AQUACEL™*Foam*

A Comparison of the *in vitro* Bio-Physical Performance Characteristics of Silicone Foam Dressings Used in Wound Management

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Introduction:

The primary requirements for modern wound dressings should be to effectively manage exudate, provide an optimal moist wound environment and to support the body's healing processes to ensure wound progression towards healing. Upon removal, a dressing should cause minimal trauma to the wound bed and peri-wound areas, in order to not disrupt the healing process. Adhesive dressings should carefully balance the need for good adherence during the wear time of the dressing with minimal trauma and pain to the patient upon removal.

In chronic wounds, exudate management is crucial, as the exudate produced is considered to be a 'corrosive biological fluid' due to its range of harmful constituents (e.g. bacteria and enzymes)[1]. The effective management of wound exudate and the importance of locking away its harmful constituents are therefore key to protecting the healing tissue and helping prevent further tissue breakdown.

Many foam dressings, of varying compositions and modes of action, are available for the management of exuding wounds. These foam dressings claim to have different physical performance characteristics; however all are primarily designed to absorb wound exudate and to provide a soft cover for the wound site, in order to manage the wound environment.

In these studies, several *in vitro* test methods have been used in order to assess the bio-physical performance characteristics of a range of foam dressings.

The influence of differences in dressing design upon the results of these tests is assessed within the Results and Discussion section.

Methods:

The foam dressings tested are described in the Table below

Name of dressing	Manufacturer	Manufacturers Description
AQUACEL™ Foam	ConvaTec	Hydrofiber™ foam wound dressing consisting of a waterproof outer polyurethane (PU) film and a multi-layered absorbent pad (a layer of PU foam and a non-woven wound contact layer (WCL) of Hydrofiber™ technology). The adhesive version has a silicone adhesive border
ALLEVYN™ GENTLE BORDER	Smith & Nephew	Absorbent hydrocellular pad, sandwiched between a perforated silicone gel adhesive WCL and a highly permeable waterproof outer film
Biatain™ Silicone Foam	Coloplast	Soft absorbent foam pad and a skin friendly adhesive border based on silicone technology. It has a semi-permeable film backing that is waterproof and provides a bacterial barrier
Mepilex™ Border	Molnlycke	Apertured silicone (Safetac™) WCL and a flexible absorbent pad in three layers: a PU foam, a non-woven spreading layer and a layer with super absorbent polyacrylate fibres. Its outer film is vapour permeable and waterproof

Table 1: Description of the foam dressings tested

1. Fluid Handling Capacity

This *in vitro* laboratory method was carried out in accordance with BS EN 13726-1:2002[2]. Briefly this involved cutting a test dressing (55mm diameter) and placing onto a Payne/Paddington cup, which was then weighed (W1). A minimum volume of 20 ml of test solution (in these studies both sodium/calcium chloride BP [Solution A] and horse serum [First Link Ltd, Cat# 12-00-850]) was added, and the whole cup was then re-weighed (W2). Horse serum was used as a test solution to more closely mimic the viscosity and composition of wound exudate. Each dressing was compressed gently to allow entrapped air within the dressing to be released prior to fixing the solid plate in place. This method modification was performed as it was observed that some dressings were not able to completely hydrate (due to air entrapment) when physically restricted within this test apparatus, although they were able to completely hydrate when not restricted. A minimum of three samples per dressing were evaluated and each cup was placed in a controlled environment incubator (37°C and relative humidity below 20%) for 24 hours, after which the cup was removed and equilibrated to room temperature before re-weighing (W3).

Moisture Vapour Loss (MVL) = W3 - W2. (A)

The solid plate was then removed from the cup, excess fluid was drained and the cup re-weighed (W4).

Fluid Absorption = W4 - W1. (B)

The Fluid Handling Capacity (FHC) was determined by the addition of A and B.

2. Intimate Contact with a Simulated Wound Surface

This *in vitro* test method has previously been described in detail elsewhere[3,4]. In summary, in this *in vitro* model a small hole was made in the wall of a Petri dish. A section of pork belly (approximately 5cm x 1cm x 1cm) was used as a simulated wound bed and placed inside along the wall of the Petri dish. A section of the dressing was then placed over the pork belly. The dressings were secured in place with tape. A 21 gauge syringe needle was then inserted at a 45° angle through the hole in the Petri dish and the pork belly, until it had been pushed through to the simulated wound bed surface, just underneath the dressing. A Microjet Micropump was set to dispense 4ml/hour of 0.01% (w/v) ortho-toluidine blue dye in Solution A through the syringe needle.

Images of this set up were captured every 20 seconds during the test, using a QImaging digital camera, until the sample was fully hydrated.

3. Fluid Retention

Free Swell Absorbency: The absorption aspect of this *in vitro* test method was carried out in accordance with BS EN 13726-1:2002[5]. In summary, for fluid retention, the hydrated dressing was placed onto a perforated metal sheet and a compression load (e.g. a weight equivalent to 40mmHg as commonly applied with a high compression bandage[6] therapy) was applied to the dressing. Any unbound liquid was allowed to drain, the dressing was then re-weighed, and this value gave the fluid retention.

Visual Assessment of Fluid Retention: In this *in vitro* visual assessment each dressing was saturated with sodium / calcium chloride (containing blue food dye) test solution. Each dressing was then placed onto clean, absorbent tissue paper on a hard flat surface. A perspex plate was then placed over the dressing and a 5kg weight was applied to the top of the Perspex plate (equivalent to 40mmHg for the size of each dressing tested). This weight was left in place for 15 seconds and then removed.

Absorbency Under Compression: This *in vitro* test method was carried out in accordance with a standard Pharmacopoeia method for water-retention capacity[7]. In summary, a sample of the test dressing was cut and weighed before placement onto a perforated metal sheet in a tank. A weight equivalent to 40mmHg pressure for the size of dressing sample being tested was then applied to the dressing and Solution A added until the perforated sheet was covered. After 24 hours, fluid was drained out of the tank, the weight was removed and the dressing sample re-weighed.

