

HemCon Guard IVa™

Antimicrobial Hemostatic IV Dressing

Summary of Clinical *in-vitro* and *in-vivo* Data

HemCon® GuardIVa™ Antimicrobial Hemostatic IV Dressing

HemCon GuardIVa 510(k) Summary

GuardIVa was cleared by the US FDA on June 8, 2010 under K093729.

Intended Use

The HemCon GuardIVa Antimicrobial Hemostatic IV Dressing is intended for use as a hydrophilic wound dressing to absorb exudate, cover and protect catheter sites. Common applications include IV catheters, other intravenous catheters and percutaneous devices. It is also indicated for control of surface bleeding from percutaneous catheters and vascular access sites.

Description of the Device

Dressing is composed of a hydrophilic polyurethane impregnated with 22-24mg of Chlorohexidine Gluconate (CHG) and a proprietary formulation of oxidized cellulose. Dressing is highly antimicrobial and hemostatic to control bleeding. The dressing is also highly absorbent to wick away exudate and blood and is able to absorb up to 11x its own weight in fluid.

❖ Summary of Independent Test Data

Antimicrobial Efficacy

Introduction

The antimicrobial effectiveness of the CHG based GuardIVa Antimicrobial Hemostatic IV Dressing was demonstrated using a variety of *in-vitro* tests. All tests were performed at independent test centers and compared GuardIVa to a variety of commercially available IV dressings.

Log Reduction

Methods

GuardIVa samples were tested to determine the degree of antimicrobial activity using a modified version of AATCC Test Method 100-2004, where GuardIVa dressings were exposed to 9 representative microorganisms commonly associated with catheter-related blood stream infections.

After incubation, the microorganisms were eluted from the dressings by shaking in neutralizing solution. The number of microorganisms present in this liquid was determined, and the percentage reduction in the population of each was calculated. The modified AATCC 100 test method was used to test dressing samples following 24 hr exposure, and up to 7 day exposure, to the test organisms.



Mechanism of Action

The antimicrobial activity of the CHG in the dressing helps to resist bacterial colonization of the dressing against a wide range of gram positive and gram negative microorganisms, including MRSA, MRSE, VRE, and *A. baumannii*. GuardIVa also controls bleeding through a proprietary oxidized cellulose compound which physically interacts with blood constituents such as platelets and provides a structural scaffold through which an artificial clot formation helps to control bleeding at the access site.

Non-Clinical Performance Data

Biocompatibility

Biocompatibility has been demonstrated per ISO10993.

Sterility

A sterility validation for GuardIVa was completed following ISO 11137:2006 requirements to demonstrate a 10⁻⁶ SAL using the Vmax25 method. Single Sterile and Bulk Non-Sterile kit configuration of the dressing available. GuardIVa can also be sterilized with EtO.

Results

In order to be considered antimicrobial a minimum of 4 log reduction in microbial count must be observed following 24 hr and again following the 7 day exposure in order to claim sustained antimicrobial activity. For all samples a minimum initial inoculum count of 1×10^6 (6 log) microbes was used. Success is measured by the dressing reducing all organisms by at least 10,000 units (10^4 or 4 log reduction).

Conclusions

- The antimicrobial effectiveness of GuardIVa was successfully demonstrated at 24 hrs and sustained for 7 days.

Table 1 – Log Reduction at 24hr and 7 days

Microorganism	Gram Stain	24 hrs Log Reduction	7 days Log Reduction
<i>Staphylococcus aureus</i> (MRSA)	+	5.50	6.31
<i>Staphylococcus epidermidis</i> (MRSE)	+	5.53	6.18
<i>Pseudomonas aeruginosa</i>	-	5.76	6.70
<i>Enterococcus faecium</i> (VRE)	+	5.52	5.51
<i>Acinetobacter baumannii</i>	-	5.55	6.16
<i>Escherichia coli</i>	-	5.58	6.38
<i>Klebsiella pneumoniae</i>	-	4.83	6.62
<i>Candida albicans</i>	n/a	4.72	4.71
<i>Aspergillus niger</i>	n/a	4.20	4.19

The clinical utility of these results is unknown.

