exudate levels. All non-healing chronic wounds should be considered to harbour biofilms and, therefore, treatments should be targeted towards this (WUWHS, 2016). Biofilms are known to prolong the chronic inflammatory response by stimulating a host response and this may result in an increase in wound exudate levels. Biofilm management should include regular cleansing, debridement, application of topical antimicrobials and regular reassessment to remove the biofilm and the source of the inflammatory response.
- Appropriate dressing selection: accurate assessment of the wound should help to determine the appropriate dressing(s) to manage wound exudate. Primary and secondary dressings may be needed, depending on the wound characteristics, and these dressings should work together to help create the ideal wound environment. For wounds with moderate-to-high exudate levels, it may be necessary to use a primary dressing such as a gelling fibre dressing to help manage the exudate effectively, to promote removal of devitalised tissue (e.g. slough) and prevent leakage of exudate onto the surrounding skin. For cavity wounds, a gelling fibre dressing may be used to lightly pack the cavity to promote the development of granulation tissue from the base of the cavity and to help manage undermining (Tickle, 2019). An appropriate secondary dressing should also be used to help further manage exudate.

Figure 2 shows the impact of poor exudate management of a grade 3 PU, in particular the impact of wound exudate on the surrounding skin. The figure also illustrates some of the challenges presented by cavity wounds; the wound bed is sloughy, the wound exudate has leaked onto the surrounding skin and there are areas of undermining present at the lower wound edge.

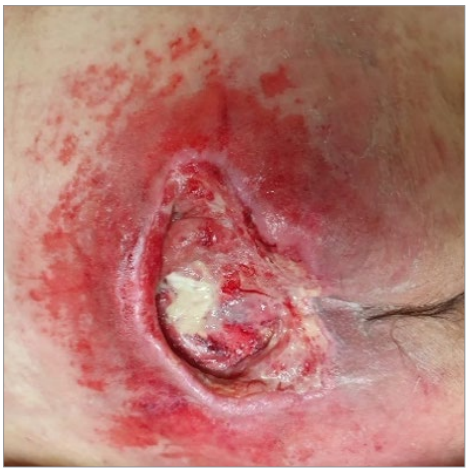


Figure 2 | A grade 3 pressure ulcer (PU) showing excoriation of the surrounding skin. The skin around the wound is red and inflammed and this is likely to be the result of damaging enzymes present in the wound exudate leaking from the dressing onto the skin. *Photograph kindly supplied by Paulo Alves, Wounds Research Laboratory, Centre for Interdisciplinary Research in Health (CIIS), Universidade Catolica Portuguesa, Oporto, Portugal*

MANAGEMENT OF CAVITY WOUNDS

Cavities can present in wounds of most aetiologies including leg ulcers, DFUs, PUs and in patients with surgical wound dehiscence (Tickle, 2019). Timmons and Cooper (2008) defined a cavity wound as one which extends beyond the layers of the dermis. Other authors suggest that a wound should be considered a cavity when there is a depth of 2cm or more from the wound edge to the wound bed (Vowden, 2016). This may seem small, however, a 2cm wound on the foot is proportionally more significant than a 2cm deep sacral wound. PUs often present as cavity wounds due to the damage caused to the underlying tissues by unrelieved pressure. Similarly, DFUs are often the result of the long-term effects of neuropathy and ischaemia, resulting in undetected pressure over the bony prominences of the foot. Cavity wounds are challenging to manage for several reasons: the patient may present with a wound that leads to a sinus or a fistula, and there may also be undermining and bridging present (Timmons and Cooper, 2008).

Accurate assessment of the patient and the wound is key to managing cavity wounds. Objective measurements of the cavity wound are important so that the progress or deterioration of the wound can be followed accurately (Tickle, 2019).

As with all chronic wounds, it is important to optimise the wound bed; this will include cleansing, debridement of sloughy and necrotic tissue and the use of dressings that support autolytic debridement between dressing changes, such as gelling fibre dressings. Cavity wounds are also at risk of infection due to the presence of exudate, sloughy tissue and the potential for exudate to 'pool' in the base of the wound, potentially leading to bacterial proliferation (Tickle, 2019). Appropriate exudate management should be a key component of cavity wound management and, as described above, the use of gelling fibre dressings can help to absorb exudate from the base of the wound and transfer it to secondary dressings when required.

Dressing selection will, however, depend on the outcome of wound assessment and wound management objectives (Tickle, 2019). Due to the tissue deficit in cavity wounds, it is essential that wound dressings are used to fill the cavity to promote granulation tissue to form from the base of the wound to the surface. It is also important to consider areas of undermining. The key principles of cavity wound management are summarised in Box 2. The properties of the ideal dressing for highly exuding and cavity wounds are listed in Table 1.

Box 2. Key principles of cavity wound management (Tickle, 2019)

- Accurately assess the wound length, width and depth, including undermining
- Optimise the wound bed through cleansing and debridement
- Manage the exudate levels using appropriate wound dressings
- Manage the wound bioburden
- Use antimicrobial dressings when necessary
- Use primary dressing to fill the cavity (do not overpack)
- Apply a suitable secondary dressing.

Table 1: Properties of the ideal wound dressing for highly exuding and cavity wounds

Dressing property	Rationale
Ability to mould to the contours of the wound and be placed into undermined areas	To promote granulation tissue and fill the dead space
Ability to absorb moderate to heavy volumes of exudate	To prevent pooling of fluid in the wound bed
Ability to transfer wound exudate to the secondary dressing	To prevent maceration of the surrounding skin and prevent the pooling of fluid in the wound bed
Ability to support autolytic debridement	To allow the softening of sloughy tissue between dressing changes
Durability/structural integrity (including high tensile wet strength)	To allow for the dressing to be safely removed from the wound in one piece (avoiding debris or micro-particles being left in the wound)
Ability to form a soft conformable gel on contact with exudate	To help provide a moist wound environment
Non-adherent wound contact layer	To minimise damage to the wound and periwound skin and pain to the patient on removal

GELLING FIBRE DRESSINGS

On contact with exudate, a gelling fibre dressing swells and takes the form of a gel, ideally conforming to the wound cavity shape (Lustig et al, 2021). Gelling fibre dressings (used in combination with a secondary dressing) absorb, retain and transfer excess wound exudate (thus protecting the periwound skin), whilst creating a moist environment to support the healing process.

Hydrolock® Technology

Exufiber® is a non-woven polyvinyl alcohol (PVA) gelling fibre dressing with Hydrolock Technology, providing an advanced fluid lock-in property for medium-to-highly exuding and cavity wounds. Exufiber Ag+ has the added benefit of silver. Hydrolock Technology refers to the unique technology that is key to the performance of Exufiber and Exufiber Ag+ gelling fibre dressings. Please refer to the relevant Mölnlycke Health Care instructions for use (IFU) for each product (Mölnlycke, 2021).

Traditional gelling fibre dressings are manufactured from carboxymethylcellulose (CMC) materials. Often, dressings made from CMC fibres have large gaps between the fibres; these gaps can fill with exudate or blood and this can impact on the structural integrity of the dressings.

Exufiber and Exufiber Ag+, on the other hand, are made from PVA fibres with unique gel-forming properties (Hydrolock Technology). These fibres are tightly entwined within the dressing, which minimises the space for wound exudate or blood to flow into; in combination with the high wet integrity of the fibres, this means that dressings with Hydrolock Technology are more likely to remain intact compared to

traditional gelling fibre dressings made from CMC fibres, which can also help with one-piece removal from the wound. This combination allows them to be manufactured without requiring reinforcement threads. On contact with wound exudate, the fibres within Exufiber and Exufiber Ag+ form a soft conformable gel, which supports an ideal wound healing environment.

Electron microscopy imaging of gelling fibre dressings illustrate the tightly entwined fibres of the Exufiber dressings (Figure 3a) and the larger gaps between the fibres of a traditional CMC dressing (Figure 3b).

Figure 3a | Electron microscopy image illustrating the tightly entwined fibres of Exufiber dressings

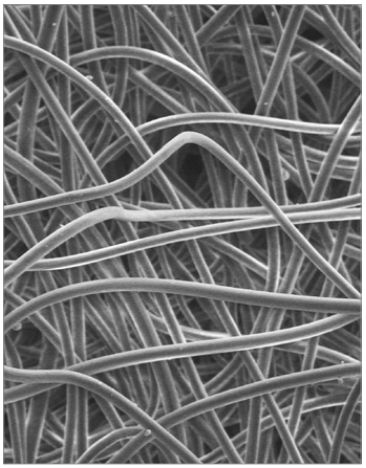
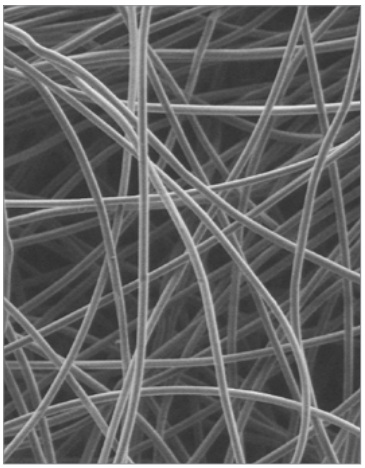


Figure 3b | Electron microscopy image illustrating a traditional carboxymethylcellulose (CMC) dressing



The unique construction of the Exufiber dressing range allows for efficient transfer of fluid from the wound bed into the dressing and supports the transfer of fluid into a secondary dressing (Mölnlycke 2018a, data on file). The combination of closely packed fibres (small capillaries) and the hydrophilic nature (attracts water) of PVA results in a capillary action, propelling liquid into the core of the dressings without assistance from external forces. This force is strong enough to overcome gravity and thus enables spreading in/through the dressing. Another important feature of the Exufiber dressing is its ability to retain absorbed fluid whilst under compression, as the fibres can hold the exudate that has been absorbed within the dressings (Chadwick and McCardle, 2015).