4. Lateral Movement of Fluid:

A plastic vial was held in place onto the centre of the WCL of each dressing, whereupon 20ml of horse serum was injected into the vial. 60 seconds later any non-absorbed fluid from the surface of the dressing was removed with the syringe and the plastic vial removed. A ruler was placed underneath the dressing and a photograph was taken with a digital camera.

The photographs were then used to measure the area of lateral fluid spread using the UTHSCSA ImageTool software package (University of Texas Health Science Center, San Antonio, Texas).

 Lateral spread is expressed as a percentage of the original vial area, and calculated as below:-

$$\% \text{ Lateral spread} = \left[\frac{\text{lateral spread area} \times 100}{\text{vial area}} \right] - 100$$

5. Bioadhesion Studies

Dressing bioadhesion studies were carried out in a cell culture model as previously described[3,8]. Both equine granulation tissue fibroblasts (cultured from debrided tissue) and adult human keratinocytes ((NHEK Clonetics™) were obtained from Lonza Biologics PLC, UK) were used in this model as a cell monolayer. A 1cm^2 piece of each dressing was cut from the central area and applied either as a dry dressing or as a wet dressing following hydration with 1ml of cell culture medium. All cut dressings were placed onto the monolayer of either fibroblasts or keratinocytes and pressed gently in place. After 24 hours the dressings were carefully removed from the surface of the culture, using minimal force to avoid damaging the cells or causing any additional cells to detach from the dressing. The cell numbers adhered onto each dressing were then determined through trypsinisation and counting using a Neubauer cell counting chamber.

6. Repeat Insult Patch Test [9]

Two hundred and twenty-seven (227) qualified subjects, male and female, ranging in age from 18 to 79 years, were enrolled for this evaluation of AQUACEL™ Foam dressings. Two hundred and six (206) subjects completed the study. The remaining subjects discontinued their participation for various reasons, none of which were related to the application of the material.

Induction Phase: Patches were applied three times per week (e.g. Monday, Wednesday, and Friday) for a total of nine applications. The site was marked to ensure the continuity of patch application. Participants removed the patches twenty-four hours after each application, the evaluation of the site was made just prior to re-application.

Challenge Phase: Approximately two weeks after the final induction phase patch application, a challenge patch was applied to a virgin test site adjacent to the original induction patch site, following a similar procedure to that described for induction. The patch was removed and the site scored at the clinic twenty-four and seventy –two hours post-application.

7. Adhesion Test

This *in vitro* method uses a cut strip of the dressing adhesive border and is based on a standard Phamacopeial method[10]. Each strip was applied to the centre of a frosted plate of polycarbonate, and rolled with an applied 20N (2kgf) force per cm width of sample, at a speed of 60cm per minute. This was then allowed to stand in a regulated controlled atmosphere (60-70% relative humidity and 18°-22°C) for 30 minutes. The force required (when applied at an angle of 180° at a constant rate of travel of 300mm per minute) to detach the strip from the polycarbonate plate was measured, such that the force required represents 15 to 85% of the full-scale deflection.

Results and Discussion:

All results are quoted as the mean ± one standard deviation.

The results for the fluid handling capacity (FHC) of the foam dressings tested are tabulated and shown in Figure 1 below.

Figure 1: Total Fluid Handling Capacity using Sodium / Calcium Chloride Test Solution[11]

	Moisture Vapour Loss (MVL) (g/10cm²/24hrs)	Absorbency (g/10cm²/24hrs)	Fluid Handling Capacity (g/10cm²/24hrs)
AQUACEL™ Foam	9.32 ± 0.49	4.97 ± 0.21	14.29 ± 0.54
ALLEVYN™ GENTLE BORDER	9.99 ± 0.82	4.63 ± 0.12	14.62 ± 0.74
Mepilex™ Border	10.65 ± 0.66	7.00 ± 0.23	17.65 ± 0.49
Biatain™ Silicone	16.52 ± 0.41	7.26 ± 0.17	23.77 ± 0.39*
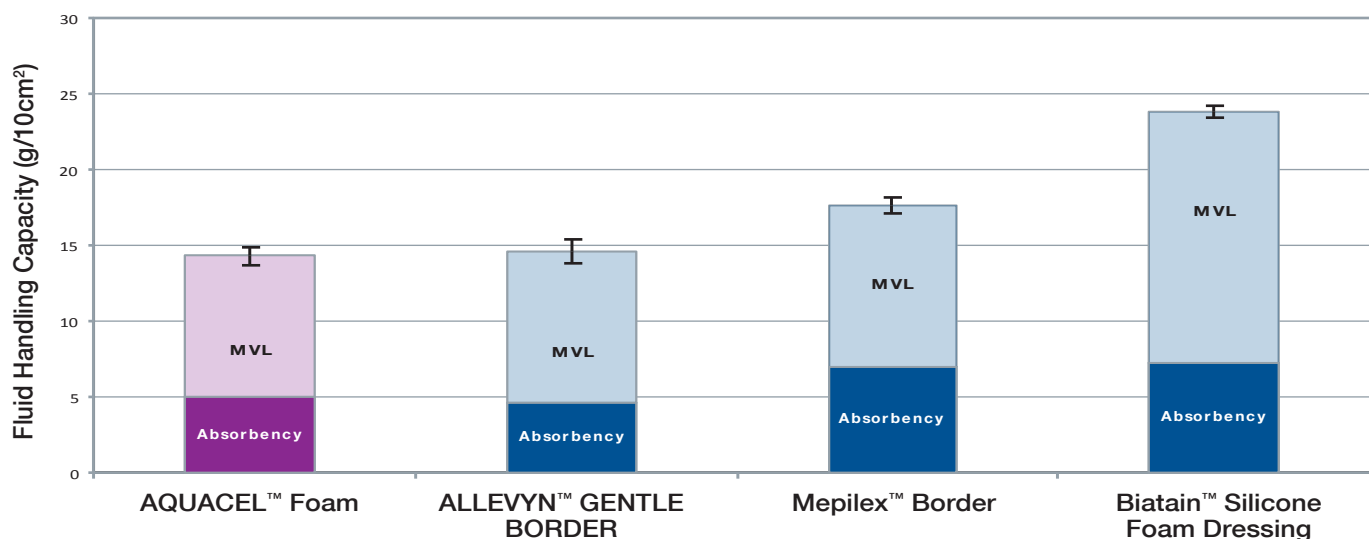
This FHC test provides the maximum volume of fluid that a dressing may be able to manage under controlled environmental conditions and when fluid is continuously in excess, it is therefore misleading to consider the exudate management potential of a dressing without also considering the rate of exudate production and consistency of the exudate.