Increasing Concentrations of Chlorhexidine Gluconate (CHG) for Antimicrobial Efficacy

Method

The aim of these studies was to determine the antimicrobial efficacy against Methicillin-resistant *Staphylococcus aureus* (MRSA) of samples of polyurethane foam containing a fixed concentration of HemCon's proprietary oxidized cellulose hemostatic agent, but increasing concentrations from 0 – 30 % of the antibacterial agent chlorhexidine gluconate (CHG). Polyurethane foam samples containing 15 % oxidized cellulose and varying concentrations of CHG were prepared. Table 4, below, outlines the various concentrations of CHG used and also indicates the corresponding actual amount of CHG (mg) present in the dressings. The antimicrobial efficacy of these foam samples was assessed against MRSA using the AATCC Test Method 100-2004.

- 1.0 ml of MRSA suspension at a minimum of 1×10^6 CFU/ml was inoculated to the test samples.
- The 24 hr microorganism log reductions against the MRSA were recorded for the foam samples.
- A minimum of 4 log reduction in microbial count must be observed following 24 hr exposure in order to be considered antimicrobial by the FDA.

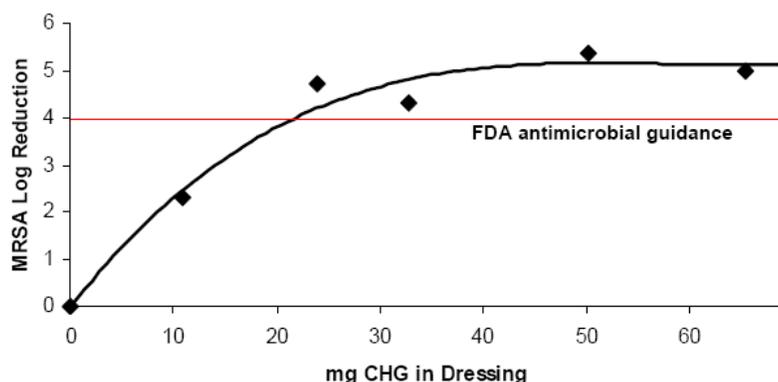
Table 4 - Concentrations of CHG

CHG (w/w)	0 %	5 %	11 %	15 %	23 %	30 %
CHG (mg)	0 mg	11 mg	24 mg	33 mg	50 mg	65 mg

Results

Figure 7 – MRSA log reduction

Antimicrobial efficacy against MRSA of the polyurethane foam dressing impregnated with increasing concentrations of CHG assessed using the log reduction of organisms test method.



Conclusions

- The antibacterial efficacy of the polyurethane foam dressing increased as the concentration of CHG increased such that when 11 % CHG (24 mg CHG per dressing) was present a 4.70 log reduction was evident.
- Increasing the concentration of CHG maintained the > 4 log reduction with MRSA, but the benefit of more CHG does not justify the additional toxicity of the increased concentration, and therefore shows no additional benefit as regards antimicrobial efficacy above 11 % CHG (24 mg CHG) (Figure 7).
- 22 – 24 g of CHG was found to be the optimum amount of CHG for GuardIVa, allowing it to maintain a minimum 4 log reduction in microbial count following 24 hr exposure.

Zone of Inhibition

Method

Kirby-Bauer Zone of Inhibition (ZOI) measurements were also used to demonstrate the sustained antimicrobial efficacy of GuardIVa over a 7 day period. Overnight cultures of representative microorganisms were prepared to a minimum inoculum count of 1×10^7 CFU / ml and spread on freshly prepared agar plates. An individual test article was placed onto the agar plate and incubated for 24 hr at 35 – 37°C. The area under the test article was swabbed and the swab was transferred onto sterile agar plates. The test article was then placed on a freshly inoculated agar plate and the procedure repeated. The test articles were transferred each day for up to 7 days. Growth from the swabs taken from the test articles indicated bacteriostatic action (slowed growth over 7 days) of the antimicrobial agent, while no growth over 7 days indicated bactericidal action. GuardIVa and BioPatch ZOI results were compared to publicly available ZOI results for other silver based antimicrobial dressings.¹

Results

Table 2 - Comparison of silver- and CHG-containing IV dressings when exposed to microorganisms over 7 days