What does this mean for the clinician and the patient?

In wounds with moderate-to-high levels of exudate, Exufiber with Hydrolock Technology can help to absorb and retain excessive exudate from the wound bed and transfer it into the secondary dressing (Mölnlycke 2018a, data on file). The use of gelling fibre dressings can, therefore, help to prevent the complications associated with excessive exudate, such as maceration of the surrounding skin, pain due to excoriation from exudate leakage, odour and the risk of infection (Wounds UK, 2013; Chadwick and McCardle, 2016). Importantly, dressings can be worn safely under compression bandaging, with minimal risk of fluid leaking onto the skin. The gel formed by the Exufiber gelling fibre dressing provides a moist wound healing environment, which can help support autolytic debridement between dressing changes, resulting in the softening and removal of sloughy tissue from the wound bed. Together with structural integrity allowing a one-piece removal without release of dressing particulates from the wound bed, the autolytic debridement helps to promote a clean wound bed. The antimicrobial dressing Exufiber Ag+ may also prevent the reformation of biofilm as part of a holistic biofilm wound management as shown *in vivo* (Davis et al, 2019a; 2019b).

Figures 4a–4d present a typical example of the use of Exufiber Ag+.

Figure 4a | Venous leg ulcer (VLU). Wound at day 0 (before debridement)

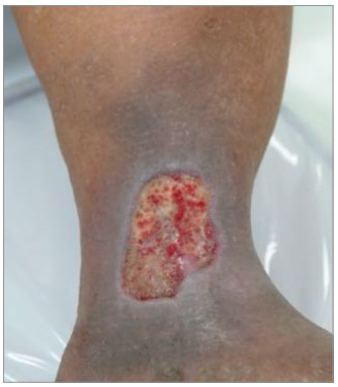


Figure 4b | Wound at day 0 (after debridement)

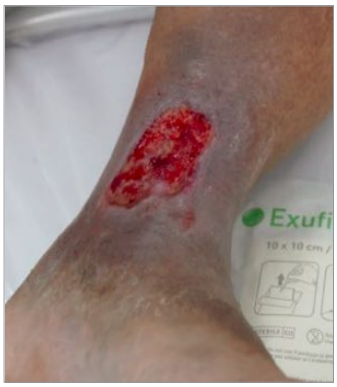


Figure 4c | The dressing regimen included Exufiber Ag+ as the primary dressing; after 9 days of treatment, Mepilex® Border Flex was used (secondary dressing) in conjunction with Exufiber Ag+ for better exudate management and periwound skin protection; dressings were applied under compression

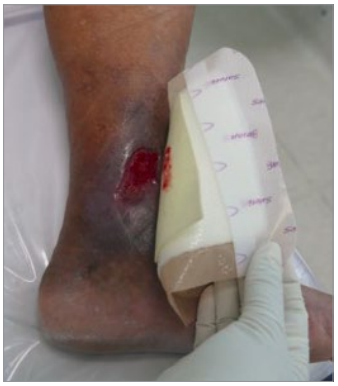
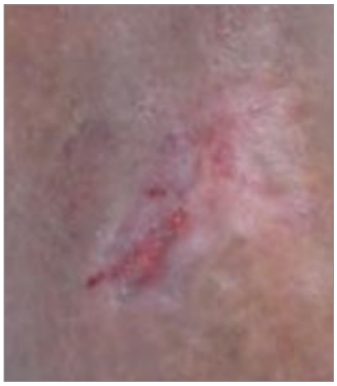


Figure 4d | At day 82, the wound had healed



Photographs kindly supplied by Dr Marcelo Ruettiimann Liberato de Moura, Hospital Sao Rafael, Salvador, Brazil

SCIENTIFIC EVIDENCE

When making decisions about clinical interventions, all available evidence should be evaluated to consider the relative weight of the available research data. When it comes to wound dressing selection, it is important to consider not only the available clinical evidence, but also the preclinical evidence, since this type of evidence helps to provide knowledge of the safety and efficacy of dressings and their mechanisms of action.

The following section aims to summarise the available evidence generated from scientific studies relating to the use of Exufiber and Exufiber Ag+.

FLUID HANDLING AND DURABILITY STUDIES

This section summaries the *in vitro* data relating to the fluid management (absorption, retention and transfer of fluid) of Exufiber and Exufiber Ag+ and the structural integrity of the dressings as modelled to imitate their use in wounds and during dressing removals.

Dressing absorption and retention capacity

As discussed above, while exudate plays a key role in wound healing, too much or insufficient exudate can delay healing. In addition to the volume of exudate, the composition of exudate typically varies during the wound healing process and is affected by several factors such as the local inflammatory activity and the microbial status. High viscosity exudate, characterised by a thick and sometimes sticky nature, can be difficult to manage (Vowden et al, 2015). Exudate viscosity, in addition to other factors such as body position and bodyweight forces, can affect the ability of a dressing to absorb and retain exudate; if not managed effectively, there may be pooling of the exudate in the wound cavity, or spill-over of exudate on periwound skin, which may result in skin maceration (Gefen and Santamaria, 2021; Lustig et al, 2021).

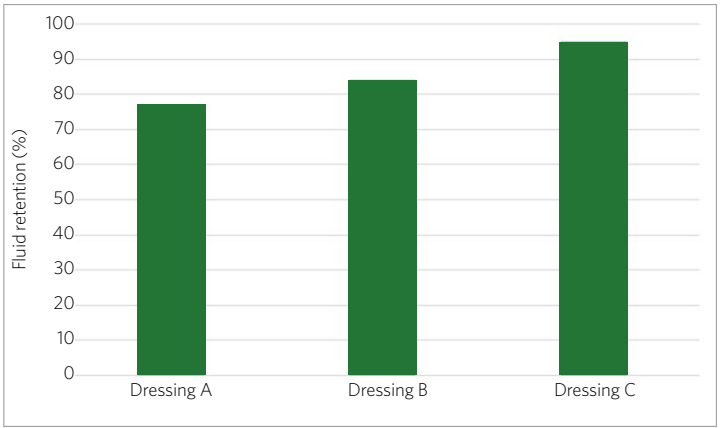
It is important that a dressing's absorption and retention capacity (i.e. its ability to 'lock in' exudate even under pressure and shear) is assessed not only in terms of fluid volume but also in terms of fluid viscosity. It is also important that wound dressings can retain or 'lock in' the absorbed exudate under pressure or frictional forces causing shear distortions, given the forces that may be applied to the dressing during normal use (for example, under compression bandages or unintentionally, as in incidental contacts of the wound area with objects or surfaces). Upon contact with fluid, Exufiber transforms into a solid gel to hold the fluid even if the pressure is elevated.

As a first laboratory approach, the absorptive capacity of Exufiber was investigated using the free swell absorption method ([SMTL TM101] Mölnlycke 2018b, data on file). In brief, a sample of the dressing (5x5cm) of known weight was placed in a Petri dish with a volume of test solution (sodium/calcium chloride containing 142 millimoles of sodium ions and 2.5 millimoles of calcium ions per litre [solution A]) equal to 40 times the weight of the test sample and was incubated for 30 ± 2 minutes. Using forceps, the sample was removed from the Petri dish, suspended for 30 seconds and reweighed. From these results, the mean weight of solution retained per 100cm^2 was calculated for sheet dressings and the mean weight of solution retained per gram of sample was calculated for packing/cavity dressings. The test was performed on 10 replicates.

Results demonstrated the ability of Exufiber to absorb and retain fluid (Mölnlycke 2018b, data on file). Furthermore, laboratory testing confirmed the ability of Exufiber to absorb fluid under continuous flow when pressure is applied (Mölnlycke 2018c, data on file; Mölnlycke 2020a, data on file), and the capacity of Exufiber to absorb fluid with different viscosities, including blood (horse blood), and using different test liquids (including a thickened solution containing guar gum) on an inclined plane at various pressures (Mölnlycke 2018c, data on file; Mölnlycke 2020a, data on file).

A different test method (SMTL TM-404) was used to determine the percentage retention of fluid. In this method, a pressure equivalent to 40mmHg was applied to the dressing for 30 seconds following absorption of the fluid. As mentioned above, this pressure was applied to mimic the pressure applied under compression bandaging used in the clinical setting. The dressing was then re-weighed to calculate the fluid retention capacity of the dressing, with the retention result calculated as a percentage. The test was performed on three replicates. Under these test conditions, Exufiber was shown to retain up to 23% more of the fluid absorbed compared to a CMC-based fibre dressing (Figure 5; Mölnlycke 2014, data on file; Mölnlycke 2018b, data on file).

Figure 5 | Dressing fluid retention, using laboratory method SMTL TM-404. *Dressing A is a CMC-based fibre dressing with silver; Dressing B is a CMC-based fibre dressing; Dressing C is Exufiber (Mölnlycke 2014, data on file)



Definition of 'sorptivity'

The capacity of a dressing structure to transfer excessive exudate away from the wound bed and onwards to the secondary dressing, through capillary action (Lustig et al, 2021).