The test solution, Solution A, is considered to have an ionic composition comparable to human serum or wound exudate, and is the laboratory standard test solution for testing wound dressings, however it is considerably different, in both viscosity and composition, to wound exudate. To more closely mimic wound exudate viscosity and composition (e.g. protein content) the test was repeated using horse serum as the test solution. The results indicated a reduction in FHC for all the dressings. The data is presented in Figure 2.

Figure 2:- Fluid Handling Capacity Using Horse Serum Test Solution[11]

	Moisture Vapour Loss (MVL) (g/10cm^2/24hrs)	Absorbency (g/10cm^2/24hrs)	Fluid Handling Capacity (g/10cm^2/24hrs)
AQUACEL™ Foam	6.52 ± 0.11	4.48 ± 0.07	11.00 ± 0.09
ALLEVYN™ GENTLE BORDER	8.02 ± 0.83	4.87 ± 0.02	12.89 ± 0.85
Mepilex™ Border	9.67 ± 0.47	4.97 ± 0.06	14.64 ± 0.49
Biatain™ Silicone	8.21 ± 1.10	4.29 ± 0.28	12.49 ± 1.34*
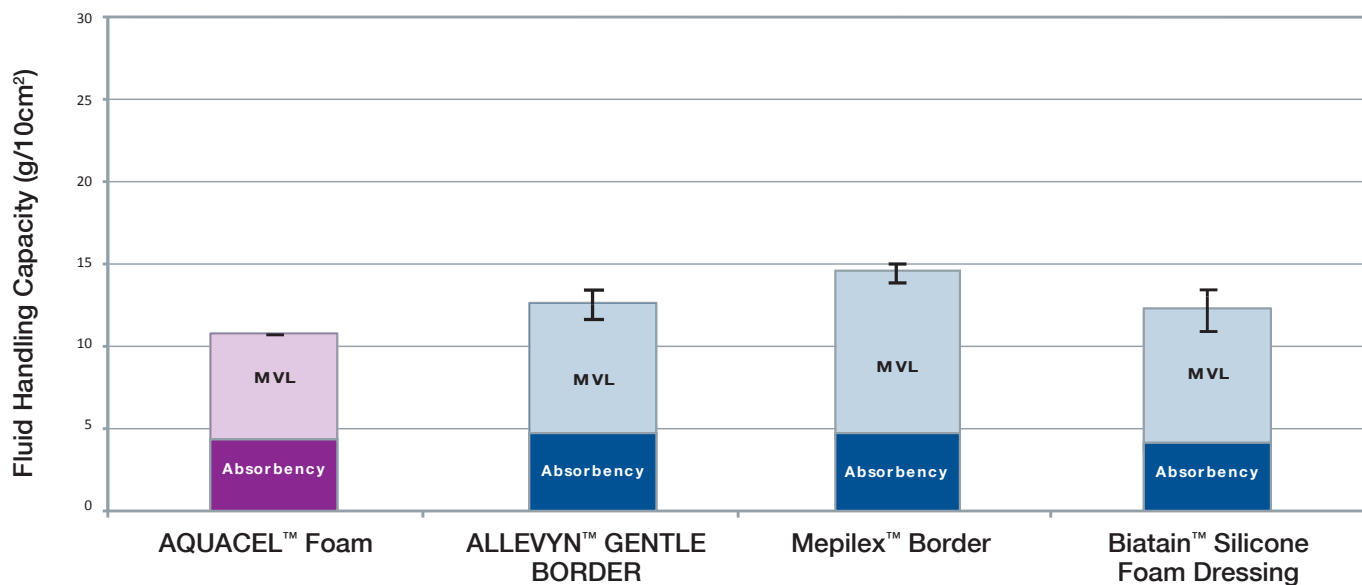
*Under the conditions of this test the film and foam layers were observed to delaminate for Biatain™ Silicone dressing, this allowed fluid to collect between these layers. This delamination is considered an artifact of the test method therefore the foam layer was slit and the absorbed fluid drained away prior to taking the final absorbency measurement.

Exudate management has historically been linked to the absorptive capacity/FHC of the dressing. Whilst greater MVL through the semi-permeable film layer increases the total FHC of the dressing, it may also increase the risk of a lightly exuding wound drying out prematurely. The importance of maintaining a moist wound environment has been established since the seminal work of Winter[12,13]. Therefore a careful balance between higher permeability to allow greater FHC whilst providing an optimal wound healing environment is important. Wound dressings should be able to 'respond' to the wound environment, influencing the cellular environment of a healing wound through the maintenance of moisture balance[14].

To allow for an optimal balance between higher MVL and the importance of a moist wound healing environment for wound progression, AQUACEL™ Foam dressing has been designed to contain a gelling wound contact layer which is able to change its physical state to form a cohesive gel upon contact with wound exudate (Figure 3).