	GuardIVa	BioPatch®	Algidex™ Ag	Silverlon®	SilverSite®	SilvaSorb®
MRSE	Bactericidal	Bactericidal	Bactericidal	Bacteriostatic	Bacteriostatic	Bacteriostatic
MRSA	Bactericidal	Bactericidal	Bacteriostatic	Bacteriostatic	Bactericidal	Bacteriostatic
VRE	Bactericidal	Bactericidal	Bacteriostatic	Bacteriostatic	Bacteriostatic	Bacteriostatic
<i>A. baumannii</i>	Bactericidal	Bactericidal	Bacteriostatic	Bacteriostatic	Bactericidal	Bacteriostatic
<i>C. albicans</i>	Bacteriostatic	Bacteriostatic	Bacteriostatic	Bacteriostatic	Bacteriostatic	Bacteriostatic
<i>P. aeruginosa</i>	Bacteriostatic	Bacteriostatic	Bactericidal	Bacteriostatic	Bactericidal	Bacteriostatic
<i>K. pneumoniae</i>	Bacteriostatic	Bacteriostatic	Bacteriostatic	Bacteriostatic	Bacteriostatic	Bacteriostatic

Figure 1(A) – Gram Positive organisms & *C. albicans* - zone of inhibition over 7 days

GuardIVa™ dressings were exposed to three Gram positive bacteria (MRSA, MRSE & VRE) and the fungus *C. albicans*

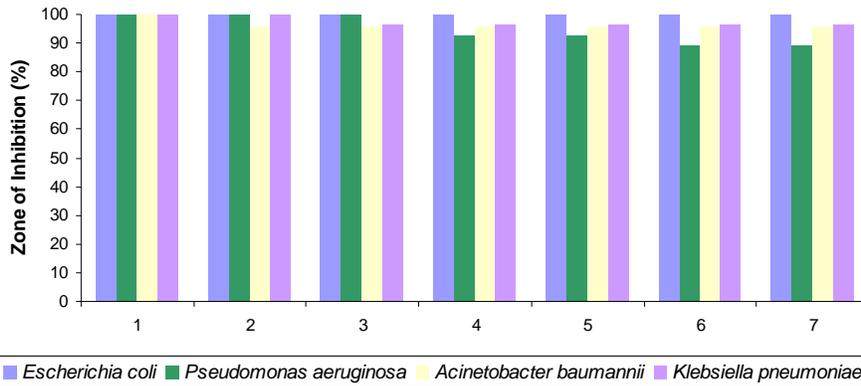
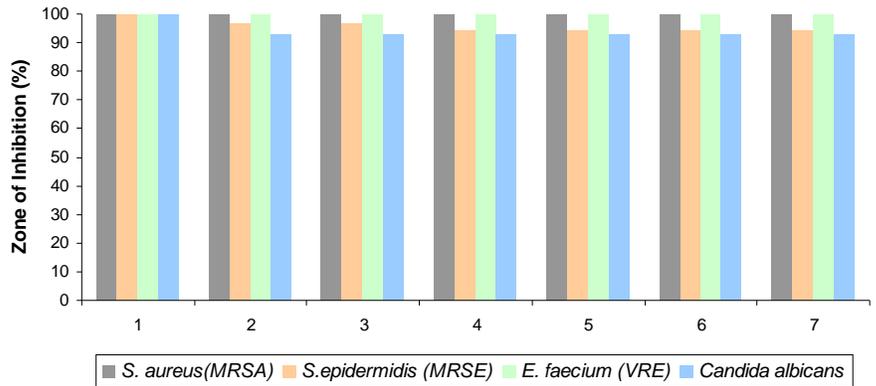
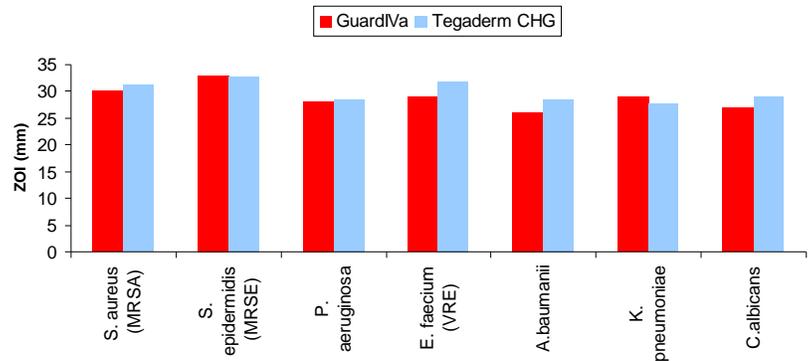


Figure 1(B) – Gram Negative organisms zone of inhibition over 7 days

GuardIVa™ dressings were exposed to four Gram negative bacteria (*E. coli*, *P. aeruginosa*, *A. baumannii* & *K. pneumoniae*).