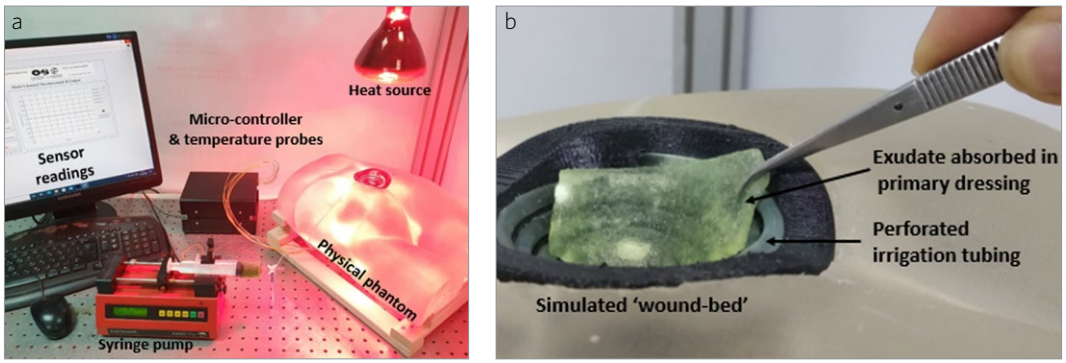
Transfer of exudate (dressing sorptivity)

Another important aspect of wound fluid management is the effective transfer of fluid from the primary dressing to the secondary dressing. The primary mechanism of action for gelling fibre dressings is capillary motion, where exudate is lifted and carried away from the wound bed surface through the capillary effect (Lustig et al, 2021). The ability of a primary dressing to effectively transport fluids away from the wound bed and towards a secondary dressing against gravity, if that is required due to the positioning of the patient and configuration of the wound, is called the sorptivity of the dressing (Lustig et al, 2021). Dressings with poor sorptivity, even if theoretically offering high retention (i.e. large saturation threshold), will not be able to utilise the theoretical retention in numerous clinical scenarios where gravity forces are opposing the required direction of exudate flow. An effective pair of primary and secondary dressings must include high sorptivity of the primary dressing for transfer of exudate to the secondary dressing, which then employs the retention reservoirs of both dressings. If there is no effective transfer of exudate between the primary and secondary dressings, a 'plugging effect' will occur, likely leading to the return of exudate to the wound bed and pooling or leaking from the dressing system causing periwound skin damage and generating a pathway for pathogens to penetrate the wound and potentially, from there, into the circulation.

Advanced *in vitro* testing

In a recently published laboratory study, Lustig et al (2021) compared the sorptivity of Exufiber and Exufiber Ag+ versus an alternative market-leading dressing. The authors designed, developed and built a robotic phantom of an exuding sacral PU, simulating an active wound environment in an anatomically and pathophysiologically realistic form (Figure 6). This method was developed to reflect the impact of real-world factors on dressing performance, including the mechanical forces applied on dressings due to patient bodyweight forces or during removal by a clinician, the technique of application and removal, the time of use between dressing changes, or the physical, chemical and biological properties of the exudate and how these interact with the materials of the applied dressing.

Figure 6 | (a) Robotic phantom set-up; (b) Simulated wound bed used within the robotic phantom model. *The photographed robotic sacral pressure ulcer system is described in detail in Lustig et al, 2021*



In this robotic phantom system, dressings are exposed to exudate-like fluids released from a simulated wound at chemical, mechanical and thermodynamic conditions that replicate real-world wounds. This facilitates objective, quantitative and standardised evaluations of dressing products and, thereby, methodological comparisons of the performances of dressings, while effectively accounting for clinical considerations that apply in practice e.g. the protocol and technique of dressing changes, the patient positioning, interactions with the support surface and other relevant medical devices.

The primary dressings were applied to a robotic phantom and put in interaction with Mepilex Border Sacrum (Mölnlycke Health Care), a multi-layered bordered foam dressing, which served as the secondary dressing. Exufiber demonstrated effective sorptivity, i.e. adequate transfer of fluids to the secondary dressing, consistently for different simulated patient body postures. In contrast, the other market-leading dressing acted more as a 'plug', which in real-world conditions, may cause hyper-hydration of the wound or periwound skin maceration, irritation and infection due to accumulation of exudate under or around the dressing when it is nearing the saturation point (Lustig et al, 2021). Consistent with the non-silver dressing data, Exufiber Ag+ retained 51% of the exudate fluid and transferred the other 49% into the secondary dressing, whereas the comparator silver-containing primary dressing transported only 31% of the fluid to the secondary dressing (n=5, p<0.05; Lustig et al, 2021).

More recently, the robotic phantom-based testing work was extended to study the performances of wound dressings used for treating a DFU (Lustig and Gefen, 2021). Non-offloaded DFUs and the wound dressings may be subjected to considerable bodyweight forces, such as during full-weight-bearing standing or while walking. An additional novel robotic phantom of an adult foot with a diabetic heel ulcer, was therefore designed and built to test the combined function of applied primary and secondary dressings in a simulated 'standing' posture versus an offloaded 'supine' posture (with the feet resting on a foam support surface). The robotic foot phantom was specifically employed to compare the performances of the primary Exufiber dressing, when combined with a secondary dressing, Mepilex Border Flex, a multilayered bordered foam dressing (Mölnlycke Health Care), against a corresponding pair from an alternative mainstream wound dressing manufacturer. Similarly to the work conducted using the robotic sacral PU phantom, fluid retention and distribution between the primary and secondary dressings of each pair were determined using weight tests (Lustig and Gefen, 2021). The findings revealed that the Exufiber and Mepilex Border Flex pair performed similarly in the two simulated postures (retention= ~97%), whereas the comparator pair exhibited a 13% decrease in retention for a 'supine' to 'standing' transition, simulating for example the process of getting out of the bed (Lustig and Gefen, 2021).

In addition, the fluid distribution between the primary and secondary dressings was measured after 5 hours of the simulated use, separately for the 'standing' and 'supine' positions. Following the 'standing' tests, the Exufiber dressing retained 39% of the total exudate-like fluid and delivered the remainder 61% away from the simulated DFU, into the secondary dressing. The other primary dressing was only able to transport approximately half the amount of the fluid (36%) into its paired secondary dressing under these simulated standing conditions, thereby leaving substantially more fluid at or near the wound. Consistently, for the simulated supine position (i.e. where the DFU was offloaded), the Exufiber dressing retained 26% of the fluid and effectively transferred the other 74% of the fluid into the secondary dressing, whereas the other primary dressing only transported 37% of the fluid to its secondary dressing (Lustig and Gefen, 2021).

The above remarkable differences between the laboratory performances of the two investigated dressing pairs makes an excellent example for why dressings should always be assessed in a clinically relevant context, reflecting real-world usage scenarios and clinical practice, so that the synergistic function of the dressing pair is measured, as opposed to examining each dressing in isolation (Lustig et al, 2021; Lustig and Gefen, 2021). For mobile patients with a DFU, it is absolutely critical that the dressing pair applied to treat their wound functions irrespectively of the activity profile of the patient (i.e. whether they offload their wound for a long time or not), so that the fluid handling efficacy of the prescribed dressings will not be influenced by the lifestyle. The Exufiber and Mepilex Border Flex pair of dressings has succeeded in experimentally demonstrating this important feature (Lustig and Gefen, 2021).

Definition of 'durability'

The capacity of dressings to maintain their structural integrity throughout the period of clinical use and during removal (Lustig et al, 2021).

Dressing structural integrity (durability)

Another element that is critical for patient safety and the effectiveness of treating the wound is the structural integrity of the dressing. It is vital that dressings have mechanical endurance (or durability), that is, that they maintain their mechanical strength and remain fully intact under the effect of any potential forces throughout the period of use, including under the elevated forces and stress concentrations that occur in the dressing structure when a clinician removes the dressing. This implies that the sustained exposure to the aggressive exudate fluids and body temperatures must not degrade the dressing materials or compromise their integrity. Any dressing debris or particulates left in the wound bed may result in a 'foreign body response' of the inflammatory system, which prolongs the inflammatory phase and consumes important healing resources, thereby delaying healing (Lustig et al, 2021).

Figure 7 shows a comparison of the progressive failure patterns of Exufiber against a comparator primary dressing product post-simulated use, through representative mechanical strength tests (conducted by means of uniaxial stretching in a materials testing machine).

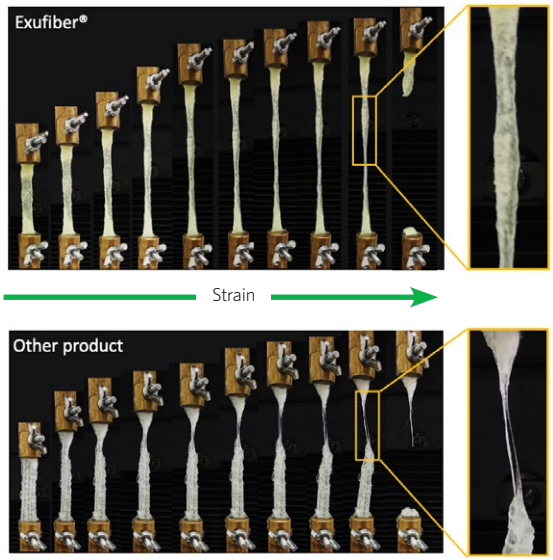


Figure 7 | Photographs of representative mechanical strength tests (through uniaxial stretching in a materials testing machine), to compare the progressive failure patterns of Exufiber against a comparator primary dressing product post-simulated use. Note that the Exufiber dressing demonstrates a more ductile behaviour until just before its ultimate failure (which promotes patient safety as this dressing remains intact), whereas in the other dressing, fibers have successively been torn. Hence, the ultimate failure in the other product ensues after loss of structural integrity and substantial fibre rupture had already occurred, which increases the risk for gradual release of particulates or debris from the used dressing into the wound

The robotic phantom of an exuding sacral PU (Lustig et al, 2021) was used to compare the performances of Exufiber and Exufiber Ag+ versus those of another market-leading product, with respect to mechanical endurance. Exufiber demonstrated considerably better mechanical endurance, approximately 5-times more than that of the other dressing.