Figure 3: Instant Gelling of Wound Contact Layer

Equally important is a dressings' ability to micro-contour to uneven wound surfaces, ensuring that there is no room for dead spaces between the wound surface and the dressing interface, thus absorbing wound exudate on a microscopic level and reducing the possibility of increased bacterial proliferation[15-17]. An *in vitro* laboratory test method was developed to assess the dressings ability to micro-contour and intimately contact a simulated wound bed. Figure 4 demonstrates that AQUACEL™ Foam dressing, through its unique gelling characteristics, has the ability to form intimate contact with a simulated wound bed (Figure 4). ALLEVYN™ GENTLE BORDER dressing and Mepilex™ Border dressing were observed to remain in contact with the simulated wound surface when the test solution was added, however small areas of non-contact between the dressing and simulated wound bed, where the test solution pooled, were observed (Figures 5 and 6). Biatain™ Silicone dressing, however, was observed to lift away from the simulated wound bed upon addition of the test solution (Figure 7).
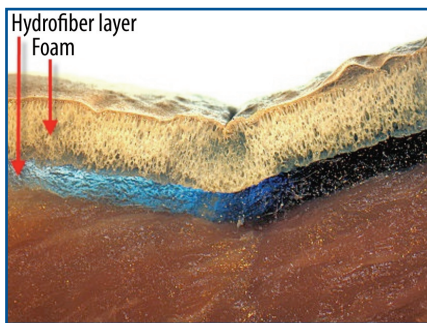

Figure 4: AQUACEL™ Foam dressing[18]

As the AQUACEL™ layer absorbed fluid and formed a cohesive gel, intimate contact with the simulated wound bed was observed. The fluid was then observed to wick into the foam layer
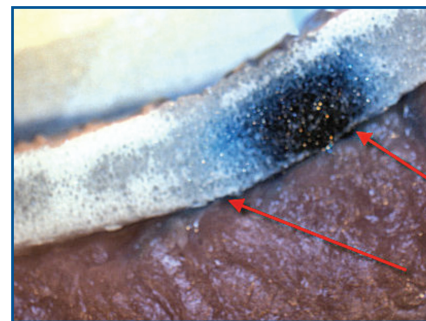

Figure 5: ALLEVYN™ GENTLE BORDER dressing[18]

ALLEVYN™ GENTLE BORDER dressing was observed to not completely conform to the simulated wound bed even when the dressing had absorbed fluid (see arrows).
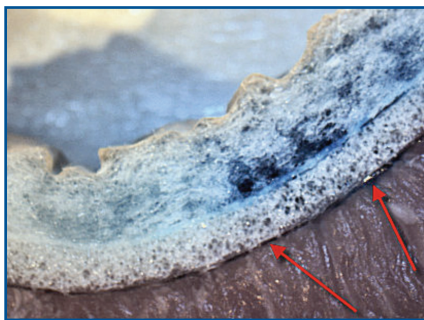

Figure 6: Mepilex™ Border dressing[18]

Upon hydration, the Mepilex™ Border dressing was observed to not completely conform to the simulated wound bed (see arrows).

Figure 7: Biatain™ Silicone dressing[18]

Upon hydration, the Biatain™ Silicone dressing was observed to lift away from the simulated wound bed (see arrow).

Under clinical conditions, dressings are often challenged to retain absorbed exudate under pressure, i.e. due to the application of compression bandaging or by the weight of a patient. Whilst many foam dressings are able to absorb large amounts of fluid within their porous structure, they are unable to retain the absorbed fluid even when low pressures are applied. Two *in vitro* test methods have been used to assess the silicone foam dressings ability to manage fluid under the application of 40mmHg pressure (equivalent to compression bandaging). Figure 8 demonstrates the dressings' ability to retain fluid after being allowed to absorb fluid unconstrained. In this *in vitro* test method, AQUACEL™ Foam dressing can be seen to retain the greatest percentage of fluid absorbed when compared to the other foam dressings tested, visual illustrations of fluid retention can be found in Figure 9.

Figure 10 demonstrates the dressings' ability to absorb fluid whilst under constant pressure. This testing is designed to replicate how a dressing may absorb fluid whilst under compression bandaging. AQUACEL™ Foam dressing can be seen to absorb the greatest volume of fluid when compared to the other foam dressings tested.

Note: Due to the swelling characteristics of Biatain™ Silicone dressing, test method modifications would be required to obtain comparative data for this dressing, retention and absorption under compression data for Biatain™ Silicone dressing have therefore not been presented.

Figure 8: Free Swell Absorbency/Retention under Compression[11]

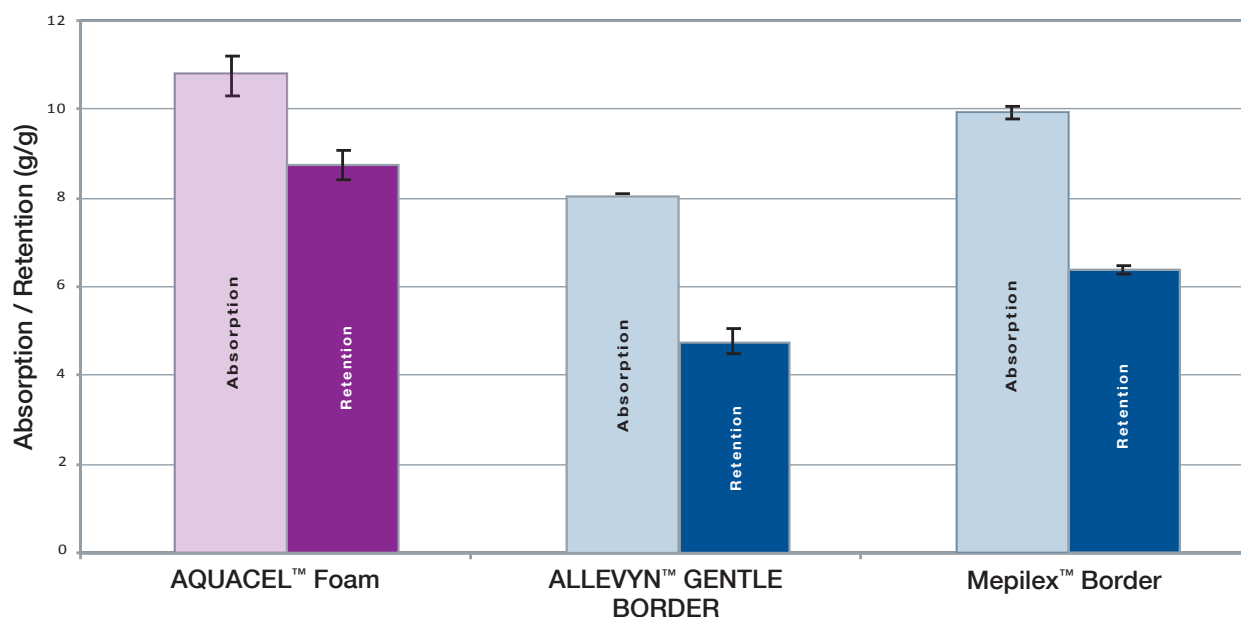|	Absorption (g/g)	Retention (g/g)	% Fluid Retained
AQUACEL™ Foam	10.75 ± 0.45	8.74 ± 0.31	81.4 ± 2.4
ALLEVYN™ GENTLE BORDER	8.03 ± 0.01	4.77 ± 0.27	59.4 ± 3.4
Mepilex™ Border	9.92 ± 0.15	6.38 ± 0.08	64.4 ± 0.7

