# Exufiber<sup>®</sup> Ag+: the science behind the technology

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# <u>Abstract</u>

## Background

Fiber dressings are used on different wound types, primarily to manage excessive fluid. Exufiber® (Mölnlycke Health Care) is a gelling fiber dressing that is composed of tightly entwined highly absorbent fibers (Hydrolock® technology) to minimize the available free space for exudate or blood to flow which, in turn, boosts the integrity of the dressing. On contact with exudate, it transforms into a gel that provides a favorable environment for healing. The addition of ionic silver to the dressing, so forming Exufiber Ag+, imparts additional antimicrobial effects, via contact with wound fluid.

#### Aims

To review the available scientific data relating to the efficacy of Exufiber Ag+.

#### Methods

Published and unpublished data held on file by Mölnlycke Health Care relating to Exufiber and Exufiber Ag+ were analyzed and summarized in order to gauge the efficacy of Exufiber Ag+, particularly in relation to other currently marketed fiber dressings.

#### Results

*In vitro* studies have demonstrated Exufiber Ag+ to have statistically significant superiority over silver-containing hydrofiber (Aquacel® Ag Extra) dressings with regards to the absorption of simulated wound fluid, simulated thick wound fluid and blood (p<0.0005). Exufiber Ag+ also demonstrated 23% greater fluid retention than Aquacel Ag Extra (p<0.0005). The two dressings were observed to be similar in terms of vertical wicking. These findings are consistent with observations of effective exudate management in the clinical setting with Exufiber. Exufiber Ag+ was tested *in vitro* against wound-relevant bacteria, fungi and yeasts, demonstrating rapid, sustained and broad-spectrum antimicrobial activity. A comparable, and in some cases superior, antimicrobial activity against *Pseudomonas aeruginosa, Staphylococcus aureus* (MRSA) and *Candida albicans* relative to four other commercially available fiber dressings was also observed *in vitro*.

#### Conclusions

The results of *in vitro* studies provide strong indicators of the ability of Exufiber Ag+ to manage high levels of excessive exudate and blood, while delivering both rapid and sustained antimicrobial activity against a broad spectrum of wound-related microorganisms. Furthermore, laboratory-based testing has highlighted the integrity of Exufiber Ag+, indicating its ease of application, stay-on-ability and ease of removal, all factors that can reduce the need for frequent dressing changes which may be costly and distressing for patients.

# **Introduction**

Exudate provides the wound with essential components for healing. However, hard-to-heal wounds are often associated with imbalances in the quantity and/or composition of exudate that can have a negative impact on the wound, leading to delayed healing and periwound skin damage if not managed correctly.<sup>1</sup> Moreover, if bioburden in these clinically and economically challenging wounds is not managed appropriately, infection can develop which may also contribute to excessive exudation, delayed healing, pain and other complications.<sup>2</sup> Modern dressings play a key role in the management of exudate and bioburden.

Exufiber<sup>®</sup> (Mölnlycke Health Care) is a non-woven gelling fiber dressing. Its tightly entwined highly absorbent polyvinyl alcohol fibers (Hydrolock<sup>®</sup> technology) minimize the available free space for exudate or blood to flow (compared with the looser composition of some other fiber dressings) which, in turn, boosts the integrity of the dressing (**Figure 1**). On contact with exudate, Exufiber transforms into a gel that facilitates moist wound healing. The moist environment promotes autolytic debridement and a favorable environment for healing.<sup>3</sup> It is designed to be of use in the management of leg and diabetic foot ulcers, pressure ulcers, partial-thickness burns, surgical wounds, donor sites, malignant wounds, dermal lesions, and additional external trauma wounds.<sup>4</sup>

The addition of ionic silver to Exufiber, so forming Exufiber Ag+, imparts additional antimicrobial properties to the dressing, leading to rapid and sustained antimicrobial effects being initiated via contact with wound fluid. The nonwoven pad is coated on both sides with 0.2 mg Ag/cm<sup>2</sup>, in the form of silver sulfate. It is released within the dressing on contact with fluid, and behaves as a preservative within the dressing to inhibit or reduce microbial growth. The released silver ions target multiple sites within or on microbial cells where they attach to thiol groups containing sulfur and hydrogen. Thiol-group binding occurs on a number of proteins that play an important role in the microbial cell. <sup>5</sup>

## <u>Aims</u>

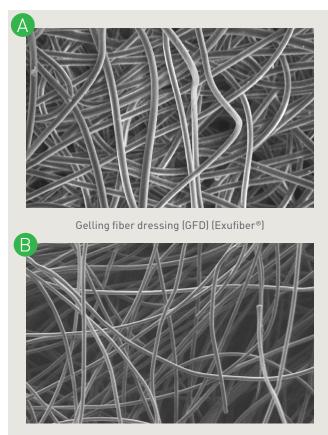
This paper summarizes an extensive review of the available scientific data relating to the use of Exufiber Ag+. Where relevant, clinical data relating to the non-silver version of the dressing (Exufiber) are also discussed to supplement the preclinical data pertaining to Exufiber Ag+.