Consistent with the experimental testing conducted using the sacral PU phantom as reported in Lustig et al (2021), measurements of the mechanical strength of the primary dressings post-simulated use were also performed after exposing the dressings to the environment of the DFU phantom system (Lustig and Gefen, 2021). The mechanical strength data for the dressings under investigation consistently revealed that after exposure to the DFU cavity and fluid conditions, the Exufiber dressing had superior strength, which was 1.7-times and statistically significantly greater than that of the comparator primary dressing exposed to the same conditions (Lustig and Gefen, 2021). Of note, where a primary dressing had shown noticeable directionality of its fibres or a seam pattern, these dressing products were tested by applying the tensile forces simulating removal of the dressing in alignment with the direction of the visible reinforcing fibres/seams, thereby allowing the tested dressings to exhibit their maximal mechanical strength (i.e. their best durability performances) (Lustig and Gefen, 2021). With that said, it is highly unlikely that a practicing clinician would pull out a fibre-reinforced (used) dressing precisely along the direction of the reinforcing fibers while removing a dressing for cleaning the wound and changing the dressing. Noteworthy, in such situations, the dressing is typically folded within the wound and would take a similar colour to that of the exudate and, therefore, alignment of the pulling forces with seams on the dressing during removals would not be feasible even if the wound care clinician would attempt to do so. In this regard, a dressing such as Exufiber, which does not have any specific primary directional stiffness or strength preferences, is highly advantageous, as it is able to effectively resist pull-out forces irrespective of the angle

and orientation at which a healthcare professional is attempting to pull the dressing away from the wound (Lustig and Gefen, 2021).

In work that is currently underway, the team of researchers led by Professor Amit Gefen at Tel Aviv University studies the dynamics (i.e. the time course) of the fluid sharing evolution between primary and secondary dressings. Their initial findings indicate that the Exufiber Ag+ dressing is substantially more effective in transferring exudate simulants to a secondary foam dressing compared with the market alternative primary dressing. Specifically, Exufiber Ag+ delivered approximately 2-fold and 1.5-fold the amounts of fluid to a secondary paired foam dressing after 10 and 15 hours within a simulated cavity wound, respectively, with reference to a comparator dressing pair. Importantly, the more fluid that is being transferred to the secondary dressing, the greater the available capacity of the primary dressing for managing new exudates that are secreted from the wound. These recent experimental results demonstrate that the extent and rate of the fluid sharing between the primary and secondary dressings strongly depend on the specific dressing materials and composition. Accordingly, primary and secondary dressings from different manufacturers would differ in their performances (alone or combined together), even if they belong to the same family of dressing products (such as gelling fibre dressings for primary dressings or multi-layered bordered foam dressings for secondary dressings).

MICROBIOLOGICAL STUDIES

The inclusion of ionic silver in its structure allows Exufiber Ag+ to provide an antimicrobial effect upon contact with wound fluid. The released silver ions target multiple sites within or on microbial cells. *In vitro* and *in vivo* testing has shown that Exufiber Ag+ has a fast, broad and sustained antimicrobial effect.

Planktonic microorganisms

An *in vitro* direct contact method was used to investigate the antimicrobial property of Exufiber Ag+ against a range of microorganisms in their planktonic form (Gerner et al, 2019a). Microorganisms were suspended in a test medium with a similar composition to that of wound exudate known as simulated wound fluid (SWF). Circular pieces of the dressing were inoculated with approximately 10^6 colony-forming units (CFUs) per dressing piece, imitating contaminated exudate being absorbed by the dressing. Results were expressed as logarithmic reductions in relation to initial concentration.

Exufiber Ag+ was shown to have an antimicrobial effect against a wide range of wound-related pathogens, including Gram-negative bacteria, Gram-positive bacteria and fungal species, with a sustained effect up to 8 days, reducing the test organisms by at least 4 logarithmic units at 4 and 8 days (Figure 8; Gerner et al, 2019a). Exufiber Ag+ was also shown to have a rapid antimicrobial effect, as demonstrated using a direct contact method, with logarithmic reductions of microorganisms evident within 3 hours (Figure 9; Mölnlycke 2020b, data on file).

The same *in vitro* method was used to compare the antimicrobial activity of Exufiber Ag+ with other gelling fibre dressings, i.e. a CMC-based fibre dressing with silver and a CMC-based fibre dressing with silver, benzethonium chloride and ethylenediaminetetraacetic acid (EDTA). The direct contact method was used to investigate the antimicrobial effect against *Pseudomonas aeruginosa*, methicillin-resistant *Staphylococcus aureus* (MRSA) and *Candida albicans* (starting inoculum of approximately $7x10^6$ – $1x10^7$ CFU/ml, inoculation volume of 0.7ml) (Figure 10).

Results demonstrated a reduction in planktonic microorganisms inside all three silver-containing dressings, with a logarithmic reduction of at least 3 at each time point, with *P. aeruginosa* being the most sensitive organism; *C. albicans* was the least sensitive organism (Figure 10). However, Exufiber Ag+ was concluded as the most efficient dressing (Gerner et al, 2019b). The authors concluded that the results demonstrated the broad and sustained antimicrobial effect *in vitro* of Exufiber Ag+, as it reduced all three test organisms below the level of detection at each time point (Gerner et al, 2019b).

A further *in vitro* method was used to determine the antimicrobial activity of Exufiber Ag+. In brief, circular pieces of the test dressing were pre-wetted in SWF and placed on top of agar gel (with 10% SWF) inoculated with test organisms (*P. aeruginosa*, *S. aureus* and *C. albicans*) at a starting concentration of approximately 10^6CFU/ml to mimic the contaminated wound bed. To test compatibility with a secondary dressing and represent the use of the dressings in clinical practice, circular pieces of an ultra-absorbent dressing were placed on top of the test and control dressings. Samples were incubated at 35°C for 24 hours, 4 days or 8 days. Microorganisms were recovered from the gel and viable counts were taken for each time point, and results expressed as logarithmic reductions in the gel in relation to the start inoculum.

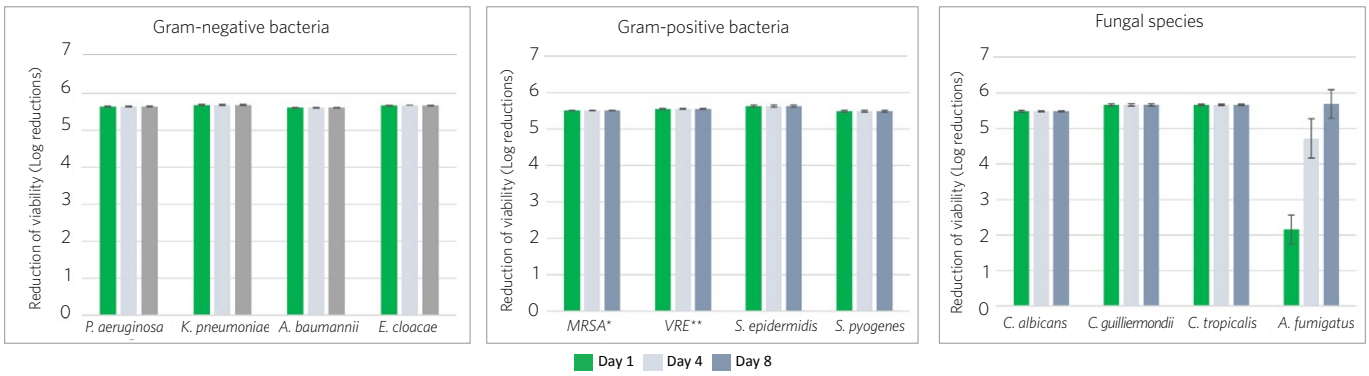


Figure 8 | Reduction of viability (logarithmic reductions) of a range of microorganisms in their planktonic form following incubation within Exufiber Ag+ samples *in vitro* over an 8-day period. Logarithmic reductions calculated in relation to start inoculum concentration. Bars show mean of three replicates; error bars show standard deviation (SD) (Gerner et al, 2019a)

*Methicillin-resistant *Staphylococcus aureus* **Vancomycin-resistant *Enterococcus faecalis*

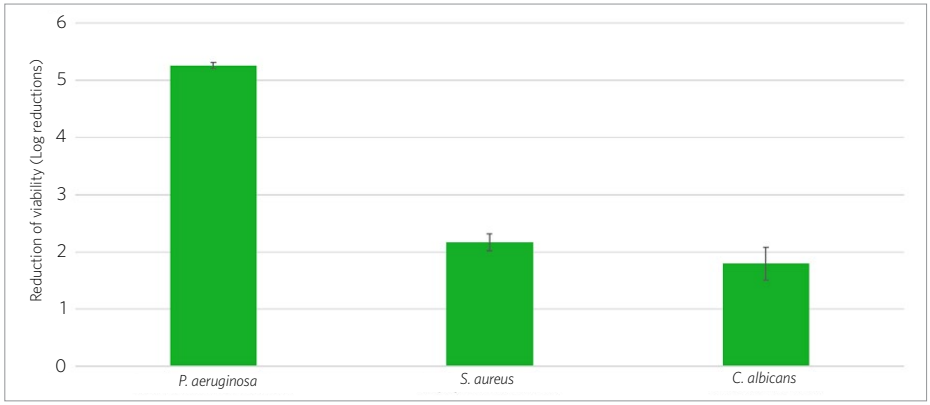


Figure 9 | Antimicrobial effect of Exufiber Ag+ against *P. aeruginosa*, *S. aureus* and *C. albicans* determined by direct contact method at 3 hours. A dressing containing the same materials as Exufiber Ag+ except for the silver component (not commercially available) was used as a negative control. Logarithmic reductions calculated in relation to start inoculum concentration. Bars show mean of three replicates; error bars show standard deviation (SD) (Mölnlycke 2020b, data on file)