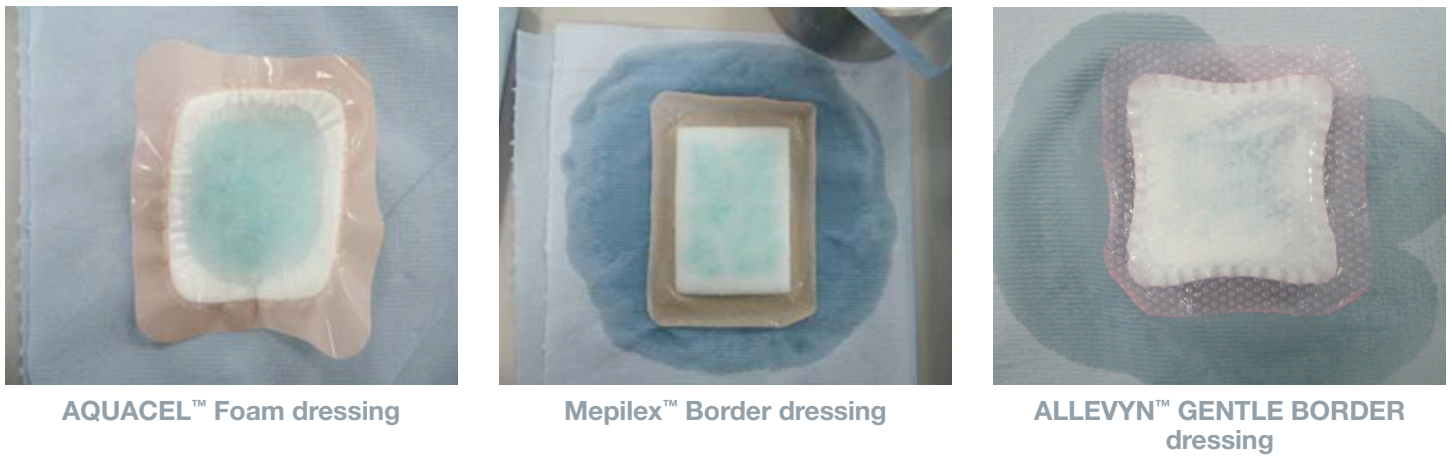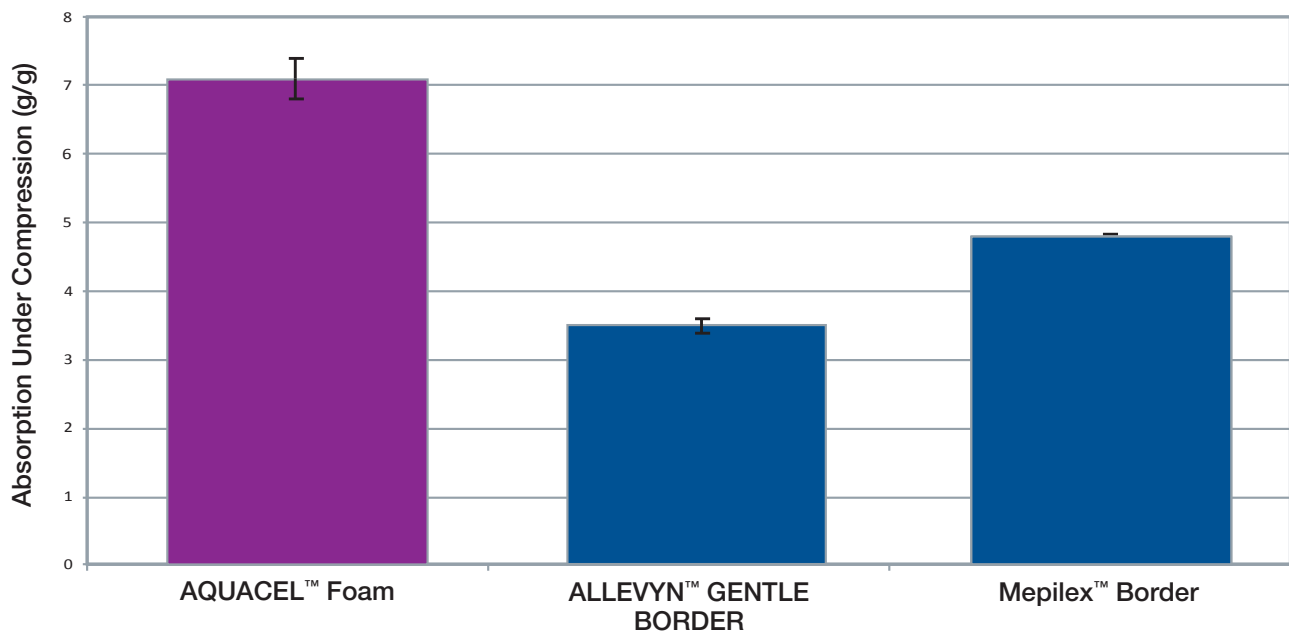**Figure 9: Visual Assessment of Fluid Retention[19]**

| AQUACEL™ Foam dressing | Mepilex™ Border dressing | ALLEVYN™ GENTLE BORDER dressing |

Figure 10: Absorbency under Compression[11]

	Absorption (g/g)
AQUACEL™ Foam	7.13 ± 0.30
ALLEVYN™ GENTLE BORDER	3.50 ± 0.08
Mepilex™ Border	4.82 ± 0.02

As part of a dressings' design characteristics to ensure effective exudate management, lateral spread of fluid to the peri-wound skin should be controlled. The peri-wound skin needs to be protected from wound exudate to help prevent maceration and potential for further skin breakdown. In order to assess a dressings' ability to manage fluid over the wound site an *in vitro* laboratory method was developed to assess fluid movement through and across dressings. Due to the unique gelling characteristics of AQUACEL™ Foam dressing, absorbed fluid is locked into the dressing structure, minimizing the lateral spread of fluid across the dressing surface. AQUACEL™ Foam dressing demonstrated the lowest percentage of lateral fluid spread when compared to the other foam dressings tested (Figure 11).