# <u>Methods</u>

Published and unpublished data held on file by Mölnlycke Health Care relating to Exufiber and Exufiber Ag+ were sourced, analyzed and summarized in order to gauge the efficacy of Exufiber Ag+, particularly in relation to other currently marketed fiber dressings.

# <u>Results</u>

The reviewed data are presented below in three categories: (1) fluid (exudate and blood) handling, (2) antimicrobial action, and (3) in-use characteristics.



Hydrofiber dressing (Aquacel<sup>®</sup>)

**Figure 1:** Micrographs of gelling fiber dressing (A) and hydrofiber dressing (HD) (B). The tightly packed entangled fibers of the gelling fiber dressing contribute to its high tensile strength (to facilitate dressing removal) and fluid retention properties (to minimize the risk of leakage and moisture-related skin damage)

# Fluid handling

A variety of *in vitro* studies have been undertaken to compare Exufiber Ag+ and silver-containing hydrofiber (Aquacel® Ag Extra) dressings in terms of their fluid-handling properties.<sup>6-12</sup> Exufiber Ag+ demonstrated statistically significant superiority (p<0.0005) over Aquacel Ag Extra with regards to the absorption of simulated wound fluid<sup>6</sup> (including under compression<sup>7</sup> and under secondary absorbent dressings),<sup>11</sup> simulated thick wound fluid,<sup>9</sup> and blood.<sup>10</sup> Exufiber Ag+ also demonstrated 23% greater fluid retention than Aquacel Ag Extra (p<0.0005).<sup>8</sup> In terms of vertical wicking ability, the two dressings were observed to be similar.<sup>12</sup> The results of these studies are summarized in **Table 1**.

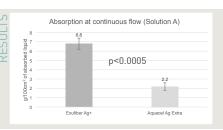
## Table 1: Laboratory testing of fluid handling

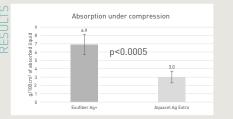
#### ABSORPTION

Measurement of quantity of test fluid (Solution A, continuous flow rate 1 ml/hour under 4 mmHg) required to spread and reach dressing edges, where there is a risk of leakage<sup>6</sup>

#### ABSORPTION UNDER COMPRESSION

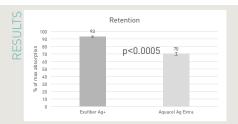
Measurement of quantity of test fluid (Solution A, continuous flow rate 1 ml/hour under 40 mmHg) required to spread and reach dressing edges<sup>7</sup>





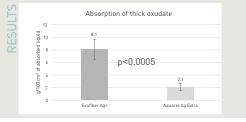
## RETENTION

Determination of amount of test fluid (Solution A) retained after application of 40 mmHg pressure to dressings that have reached maximum absorption<sup>8</sup>



## ABSORPTION OF THICK EXUDATE

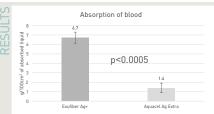
Measurement of quantity of viscous test fluid (Solution A plus 0.5% guar gum, continuous flow rate 10 ml/hour) required to spread and reach dressing edges?





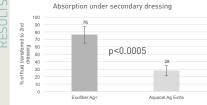
#### ABSORPTION OF BLOOD

Measurement of quantity of test fluid (horse blood, continuous flow rate 10 ml/hour) required to spread and reach dressing edges<sup>10</sup>



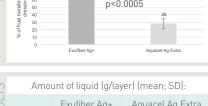
## ABSORPTION UNDER SECONDARY DRESSING

Measurement of quantity of test fluid (Solution A, continuous flow rate 10 ml/hour) transferred to a secondary absorbent dressing<sup>11</sup>