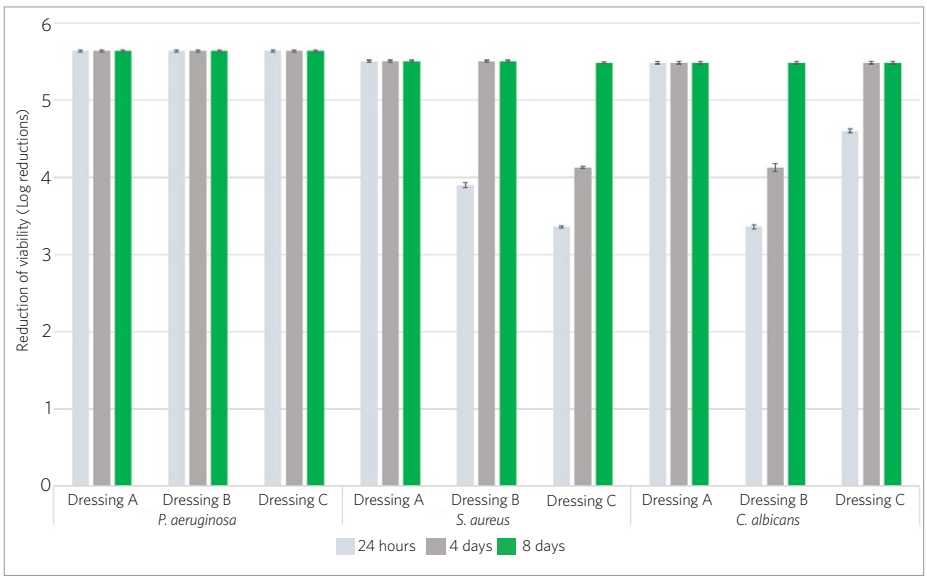


Figure 10 | Reduction of viability of *P. aeruginosa* ATCC 15442, methicillin-resistant *S. aureus* (MRSA) ATCC 44300 and *C. albicans* ATCC 20231 by three silver-containing dressings determined in a direct contact method at 24 hours, 4 days and 8 days. A dressing containing the same materials as Exufiber Ag+ except for the silver component (not commercially available) was used as a negative control. Logarithmic reductions calculated in relation to start inoculum concentration. Bars show mean of three replicates; error bars show standard deviation (SD) (Gerner et al, 2019b). *Dressing A is Exufiber Ag+; Dressing B is a CMC-based fibre dressing with silver; Dressing C is a CMC-based fibre dressing with silver, benzethonium chloride and ethylenediaminetetraacetic acid (EDTA)

Logarithmic reductions within the gel were observed for all three test organisms, demonstrating the antimicrobial effect. Furthermore, when the secondary dressing was applied on top of the gelling fibre dressing in this model, logarithmic reductions were not significantly affected (Figure 11; Gerner et al, 2019a).

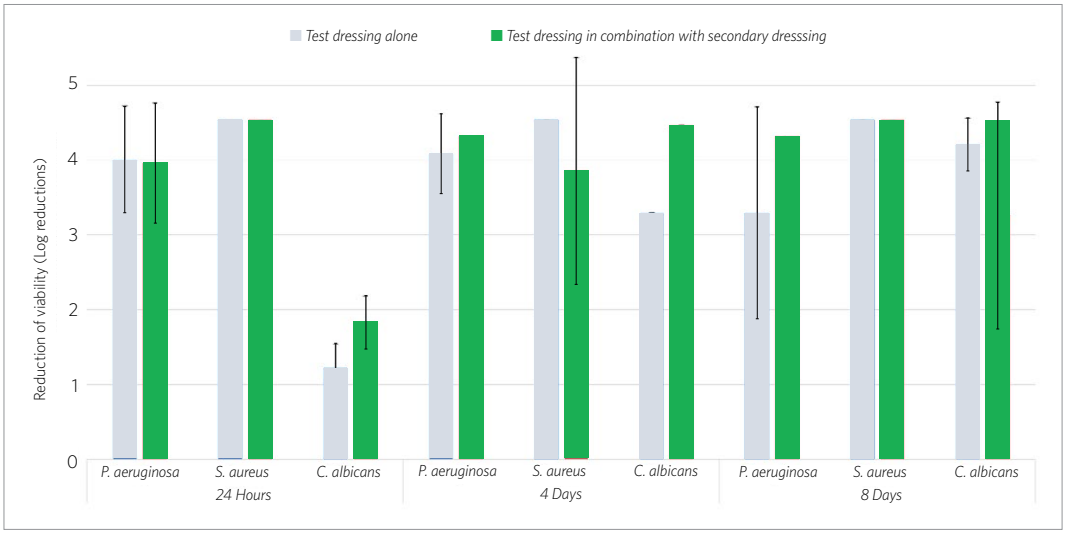


Figure 11 | Reduction of viability (logarithmic reductions) of three test microorganisms in the *in vitro* agar gel model, with Exufiber Ag+ samples alone and in combination with secondary dressing samples. Logarithmic reductions calculated in relation to start inoculum concentration. Bars show mean of three replicates; error bars show standard deviation (SD) (Gerner et al, 2019a)

Biofilm

It is considered that biofilms are ubiquitous in chronic non-healing wounds (Malone et al, 2017). Given the detrimental impact of biofilms on wound healing, it is also important to assess the antimicrobial effect of a dressing against microorganisms within a biofilm.

The collagen gel biofilm method (Werthén et al, 2010) was used to investigate the antimicrobial effect of three test dressings against *S. aureus* biofilm: Exufiber Ag+ (Dressing A), a CMC-based fibre dressing with silver (Dressing B) and a dressing with silver ions bound to charge groups of CMC fibres and containing benzethonium chloride and EDTA (Dressing C).

Both Dressing A and Dressing C reduced *S. aureus* biofilm by approximately 5 logarithmic units in relation to the control after 24 hours treatment; Dressing B reduced biofilm by approximately 1 logarithmic unit (Figure 12; Gerner et al, 2019b). The three dressings differ in chemical composition and silver content, which can lead to differences

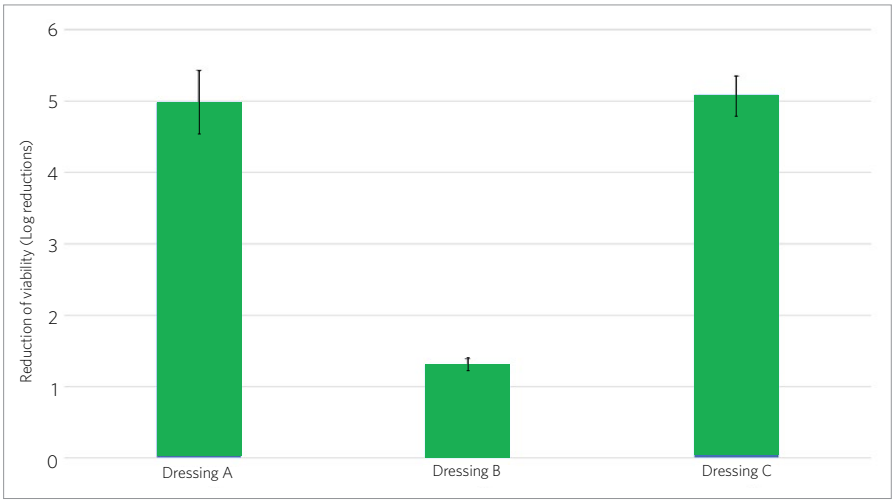


Figure 12 | Reduction of viability of *S. aureus* ATCC 6538 biofilm by three silver-containing dressings at 24 hours, determined in a collagen biofilm model. A non-silver containing fibre dressing (not commercially available) was used as a negative control sample. Logarithmic reductions calculated relative to the control after 24 hours treatment. Bars show mean of three replicates; error bars show standard deviation (SD) (Gerner et al, 2019b). *Dressing A is Exufiber Ag+; Dressing B is a CMC-based fibre dressing with silver; Dressing C is a CMC-based fibre dressing with silver, benzethonium chloride and EDTA

in Ag+ release and bioavailability (Davis et al, 2019a). In this laboratory study, Exufiber Ag+ effectively reduced *S. aureus* bioburden in a wound-relevant biofilm *in vitro* model, indicating the effectiveness of silver alone against biofilm (as compared to the dressing with silver, benzethonium chloride and EDTA as active substances; Gerner et al, 2019b).

Wound bioburden and healing *in vivo* (animal model)

Recent pre-clinical evidence has demonstrated the effect of Exufiber Ag+ in the treatment of *P. aeruginosa in vivo*. Using a well-established porcine wound biofilm model, Davis et al (2019a) studied the effect of Exufiber Ag+ compared to a CMC-based fibre dressing with silver, benzethonium chloride and EDTA and untreated control against *P. aeruginosa* biofilm. Porcine deep partial-thickness wounds were inoculated with *P. aeruginosa* ATCC 27312 and covered with a polyurethane film dressing to promote biofilm formation; the resultant 24-hour biofilms were treated with the test dressings. Microbiological, biofilm and histological wound assessments were performed on days 3, 5 and 7 post-infection (Davis et al, 2019a). After treatment with Exufiber Ag+, wounds had a significant reduction of *P. aeruginosa* biofilm when compared to all other treatment groups at each assessment time point (Figure 13). Furthermore, immunostaining for visualisation of wound biofilm highlighted *P. aeruginosa* biofilm detachment away from the newly formed epidermis in deep partial-thickness porcine wounds treated with Exufiber Ag+ (Davis et al, 2019a). In addition, wounds treated with a non-silver containing fibre dressing (not commercially available) or Exufiber Ag+ showed more granulation tissue formation and white cell infiltration on day 3 than wounds treated with the CMC-based fibre dressing with silver, benzethonium chloride and EDTA and the untreated control (no significant difference was observed at the other time points; Davis et al, 2019a).