Figure 11: Lateral Movement of Fluid Across the Wound Dressing Surface[11]

	% lateral fluid spread
AQUACEL™ Foam	16.6 ± 4.0
ALLEVYN™ GENTLE BORDER	83.6 ± 8.2
Mepilex™ Border	104.2 ± 1.5
Biatain™ Silicone	70.5 ± 10.2
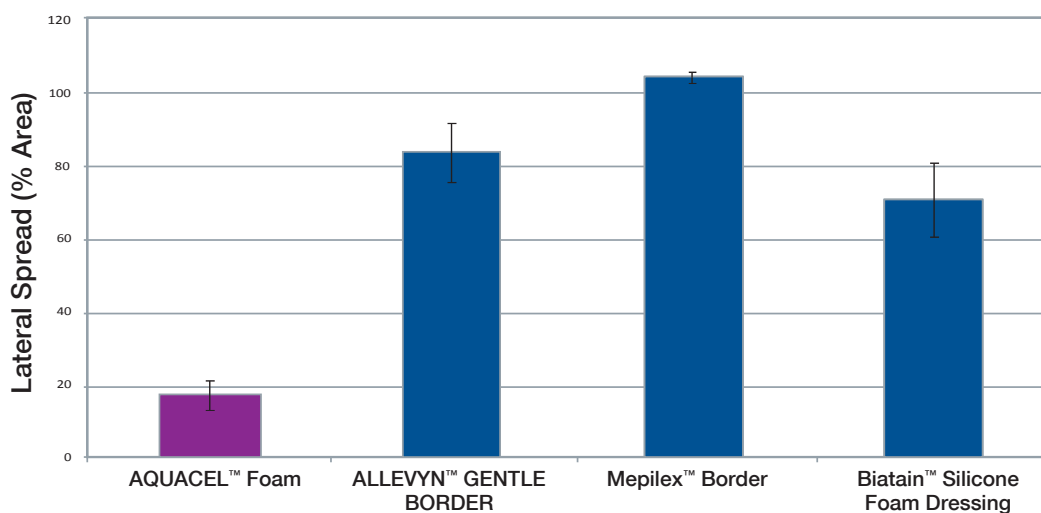
Studies have shown that the peri-wound skin area of ischaemic diabetic patients is often compromised[20,21]. It is therefore important that an appropriate dressing is chosen, with the selected dressing having the capacity to absorb exudate and to retain the exudate within its structure. Dressings containing a Hydrofiber™ layer have been found *in vitro* to lock harmful components, such as bacteria and proteolytic enzymes, within their gelling structures[22-24].

Exudate management is not the only consideration, dressings may adhere to the wound surface upon dressing removal, which may cause pain and also disrupt the healing process[25]. In this *in vitro* assessment, the dressings' bioadhesive properties to granulation tissue fibroblasts (to mimic a wound) were evaluated. The results are presented (Figure 12) for both the removal of a dry dressing and a hydrated wound contact layer from a fibroblast cell culture. This *in vitro* model was further developed to assess the potential for the dressings adhesive border to adhere to fragile newly formed epithelium or peri-wound skin. In this *in vitro* assessment, the dressings' bioadhesive properties were also assessed using keratinocytes (to mimic peri-wound tissue). Results are presented in Figure 13 for the removal of the dressing adhesive border from a keratinocyte cell culture.

It is acknowledged that these studies are only conducted over a short period of time (e.g. 24 hours) and do not take into account the many complex cellular and adhesive associated events that take place in a wound environment, but these studies do allow specific dressing/cell interactions to take place in a controlled environment allowing direct dressing to dressing comparisons. The results for both cell types demonstrate that there were significantly less cultured cells adhered to the AQUACEL™ Foam dressing when compared to the other silicone foam dressings tested (P<0.0001).

Equally important, the dressing should not irritate the wound or peri-wound skin as this could potentially contribute to further wound or peri-wound skin breakdown. *In vivo* repeat insult patch tests were performed on the silicone adhesive contained within AQUACEL™ Foam dressings. Under the conditions of this 206 healthy volunteer study, the Gentle Silicone border in AQUACEL™ Foam dressing was found to be skin friendly and demonstrated low potential for dermal irritation or allergenic contact sensitization.

Figure 12: Bioadhesion of Cultured Fibroblasts to the Dressing Wound Contact Surfaces[26]