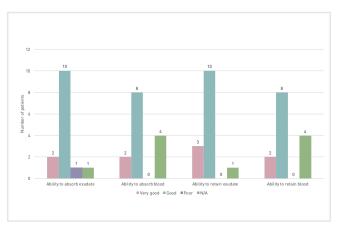
#### VERTICAL WICKING

Determination of quantity of test fluid (Solution A, continuous flow rate 0.3 ml/hour) spread through 4 dressings placed on top of one another<sup>12</sup>



RESUL		Exufiber Ag+	Aquacel Ag Extra
	Layer 1	1.72 (0.71)	1.38 (0.37)
	Layer 2	1.50 (0.38)	0.97 (0.19)
	Layer 3	1.53 (0.22)	1.52 (0.17)
	Layer 4	2.49 (0.35)	3.24 (0.31)

These findings are consistent with observations of effective exudate management with Exufiber when used on a variety of chronic wound types.<sup>3,4,13,14,15</sup> For example, in a clinical study involving patients with pressure ulcers (stages II-IV), Exufiber was used for up to 6 weeks. Overall, there was a general trend of improvement in the periwound skin and the investigators rated the dressing highly in terms of its exudate handling properties (**Figure 2**).<sup>14</sup>



**Figure 2:** Investigator evaluations (n=14) of exudate management properties of Exufiber<sup>14</sup>

# Antimicrobial action

## Planktonic microorganisms

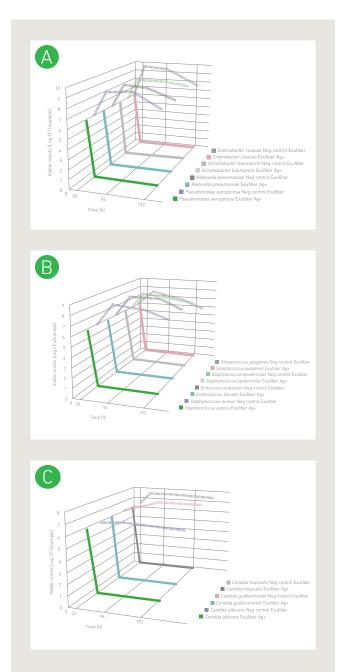
Exufiber Ag+ was tested *in vitro* against species of Gramnegative bacteria (n=4), Gram-positive bacteria (n=4), and fungi/yeasts (n=4) using a direct contact method based on test method ISO 20743:2013.<sup>16</sup> Exufiber Ag+ demonstrated both rapid and sustained antimicrobial activity, effectively reducing the prevalence (by at least 5 logarithmic units or to below the level of detection) of 11 of the test organisms, and reducing *Aspergillus fumigatus* by a 4.1 logarithmic unit reduction (**Figure 3**).<sup>17,18</sup> Using the same method, Exufiber Ag+ was demonstrated to have comparable, and in some cases better, rapid and sustained antimicrobial activity against *Pseudomonas aeruginosa, Staphylococcus aureus* (MRSA) and *Candida albicans* as four other commercially available fiber dressings (Aquacel Ag Extra, Aquacel Ag+ Extra, Durafiber<sup>™</sup> Ag, and Opticell<sup>®</sup> Ag+) (**Figure 4**).<sup>18,19</sup>

The rapidity of antimicrobial effect of Exufiber Ag+ was further demonstrated by means of *in vitro* tests using a direct contact method based on test method ISO 20743:2013, with logarithmic reductions of microorganisms evident within 3 hours (**Figure 5**).<sup>17</sup>

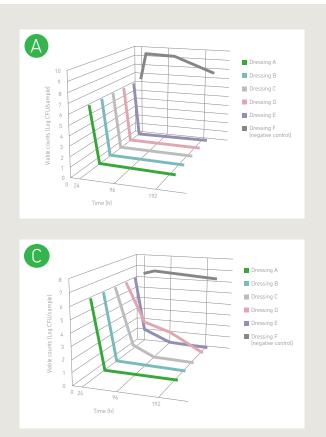
Additionally, an *in vitro* test has been performed to investigate if there is a difference in antimicrobial properties of Exufiber Ag+ when used with and without an absorbent secondary dressing. From this study, it was concluded that the antimicrobial effect of Exufiber Ag+ is not significantly reduced when used in combination with a secondary dressing, so indicating that insubstantial levels of silver are relocated from Exufiber Ag+ to the secondary dressing (**Figure 6**).<sup>17</sup>