The same research group also presented data relating to treatment of MRSA wound biofilms with Exufiber Ag+ *in vivo* (Davis et al, 2019b) (Figure 13). Wounds treated with Exufiber Ag+ had statistically significantly ($p<0.05$) lower counts of MRSA compared to baseline and untreated control at each assessment day. Wounds treated with Exufiber Ag+ also had statistically significantly ($p<0.05$) lower MRSA counts in the biofilm model compared to all other treatment groups on day 5 and day 7 (Davis et al, 2019b).

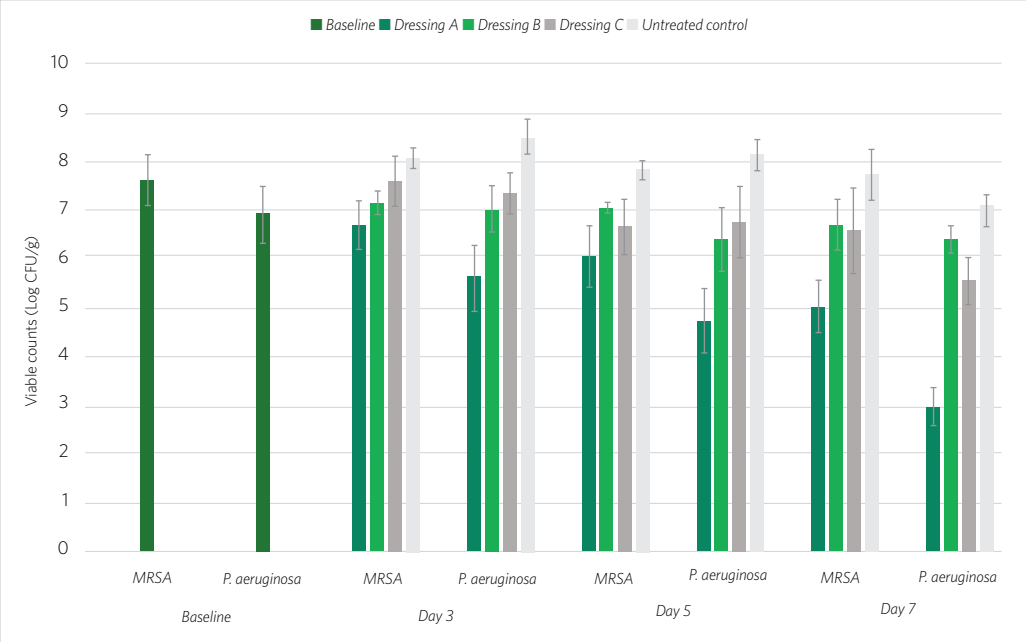


Figure 13 | Viable counts (Log CFU/g) of *P. aeruginosa* and MRSA biofilm by three dressings at baseline and days 3, 5 and 7. Bars show mean of three replicates; error bars show standard deviation (SD) (Davis et al, 2019a; Davis et al, 2019b). *Dressing A is Exufiber Ag+; Dressing B is a non-silver containing fibre dressing (not commercially available); Dressing C is a CMC-based fibre dressing with silver, benzethonium chloride and EDTA

CLINICAL EVIDENCE

This section reviews the clinical evidence relating to the use of Exufiber and Exufiber Ag+ as part of the management of a range of wound types. While the conventional approach to evidence-based medicine is to focus on randomised controlled trials (RCTs), practice-based medicine allows for flexibility, for example, wound dressing choice based on individual patient needs. A number of clinical studies have been carried out to evaluate the use of Exufiber and Exufiber Ag+ on a range of wound types, including DFUs and VLUs. All available clinical evidence from across the entire evidence hierarchy has been considered and evaluated (Table 2).

Chadwick and McCardle (2016) evaluated the use of Exufiber in the management of DFUs, with improvement in periwound skin condition, increased wound epithelialisation and excellent absorption and retention of exudate by the dressing observed. Similar results were recorded by Smet et al (2015) in a non-comparative study of patients with stage 2-4 PIs that were dressed with Exufiber. The authors of this study highlighted that the benefits of Exufiber were in supporting wound healing, improving the state of the periwound skin and its ability to manage wound exudate effectively. The authors also commented on the ease of removal of the dressing from wound cavities in once piece, which as stated previously, is a key requirement of a cavity dressing.

In a technical performance survey (Davies and McCarty, 2017), 320 clinicians were asked to evaluate the performance of Exufiber following its use in a variety of patient groups including those with VLUs. The survey respondents generally rated Exufiber positively in terms of the high retention capacity, conformability and ease of removal of the dressing in one piece.

A multi-centre RCT was performed in 35 centres across Europe to demonstrate non-inferiority with a comparator CMC fibre-based dressing in a group of patients with VLU and mixed aetiology wounds (Mölnlycke 2021, data on file). Patients were followed-up for 6 weeks after initial assessment and, although the difference was not significant statistically, there was a trend in terms of greater wound size reduction in those offered Exufiber: the Exufiber patient group (n=100) showed a 50% wound area reduction in 6 weeks compared with 42% wound area reduction in the comparator CMC fibre-based dressing patient group. As with the previous studies, Exufiber demonstrated high levels of clinician and patient satisfaction in relation to ease of use, exudate management, removal of sloughy tissue and also in managing less viscous fluid, such as blood.

A study by Lev Tov et al (2020) was carried out to examine the clinical effectiveness of Exufiber Ag+. This study included 102 patients who were studied over a 4-week period. Exufiber Ag+ demonstrated excellent exudate management, with approximately half (52.6%) of patients experiencing only one dressing change per week. None of the patients that used Exufiber Ag+ required dressing changes due to leakage, which as stated previously, can lead to maceration of the periwound skin. All patients demonstrated a progression towards healing, through increased epithelialisation and a decrease in sloughy tissue over the course of the study. A small subset analysis of patients was compared with a CMC-based fibre dressing with silver, benzethonium chloride and EDTA; however, there were no differences in the overall performance of the two products.

Table 2: Summary of the clinical evidence relating to Exufiber and Exufiber Ag+

Dressing	Reference	Design method	Main outcome measures	Main results
Exufiber	Chadwick and McCardle, 2016	Open, non-comparative, multi-centre study on highly exuding DFUs (*n*=21) 12-week study period	Performance and safety of Exufiber when used as part of the management regimen for highly exuding DFUs: • Condition of periwound area, dressing-related pain, wound status (wound size and healing phase) • Investigator/nurse and patient opinions of the dressing • Technical performance (presence of dressing residue following removal, handling of wound exudate)	• Number of patients with healthy/intact periwound skin increased from baseline to the final visit • Statistically significant reduction in wound area (cm^2), p=0.0094 and wound volume (cc), p=0.0056, from baseline to the final visit • Steady decrease in wound exudate • Small decline in mean percentage of granulation tissue, gradual increase in mean percentage of epithelialisation tissue, percentage of non-viable tissue remained very low • Pain levels were very low throughout the study period, bearing in mind issues with neuropathy • No occurrences of product degradation on the skin • No reported AE/ADE judged to be related to the investigational product • The technical performance of the dressing was demonstrated by an ability to absorb and retain exudate • The dressing was found to be easy to use and transferable into existing clinical wound dressing tool kits • The dressing was found to be simple to apply and it was reported to be comfortable to wear and absorbed exudate effectively
Exufiber	Smet et al, 2015	Open, non-comparative, multi-centre clinical investigation on exuding stage 2–4 PIs (*n*=21, 15 completed the study) 6-week study period	Performance and safety of Exufiber in the management of exuding stage 2–4 PIs: • Periwound skin assessment • Pain at dressing change • Wound condition • Technical performance of the dressing (ability to handle exudate, presence of dressing residue following removal) • Patient/investigator satisfaction • Number of dressing changes per week	• Mean number of dressing changes per week (excluding secondary dressings) was 2.7 • Signs of poor periwound skin condition were minimised throughout the investigation period • Reduction in wound size throughout the investigation period • Improvements in wound bed condition and condition of periwound skin throughout the investigation period • Authors concluded that the healing outcomes are also indicators of the dressing's ability to manage excess exudate • Dressing-associated pain decreased from baseline to the final visit (despite stage 4 PIs being included in the investigation) • No residues were left in the wound on removal of the dressing • No reported AEs or ADEs during the study judged to be related to the investigational dressing • Investigators rated the dressing highly in terms of ease of removal, conformability and overall experience • Study participants rated the dressing highly in terms of comfort and ease of movement during wear
Exufiber	Davies and McCarty, 2017	Survey of 320 clinicians across Germany	Technical performance of Exufiber in terms of a range of in-use dressing characteristics: • Exudate handling • Ease of use • Patient comfort	• Respondents to the survey had used the dressing on a variety of wound types, including leg ulcers, PIs and DFUs • Exufiber was rated highly in terms of exudate absorption and retention capacity, conformability, ease of removing the dressing in one piece and patient comfort during wear
Exufiber Ag+	Lev-Tov et al, 2020	Prospective, multi-centre investigation (medium to high exuding wounds of adults) Three treatment groups (Exufiber Ag+, Exufiber, CMC-based fibre dressing with silver, benzethonium chloride and EDTA) In total, 102 out of 109 patients completed the study (*n*=62 in the Exufiber Ag+ group, *n*=11 in the Exufiber group, *n*=12 in the CMC-based fibre dressing with silver, benzethonium chloride and EDTA group) 4-week study period (or shorter if the wound was dry or healed), weekly dressing changes	Impact of Exufiber Ag+ on: • Exudate management • Wound status • Periwound skin condition • Comfort Safety and tolerability	• Exufiber Ag+ was well-tolerated and performed well in terms of exudate handling, technical performance and patient experience • Statistically significant decrease in exudation from baseline to final visit in the Exufiber Ag+ cohort (p=0.0019) • Most wounds treated with Exufiber Ag+ did not have a primary dressing change due to leakage; 52.6% of subjects had no primary dressing change for 7 days or more • No dressing changes due to leakage occurred in the Exufiber cohort, whereas there were two in the CMC-based fibre dressing with silver, benzethonium chloride and EDTA cohort at visit 3 • Exufiber Ag+ performed well in terms of progression towards wound healing; an increase in epithelialisation and a decrease in slough for all cohorts was reported by visit 5, statistically significant increase in the percentage of epithelialisation (p=0.0027) in the Exufiber Ag+ group • Overall handling and technical performance of Exufiber Ag+ was rated as 'good' or 'very good' (visit 5) by all investigators and patients • 36 AEs reported in 29 participants, no device-related serious AEs occurred • A small subset analysis of patients was compared with a CMC-based fibre dressing with silver, benzethonium chloride and EDTA; however, there were no differences in the overall performance of the two products

AE: Adverse event, ADE: Adverse device effect

CASE STUDIES

The following case studies demonstrate the use of Exufiber and Exufiber Ag+ as part of the management of complex wounds. The reports help to illustrate some of the challenges faced by those involved in the management of patients with complex wounds and how Exufiber and Exufiber Ag+, in conjunction with other interventions, can contribute towards effective exudate management and successful clinical outcomes.