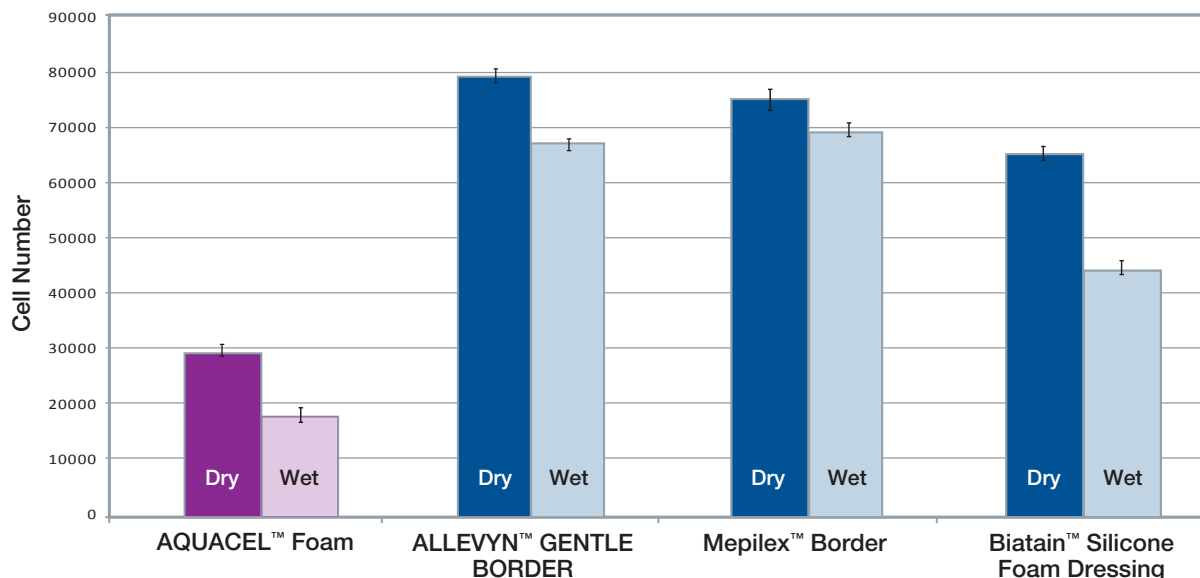|	Bioadhesion (Cell Number)	
	Dry	**Wet**
AQUACEL™ Foam	29500 ± 1049	17000 ± 1265
ALLEVYN™ GENTLE BORDER	79333 ± 1033	68667 ± 1033
Mepilex™ Border	75667 ± 1366	69333 ± 1033
Biatain™ Silicone	66000 ± 1265	44000 ± 1265

**Figure: 13 Bioadhesion of Cultured Keratinocytes to the Dressing Skin Contact Adhesive Surface[27]**

	Bioadhesion - Dry (Cell Number)
AQUACEL™ Foam	33167 ± 983
ALLEVYN™ GENTLE BORDER	81167 ± 1169
Mepilex™ Border	78167 ± 1169
Biatain™ Silicone	68667 ± 1033
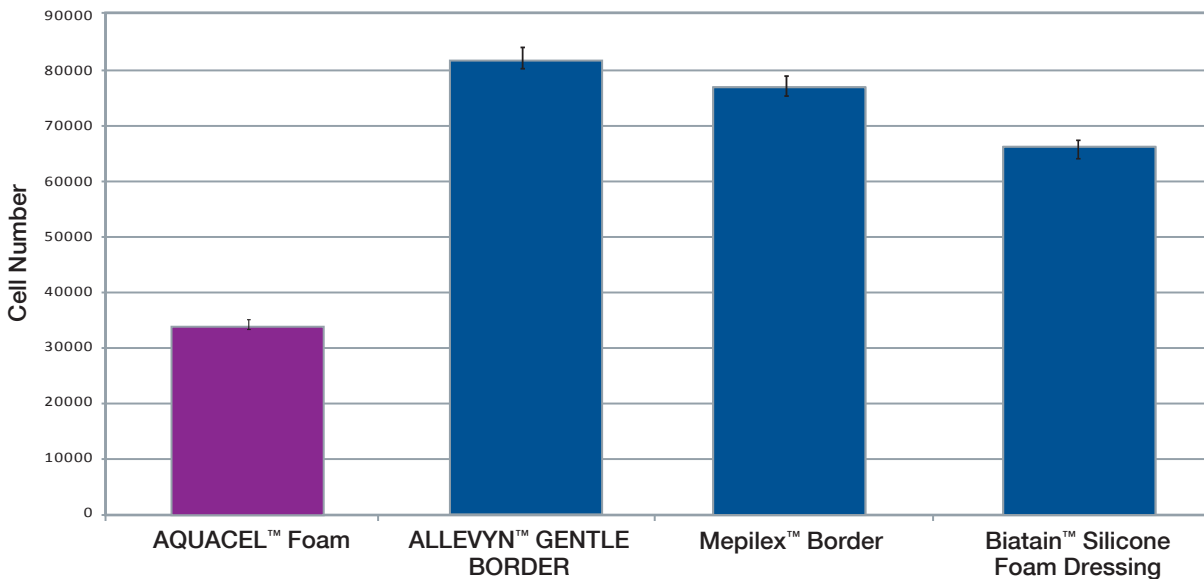
Whilst pain and trauma both during wear time and upon dressing removal are of primary importance both to the care-giver and the patient, it is important that an applied adhesive dressing has sufficient adhesive strength to remain in place throughout its intended wear time. The balance between no pain and low pain/trauma upon dressing removal, and the level of dressing adhesion to skin has been enhanced through the introduction of silicone adhesive technologies. Figure 14 shows that in this *in vitro* test, AQUACEL™ Foam dressing showed stronger adhesion to a standard polycarbonate test plate, compared to the other silicone foam dressings tested.

Figure 14: Adhesion Characteristics[11]