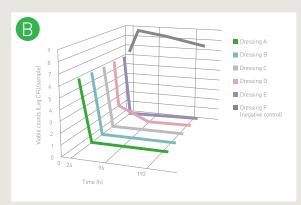
#### **Biofilms**

An *in vitro* study has been conducted to compare Exufiber Ag+, Aquacel Ag Extra and Aquacel Ag+ Extra in terms of their ability to reduce biofilms. Exufiber Ag+ was shown to be comparable to Aquacel Ag+ Extra, but significantly superior to Aquacel Ag Extra in reducing the viability of a *S. aureus* biofilm (p<0.001) (**Figure 7**).<sup>20</sup>



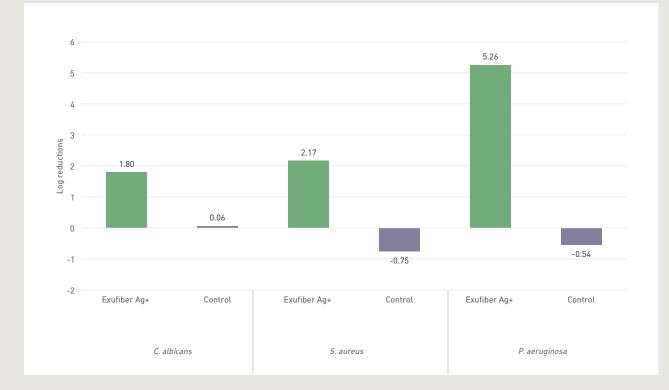
**Figure 3:** Antimicrobial effect of Exufiber Ag+ (solid lines) against Gram-positive bacteria (A), Gramnegative bacteria (B) and fungi/yeasts (C), determined by direct contact method. A non-silver dressing containing the same materials as Exufiber Ag+ except for the silver substance was used as a negative control (dashed lines)<sup>18</sup>





**Figure 4:** Antimicrobial effect of fiber dressings against *P. aeruginosa* (A), *S. aureus* (MRSA) (B) and *C. albicans* (C), determined by direct contact method. A non-silver dressing containing the same materials as Exufiber Ag+ except for the silver substance was used as a negative control<sup>19</sup>

Key: Dressing A = Exufiber Ag+; Dressing B = Aquacel Ag Extra; Dressing C = Aquacel Ag+ Extra; Dressing D = Durafiber Ag; Dressing E = Opticell Ag+; Dressing F = Negative control (Exufiber Ag+ without Ag).



**Figure 5:** Antimicrobial effect of Exufiber Ag+ against *P. aeruginosa, S. aureus and C. albicans;* determined by direct contact method at 3 hours. A non-silver dressing containing the same materials as Exufiber Ag+, except for the silver substance, was used as a negative control.<sup>17</sup>

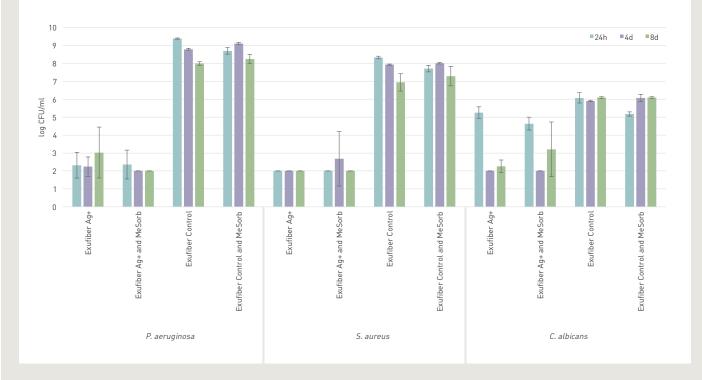


Figure 6: Antimicrobial effect of Exufiber Ag+ with and without secondary dressing [MeSorb®]<sup>17</sup>

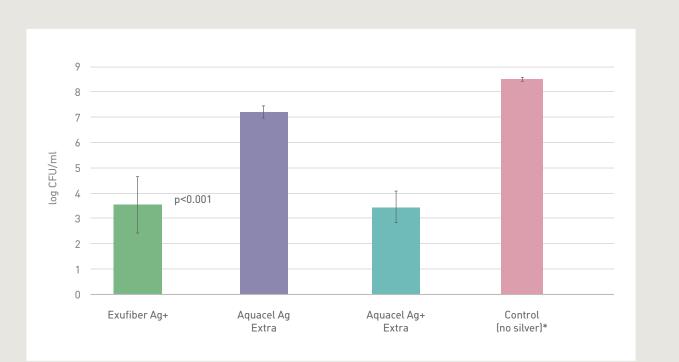


Figure 7: Validity of a three-dimensional S. aureus biofilm after 24 hours' exposure to dressings in vitro<sup>20</sup>