Figure 2 – Antimicrobial efficacy of GuardIVa assessed using the Zone of Inhibition (ZOI) test method

GuardIVa dressing provides a comparable zone of inhibition to Tegaderm™ CHG², against common pathogens.



Conclusions

- GuardIVa demonstrated sustained zone of inhibition over 7 days with representative microorganisms.
- GuardIVa showed comparable zone of inhibition results as Tegaderm CHG.
- GuardIVa and BioPatch, the CHG-containing IV dressings, were determined to be bactericidal (no growth) against four of the microorganisms and bacteriostatic (slowed growth) against three of the microorganisms tested over 7 days

Hemostatic Properties

Method

The *in vivo* hemostatic efficacy of GuardIVa was determined using a rabbit ear model. The study was divided into two periods. Within the first test period (D +1) the test item (GuardIVa) was tested on the left ear of the rabbit, the right ear was used as control (Pur-Zellin® cellulose swab, HARTMANN-RICO a.s.). Within the second period (D +3) GuardIVa was tested on the right ear of the rabbit, the left ear was used as a control. Bleeding was caused by puncture of a lateral ear vein with an injection needle (external diameter always 0.9 mm). On D +1 the puncture was performed at an acral part of the ear, on D +3 the puncture was performed cranially. Distance between both punctures was 2 – 3 cm. The test and control were applied immediately after the puncture wounds were made. Test items and controls were weighed before their use and immediately after cessation of bleeding. Also the time from start to the end of bleeding was measured.

Results

Table 3 - *in vivo* hemostatic properties of GuardIVa

	GuardIVa	Gauze Control
Time to Haemostasis	48 sec	113 sec
Blood Loss	0.17 g	1.30 g

Figure 4 - Time To Hemostasis (sec)

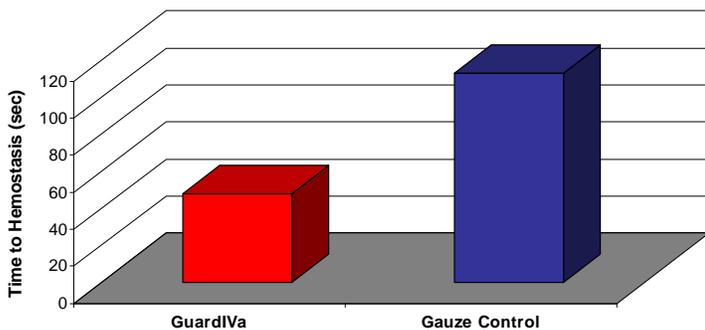
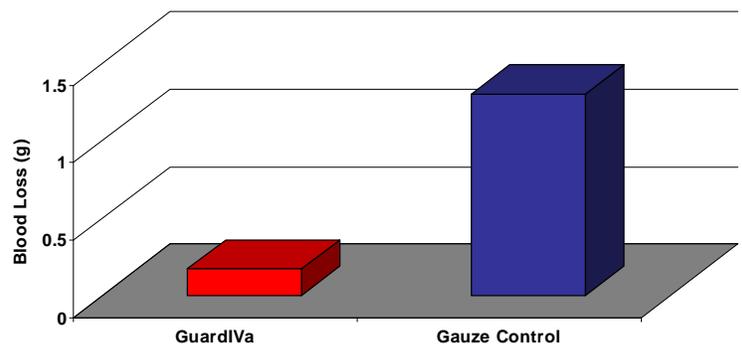
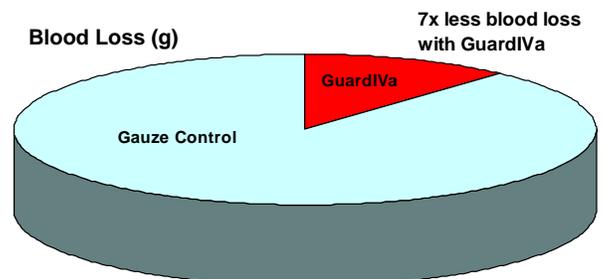


Figure 5 – Blood Loss (g)



Conclusions

- In this *in vivo* study, wounds treated with GuardIVa significantly reduced time to haemostasis and had up to 7 times less blood loss compared to the gauze dressing.
- Hemostatic efficacy of GuardIVa, which contains a proprietary oxidised cellulose hemostatic compound was demonstrated.