CASE STUDY 1 Abscess

Paulo Alves, Wounds Research Laboratory, Centre for Interdisciplinary Research in Health (CIIS), Universidade Catolica Portuguesa, Oporto, Portugal; João Castro, Chief Nurse/Technical Director Multivaze, Wecare Saude, Unidade de Cuidados Continuados Integrados e Paliativos, Póvoa de Varzim, Portugal

Patient/wound history

An 85-year-old female presented with a 1-week old abscess (Figure 14a). The patient had a current medical history of cerebrovascular accident, dementia and hypertension. She was dependent on a high degree of activities of daily living. She was receiving enteral nutrition via a nasogastric tube.

The ulcer was located on the right thigh and measured 20.36cm^2 (5.2cm length x 4.3cm width), with a depth of 5cm after debridement. The ulcer appeared as an abscess following the intramuscular administration of an anti-inflammatory agent. The wound was initially covered with dry eschar tissue (sloughy tissue was observed at subsequent visits). Exuberant signs of inflammation were observed (swelling, redness, pain, raised periwound temperature). There was no exudate prior to surgical debridement. Following eschar removal, moderate levels of viscous exudate, without odour, were observed.

Wound treatment regimen

To manage the exudate and assist with wound bed preparation, Exufiber was applied (Figure 14b), with Mepilex Border Flex (multi-layered bordered foam) used as a secondary dressing. The dressing conformed to the shape of the body. Dressing changes were initially undertaken every 3 days for 2 weeks until major growth of the granulation tissue was observed. Subsequently, dressings were changed once per week. After 10 days, Granulox® (a topical haemoglobin spray) was applied to the debrided wound, prior to the application of the dressings.

Follow-up assessments

Over the treatment period, the ulcer area and depth steadily decreased (Figures 14c–14f). The condition of the wound bed tissue steadily improved, with 100% granulation tissue present. There were no clinical signs of local wound infection. Wound exudate reduced from moderate to low levels. The periwound skin remained dry without maceration, despite the high levels of exudate at the outset. Pain during treatment was noted at the start of the evaluation period but started to decrease in the early stages of follow-up. Dressing change-related pain was reported as low-to-none.

Clinical outcome

At the final evaluation, the wound had healed (Figure 14g). The clinicians commented that Exufiber could be easily removed intact and facilitated autolytic debridement due to good exudate management.

Figure 14a | Wound at the start of the evaluation (day 1)

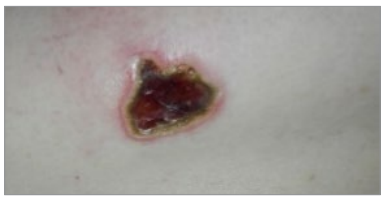


Figure 14b | Exufiber *in situ* in the wound cavity (follow-up visit, day 4)

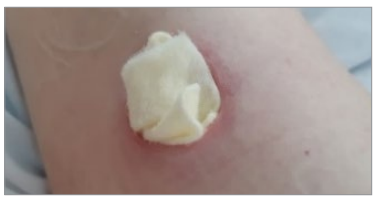


Figure 14c | Clean wound bed covered with healthy granulation tissue (follow-up visit, day 10)

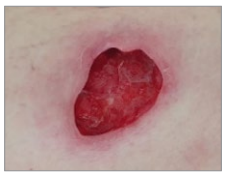


Figure 14d | Ulcer depth reduced to 4cm (follow-up visit, day 23)

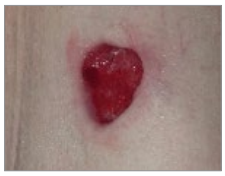


Figure 14e | Ulcer depth reduced to 1cm (follow-up visit, day 63)

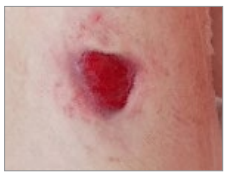


Figure 14f | Wound depth significantly reduced, wound edges epithelialising and contracting and periwound skin healthy and intact (follow-up visit, day 74)

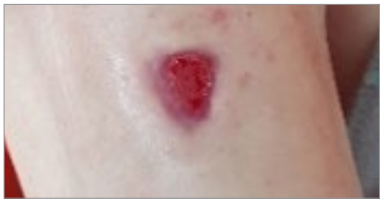
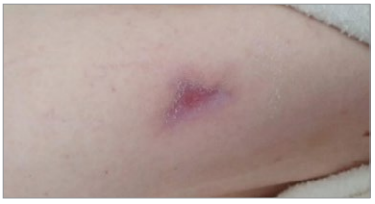


Figure 14g | Ulcer healed (end of evaluation, day 103)



CASE STUDY 2 Diabetic foot ulcer (DFU)

Paulo Alves, Wounds Research Laboratory, Centre for Interdisciplinary Research in Health (CIIS), Universidade Catolica Portuguesa, Oporto, Portugal); João Castro (Chief Nurse/Technical Director Multivaze, Wecare Saude, Unidade de Cuidados Continuados Integrados e Paliativos, Póvoa de Varzim, Portugal

Patient/wound history

A 96-year-old female presented with a five-week old DFU (Figure 15a). The patient had a current medical history of arterial hypertension, type 2 diabetes mellitus, peripheral vascular disease and dementia. The ulcer was located on the left heel and measured 54.24cm^2 (11.3cm length x 4.8cm width x 0.8cm depth). Fifty percent of the wound bed was covered with sloughy tissue. Clinical signs of wound infection (stagnated wound, erythema, swelling, raised periwound temperature, pain, odour and increased exudate) were observed. Wound exudate was high, viscous and yellow/green in appearance. The periwound region was flushed but integrated, with tenuous signs of cellulitis. The wound had previously been surgically debrided, followed by the application of hydrogel and silver/activated charcoal-containing foam dressings. Antibiotic therapy was also administered.

Wound treatment regimen

Over the initial 2 weeks of the evaluation, the ulcer was treated with Exufiber Ag+ (Figure 15b). Thereafter, Exufiber and Granulox were applied. Throughout, Mepilex® Border Heel was used as a secondary dressing. At the follow-up visits, the dressings were changed; dressing changes were performed according to local clinical practice or when the dressing became saturated.

Follow-up assessments

Over the evaluation period, the ulcer area and depth steadily reduced; after 7 weeks, the wound measured 25.42cm^2 (6.2cm length x 4.1cm width), a reduction of 50%. The condition of the wound bed steadily improved, with 100% granulation tissue present. After 2 weeks of treatment and thereafter, all clinical signs of local wound infection were absent. Wound exudate levels decreased substantially; exudate became less viscous and clear/yellow in appearance. The periwound skin was hydrated and intact, without signs of injury or maceration (Figure 15c).

Clinical outcome

At the final evaluation, the wound had significantly reduced in size (Figure 15d). The clinicians commented that both Exufiber Ag+ and Exufiber afforded excellent wound exudate management.

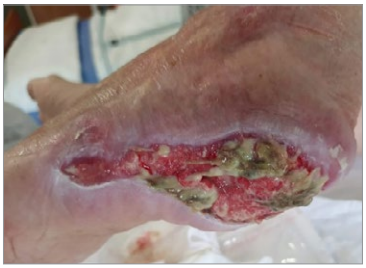


Figure 15a | Wound at the start of the evaluation (day 1)

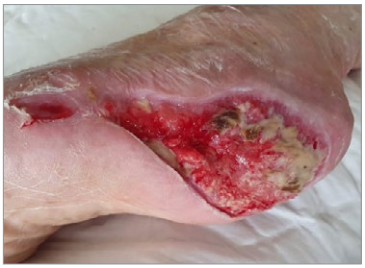


Figure 15b | Wound at day 7. After 1 week of treatment with Exufiber Ag+

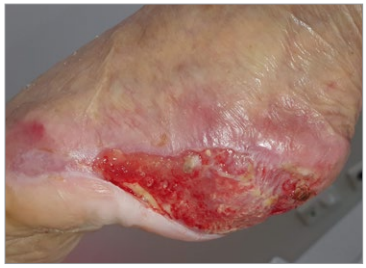


Figure 15c | Wound at day 14. Signs of infection and biofilm were absent so Exufiber Ag+ was discontinued; treatment with Exufiber and Granulox was initiated

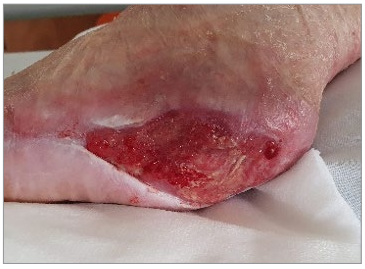


Figure 15d | Wound at the end of the evaluation (day 48); 50% reduction in wound size with granulating wound bed and low exudate

CASE STUDY 3 Leg ulcer

This case study report has been prepared by Mölnlycke's Global Medical Affairs and Safety team, based on information and photographs taken from a Mölnlycke-sponsored clinical investigation (Clinical Trials.gov identifier: NCT02921750)

Patient/wound history

A 63-year-old male presented at the clinic with a leg ulcer (Figure 16a). The patient had a current medical history of obesity and benign prostatic hyperplasia (medication prescribed). Past medical history included gonarthrosis and prolapsed disc. The ulcer, located on the right inner ankle, measured 1.76cm^2. It was critically colonised with *Staphylococcus aureus* and *Escherichia coli*. The ulcer had been present for 10 weeks. The wound bed composed of 20% granulation tissue and 80% slough/fibrin. There were no clinical signs of wound infection. Exudate levels were moderate and serous in nature and the periwound skin was healthy and intact. Compression therapy was not used prior to enrolment.