	Average Force (N / 2.5cm)
AQUACEL™ Foam	2.67 ± 0.19
ALLEVYN™ GENTLE BORDER	0.99 ± 0.12
Mepilex™ Border	1.83 ± 0.11
Biatain™ Silicone	1.89 ± 0.06
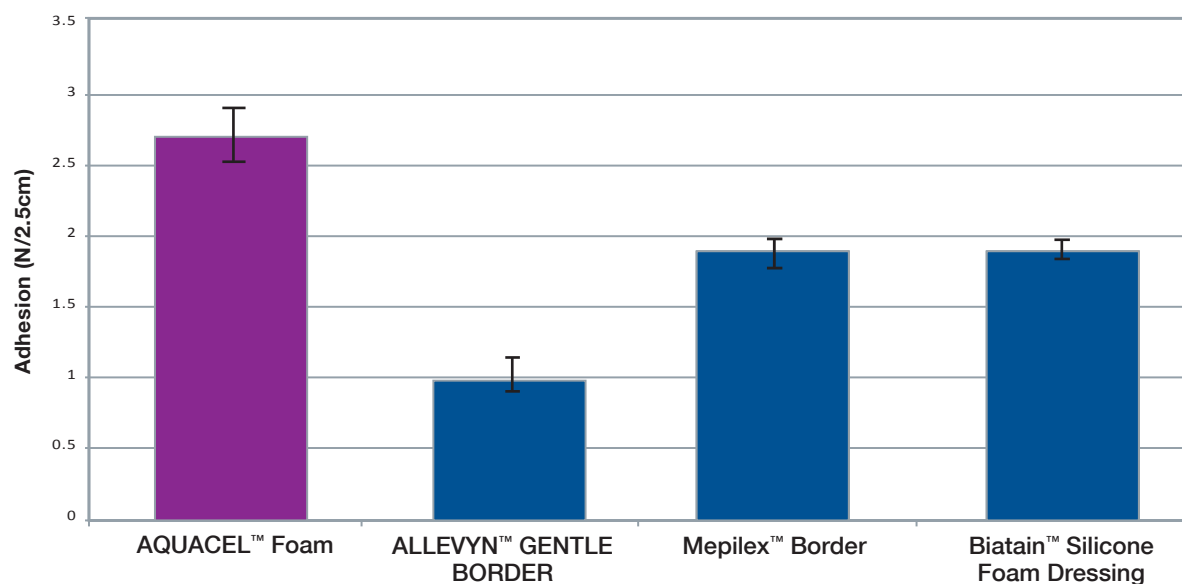
Foam dressings are frequently also used as cover (secondary) dressings, for example when exudate levels are high or when there is wound depth i.e. a cavity which requires to be packed with a primary dressing.

AQUACEL™ Foam dressing has been designed to work in partnership with AQUACEL™ / AQUACEL™ Ag dressings by allowing optimal fluid transport between the dressings to aid with effective exudate management. To assess the ability of foam dressings to manage fluid in combination with an AQUACEL™ primary dressing, an *in vitro* visual assessment was performed using the previously described intimate contact with a simulated wound surface method.

From this *in vitro* testing, the AQUACEL™ primary wound contact dressing covered with a secondary AQUACEL™ foam dressing combination was shown to handle fluid effectively, with the fluid transferring into all layers of this dressing combination (Figure 15).

The other foam dressings tested did not appear to effectively accept fluid from the AQUACEL™ primary wound contact dressing in this *in vitro* testing (Figures 16, 17 and 18).
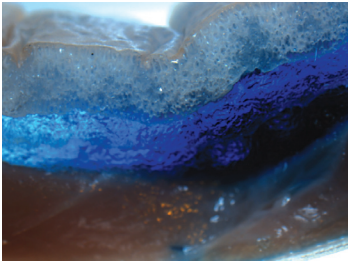
Figure 15: AQUACEL™ Foam dressing[28]

During hydration of the AQUACEL™ primary wound contact dressing, fluid passed vertically into both the Hydrofiber™ and polyurethane foam layers of the AQUACEL™ foam dressing. There was clearly visible fluid transfer between the AQUACEL™ primary dressing and the AQUACEL™ foam cover dressing in this *in vitro* test.
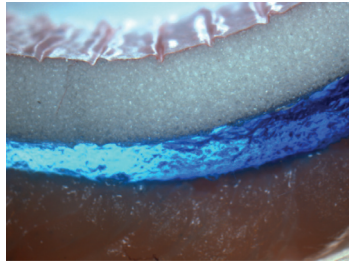
Figure 16: ALLEVYN™ GENTLE BORDER dressing[28]

The AQUACEL™ primary wound contact dressing fully hydrated. However, fluid transfer was not evident between the AQUACEL™ primary dressing and the ALLEVYN™ GENTLE BORDER cover dressing in this *in vitro* test.
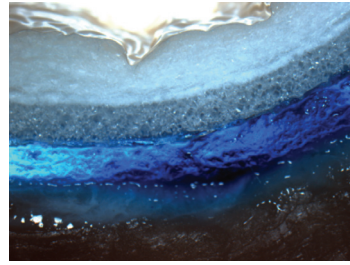
Figure 17: Mepilex™ Border dressing[28]

The AQUACEL™ primary wound contact dressing fully hydrated. However, the Mepilex™ Border dressing did not appear to hydrate effectively and fluid transfer between the dressings was not highly evident.
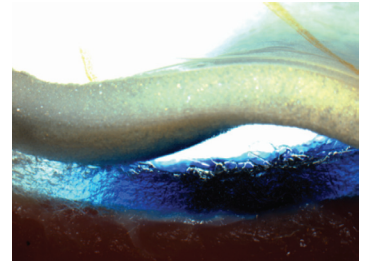
Figure 18: Biatain™ Silicone dressing[28]

The AQUACEL™ primary wound contact dressing fully hydrated. However, the Biatain™ Silicone dressing was observed to lift away from the AQUACEL™ primary dressing and so there was not effective contact between the two dressings for fluid transfer.

The findings from these test studies confirm the importance of dressing design in providing an effective foam dressing which will provide: - effective exudate management, in terms of fluid handling capacity; fluid retention and low lateral fluid spread across the dressing surface; balanced adhesion characteristics, in terms of adhesiveness and wear time, combined with atraumatic removal and low bioadhesion, and the provision of an intimately-contacting wound interface to provide an optimal moist wound healing environment all the way across the surface of the healing wound.

The AQUACEL™ Foam dressing has been designed to meet these important requirements, with an effective fluid transition being assured between the Hydrofiber™ wound contact layer and the foam layer within the dressing. Additionally, the silicone adhesive has been positioned at the border of the dressing for effective skin adhesion, without disruption of the Hydrofiber™ – wound interface.

Conclusions:

The importance of good exudate management and the ability of a dressing to provide an optimal wound healing environment are key requirements for wound progression. The *in vitro* laboratory studies performed here demonstrate that the different foam dressings tested have different physical characteristics, these differences in physical characteristics may be indicative to their clinical performance.

AQUACEL™ Foam dressing has been designed to effectively manage exudate, provide an optimal moist wound environment to support the body's healing process to ensure timely wound progression towards healing, and to cause minimal trauma to the wound bed and peri-wound area upon dressing removal. The adhesive version of AQUACEL™ Foam dressing has been designed to carefully balance the need for good adherence during its wear time with minimal trauma and pain upon removal.

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