Support of Normal Wound Healing

Method

Dermal wound healing experiment in rats: Each of 10 rats received three dorsal full thickness wounds to the depth of the subcutis created with a 10 mm dermal punch. Following wound creation, each of the three wounds on each animal was covered with a test sample (GuardIVa), a control dressing (BioPatch) or left untreated. The wound sites on each animal were covered with a secondary dressing. Animals were observed daily to ensure integrity of the wound, to observe signs of general clinical health and to record wound measurements. The same dressing that was removed was replaced on the wound after each measurement had been taken. Dressings were changed as necessary depending on the degree of saturation with exudate and wear time was limited to a maximum of 7 days exposure of a single treatment on the wound. Results in Figure 6.

Also, the effect of the test item (GuardIVa) and the control dressing on edema development was assessed during the dermal wound healing experiment in rats described below in Figure 7.

Results

Figure 6 - GuardIVa Supports Normal Wound Healing

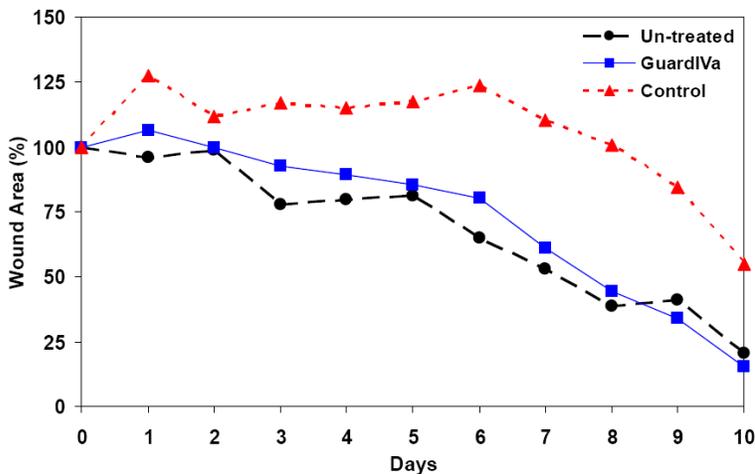
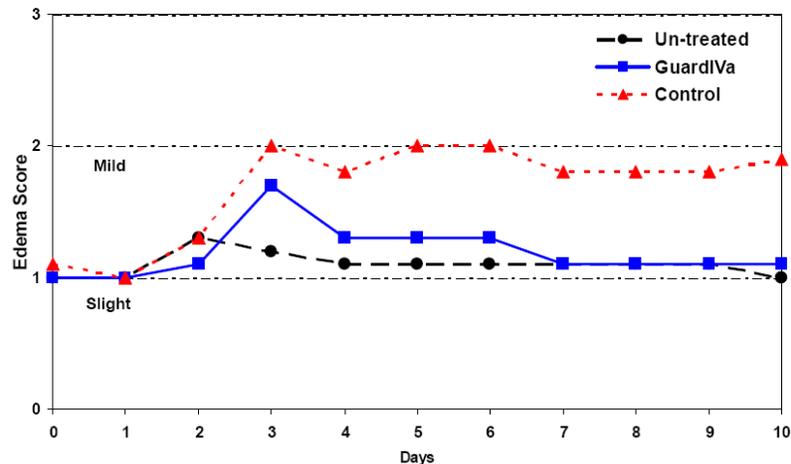


Figure 7 - Comparison of Edema Development



Conclusions

- Wounds treated with the test item (GuardIVa) healed at a rate comparable to un-treated wounds when compared to wounds treated with the control dressing.
- A lesser edema response was reported for untreated wounds and those treated with GuardIVa, than for the wounds treated with the control dressing. The wounds treated with the control dressing showed a more pronounced edema score.
- The wound sites were also assessed for signs of erythema development but none were visible at the untreated sites or at the sites treated with GuardIVa or control.

References

1. Bhende, Shubhangi, et al.. "In vitro Antimicrobial Effectiveness of 5 Catheter Insertion-Site Dressings" *The Journal of the Association for Vascular Access*. Winter 2007. Vol 12 #4.
2. Schwab DL et al., "Growth inhibition of micro-organisms involved in catheter-related infections by an antimicrobial transparent IV dressing containing chlorhexidine gluconate" *19th European Congress of Clinical Microbiology and Infectious Diseases*. P1194.