Wound treatment regimen

The ulcer was treated with Exufiber and compression therapy. The patient attended six follow-up visits over a 67-day period. At the follow-up visits, the dressing was changed. Dressing changes were performed according to local clinical practice or when the dressing became saturated.

Follow-up assessments

Over the treatment period, the size of the wound steadily reduced. At the third (day 26) and fourth (day 39) follow-up visits, the wound measured 1.61cm^2 (9.2% reduction) and 0.6cm^2 (66% reduction), respectively. The condition of the wound bed tissue steadily improved over the treatment period. Clinical signs of local wound infection were absent throughout. At the first follow-up visit and until the fifth follow-up visit (week 8), wound exudate was low but serosanguinous in nature; thereafter, wound exudate was absent. Moderate to mild redness of the periwound skin was recorded at the initial three follow-up visits, but thereafter the periwound skin was healthy and intact (Figures 16b and 16c).

Clinical outcome

At the final evaluation, the wound had healed (Figure 16d).

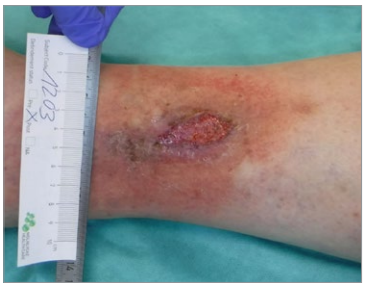


Figure 16a | Wound at start of evaluation (day 1), following debridement. A 10-week old leg ulcer with moderate levels of serous exudate. The periwound skin was healthy and intact

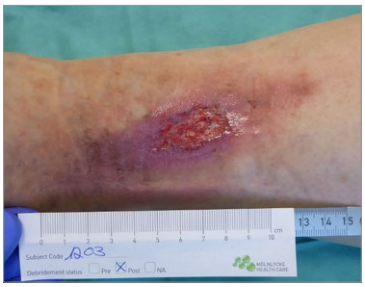


Figure 16b | Wound at first follow-up visit (day 5), following debridement. After five days of treatment with Exufiber, the wound bed was composed of 50% granulation tissue, 10% epithelialisation and 40% slough/fibrin. Moderate redness of the periwound skin was recorded

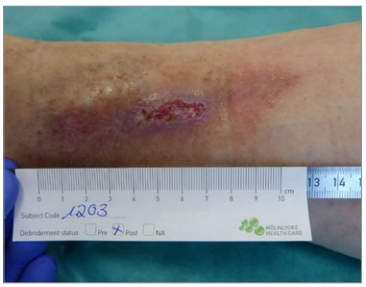


Figure 16c | Wound at fourth follow-up visit (day 39), following debridement. After 39 days of treatment with Exufiber, the wound measured 0.6cm^2, a 66% reduction in wound area. The periwound skin was healthy and intact

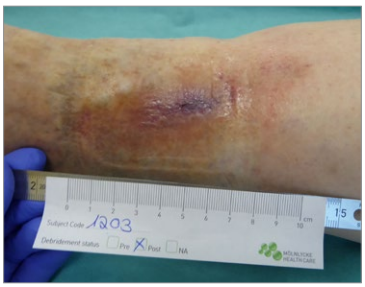


Figure 16d | Ulcer healed (end of evaluation, day 42), following debridement

CASE STUDY 4 Diabetic foot ulcer (DFU)

This case study report has been prepared by Mölnlycke's Global Medical Affairs & Safety team, based on information and photographs taken from a Mölnlycke-sponsored clinical investigation (ClinicalTrials.gov identifier: NCT03249909).

Patient/wound history

A 53-year-old male patient presented with a DFU on the plantar region of the left forefoot, that measured 800mm^2 (Figure 17a). It had been present for a duration of 6 weeks and had previously been treated twice weekly using an absorbent dressing and gauze. The ulcer exhibited signs of infection and moderate levels of serous wound exudate. The patient was obese with a body mass index of 30.52kg/m^2 and had a current medical history of type 2 diabetes mellitus and diabetic polyneuropathy (ongoing medication). There was no significant surgical history.

Wound treatment regimen

Following sharp debridement of the wound, Exufiber Ag+ was applied as the primary dressing.

Follow-up assessments

After the initial week of treatment, the wound area was significantly reduced by 48% to 420mm^2; thereafter, the wound area continued to steadily reduce (2-weeks — 180mm^2; 3-weeks — 60mm^2), and at the final visit the wound area measured 8mm^2, a reduction of 99% from baseline. Throughout the evaluation period, the wound bed was composed of 100% granulation tissue and the wound showed no clinical signs of infection. High levels of serosanguinous wound exudate were reported throughout the study period. During the first and fourth week of treatment, maceration of the periwound skin was reported, but at the final evaluation the periwound skin was healthy and intact.

Clinical outcome

After 28 days of treatment, the condition of the wound had significantly improved with a 99% reduction in wound area (Figure 17b).

The clinicians rated Exufiber Ag+ as 'Good' for its ability to maintain a balanced environment. On average, they rated its ease of application, conformability and retention of soft gelling properties, and its 'one-piece' removal as 'Good'. The clinicians commented on the dressing's ability to both absorb exudate/blood and to retain exudate/slough, with no dressing leakage, thereby facilitating the progress towards a 'clean' wound bed. The patient rated Exufiber Ag+ as 'Good' for comfort and ease of mobility during wear, and its ability to stay in place.

Figure 17a | Initial presentation of the wound, following debridement. The wound measured 800mm^2

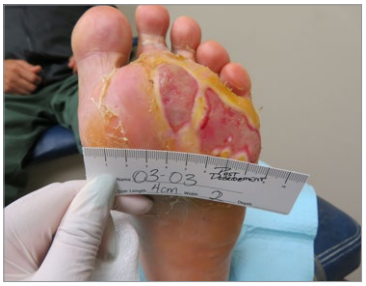
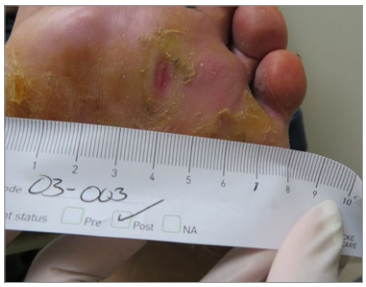


Figure 17b | The wound at the final evaluation (28 days), following debridement: wound area measured 8mm^2, representing a 99% reduction from baseline



CONCLUDING REMARKS

Wound dressings have been created to manage a number of clinical conditions, including cavity wounds and wounds where exudate levels may vary from low levels in a relatively dry wound to highly exuding wounds where there is a genuine risk of damage to the surrounding skin. Likewise, dressings should be evaluated according to their ability to manage a clinically relevant range of exudate viscosities (from watery to thick and sticky) and pH levels (from alkaline to acidic). To this end, it is essential that wound dressings undergo significant testing both within the laboratory, 'phantom' wound models and, of course, clinical studies.

There is a need to test all aspects of dressing performance, including durability of the gelling fibre product post-simulated use in different wound types, absorbency and retention, ability to transfer exudate to the secondary dressing, and ability to assist in debridement. The combination of testing in all of these areas goes some way to demonstrate the effectiveness of the product in the pre-clinical setting. Without rigorous pre-clinical testing, there would be a risk that the products would not function in the correct manner when applied to patients, and it would not be feasible to isolate the reason for the poor performances or failure of the applied dressing. However, this then has to be followed-up with clinical investigations, which are informed by the laboratory test results.

Clinicians need the ability to choose the correct wound dressings for a variety of patients with a range of wound types and healing stages. It is incumbent on the companies who manufacture the dressings to ensure that as much testing can be carried out both pre-clinically and in patients prior to dressings going on to the market. Clinicians and patients alike have to trust the products they use to minimise the risk of wound deterioration, including maceration of the surrounding skin and in some cases wound infection. It is vital that laboratory testing is clinically relevant and captures or simulates, to the extent possible, the wound aetiology and pathophysiology, the clinical practice of application and removal of the dressings, the activity pattern and the lifestyle of the relevant patients and perhaps other real-world considerations such as interactions with applied medical devices (e.g. compression stockings). Laboratory testing such as reported here takes these considerations into account through development and utilisation of robotic phantom systems that are able to simulate both the wound and the clinical practice of treating the wound.

The evidence included in this supplement highlights some of the key pre-clinical and clinical studies conducted to evaluate the performance of Exufiber and Exufiber Ag+ gelling fibre dressings. It is clear that, in keeping with the clinical parameters set, the dressings are able to deliver excellent performance in relation to management of exudate, transfer of exudate, assisting with autolytic debridement and one-piece removal.

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