# In-use characteristics

## Integrity

Exufiber Ag+ has a high wet tensile strength (mean: 2.3 N) enabling easy one-piece dressing removal.<sup>21</sup> It is also associated with limited fiber shedding, with similar amounts of fiber loss in the dry state, both when shaking (9.7 vs 6.53) and cutting (2.9 vs 2.33), as for Aquacel Ag Extra. Exufiber Ag+ also loses significantly less fibers in the dry state when shaking (9.7 vs 31.5) and cutting (2.9 vs 27.7) (compared with an alginate dressing) (p<0.0005).<sup>22</sup>

Additionally, Exufiber Ag+ is associated with limited shrinkage during wear, similar to Aquacel Ag Extra in terms of percentage change in area (-31% vs -37%), indicating that the dressings will maintain sufficient coverage upon absorption of exudate.<sup>23</sup> It is important that clinicians choose the correct size of dressing to cover the entire wound. The dressing should overlap the dry surrounding skin by at least 1-2cm for smaller sizes and 5cm for larger sizes, in order to take into account that the edges of the dressing will contract as it absorbs fluid. Exufiber Ag+ can also be re-wet on drying out and becoming stuck in the wound, which supports easy removal of dried dressings.<sup>24</sup>

#### **Dressing removal**

Exufiber Ag+ can be left in place for up to 7 days, depending on the condition of the wound and clinical requirements, thereby reducing the need for frequent dressing changes and associated costs.<sup>25</sup> A clinical study of Exufiber indicates that Exufiber Ag+ can be expected to minimize pain on dressing removal.<sup>14</sup> Likewise, clinical observations strongly indicate that Exufiber Ag+ can be expected to demonstrate a variety of positive in-use characteristics, such as conformability and ease of removal, in the management of different wound types.<sup>3,4,13,14,15</sup>

# Discussion and conclusions

Although the studies relating to Exufiber Ag+ considered here are confined to *in vitro* findings, their significance in a 'real world' clinical setting can be pondered upon in the knowledge that certain attributes of such preclinical findings point to clinically relevant outcomes. For example, in terms of the microbiological aspects of these studies, three major findings relate to: (1) rapidity of onset of antimicrobial activity, (2) broad spectrum of activity covering multiple bacterial and fungal species, and (3) sustained activity. Clearly, rapid onset might be interpreted in clinical terms as resolving acute occurrences of microbial invasion in a timely fashion, so reducing long-term risk to sufferers and the possibility of developing chronic or 'hard-to-heal wounds'. Importantly, in view of today's concerns over the development of antibiotic resistance, the use of ionic-silver-based dressings with proven sustained effect, at any level, may possibly translate into reduced risk of resistance in the clinical setting by way of avoiding exposure of bacterial and fungal populations to sublethal concentrations. Additionally, when considering the findings of in vitro research relating to biofilm reduction, the findings indicate that Exufiber Ag+ is potentially more effective than other silver-containing fiber dressings in reducing biofilm burden. Particularly encouraging is its apparent efficacy in combatting MRSA which is a persistent problem in today's clinical settings. Again, in terms of sustained activity, the implications for clinical practice are clear in that it will increase the effective wear time of such dressings and in doing so reduce anxiety and pain for patients by reducing the requirement for frequent dressing changes. Both anxiety and pain are recognized to slow or stall the healing process. By the same token, valuable nursing and medical resources will be spared in terms of time required to make more frequent dressing changes.

In terms of findings made with respect to fluid handling properties and issues of in-use characteristics, there is already substantial clinical experience of Hydrolock technology being used in the clinical setting with Exufiber, and these are generally favorable – it is no leap of the imagination to suggest that the addition of ionic silver to this technology will result in any less favorable results in the clinic. For example, wound management often involves the dressing of awkward stress areas and in these cases its conformability in *in vitro* studies should mirror that of Exufiber.

To conclude, the results of *in vitro* studies presented in this paper provide strong indicators of the ability of Exufiber Ag+ to manage high levels of excessive exudate and blood, while delivering both rapid and sustained antimicrobial activity against a broad spectrum of wound-related microorganisms. Furthermore, laboratory-based testing has highlighted the integrity of Exufiber Ag+, indicating its ease of application, stay-on-ability and ease of removal, all factors that can reduce the need for frequent dressing changes which may be costly and distressing for patients.

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