

AMD™ Dressings and Silver Topicals

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INTRODUCTION

AMD dressings contain Polyhexamethylene Biguanide (PHMB) as an active component that imparts antimicrobial activity to the dressing. Typical concentration of PHMB on AMD dressing is 0.2% (2000 ppm) per dry weight. In clinical use, it is anticipated that occasionally AMD dressings may be utilized in combination with other topical products such as Thermoazene which is a topical formulation containing silver sulfadiazine (SSD) as an antimicrobial agent. Clinically, SSD may be applied on the wound and covered by AMD-like gauze dressings or SSD may be directly applied on the gauze dressing. In such modes of use, incompatibility of products could lead to reduction in antimicrobial activity. This study was performed to assess compatibility of SSD with PHMB in AMD dressings. *S. aureus* was used as a test organism in this study. In one experiment, SSD and PHMB solution were mixed with each other at different concentrations and changes in antimicrobial activity of the resulting mixtures were assessed. In the second experiment, SSD and AMD dressings were exposed to microbial challenge separately and in combination, with antimicrobial activity compared. In the third experiment, SSD was applied onto AMD dressings and antimicrobial activity was assessed using Zone of Inhibition (ZOI) observations.

MATERIAL AND METHODS

Test Samples

KERLIX™ AMD, Antimicrobial Large Roll # 3331

Lot # 51882701, exp 2010-07

SSD (KENDALL THERMAZENETM Silver Sulfadiazine Cream, 1 %) P.C. 473400 Lot # 521524 exp. 2008-08

Reagents

PHMB - Cosmocil CQ made by Avecia, Lot # 1L15-038, 20.40% NB # 2908 p. 85

Difco D/E Neutralizing Broth # 281910, Lot 3301560, exp 2006 - 09 - 03

Phosphate Buffer,

Challenge Organism

Staphylococcus aureus, ATCC 25923

METHODS

Preparation of Test Article

0.75 inch circular disks were aseptically cut from each test dressing.

Challenge Assay (SSD and PHMB, in solution)

A stock solution of SSD was prepared in Phosphate buffer at 1 g/ml concentration. This solution was serially diluted to a working solution of 1 µg/ml solution. A working solution of PHMB was prepared by diluting 20% PHMB solution in Phosphate buffer to 2 µg/ml concentration. These 1 µg/ml SSD solution and 2 µg/ml PHMB solutions were mixed together in different proportions resulting in concentrations listed in Table 1. To each of these mixtures an inoculum of *S. aureus* was added resulting 10⁶ cfu/ml challenge level. Similarly, several different working solutions of SSD and PHMB were also challenged with *S. aureus* at 10⁶ cfu/ml challenge level. These solutions were incubated at 37° C for 24 hours. Following incubation, 1 ml aliquot from each solution was taken and added to 9 ml neutralizer (D/E broth). This solution was serially diluted and plated for bacterial counts.

Table 1: Test Solutions

Test group	SSD solution, ml (1 µg/ml)	PHMB solution, ml (2 µg/ml)	Phosphate buffer, ml	Inoculum, ml
A	4.95	—	4.95	0.1
	—	4.95	4.95	0.1
	4.95	4.95	—	0.1
B	1.0	—	8.9	0.1
	—	2.5	7.4	0.1
	1.0	2.5	6.4	0.1
C	1.0	—	8.9	0.1
	—	1.0	8.9	0.1
	1.0	1.0	7.9	0.1

Table 2: Combination of SSD and AMD dressings

Combination	SSD	AMD	PHMB solution, 0.2%	Phosphate buffer	D/E broth	S. aureus, 10 ⁷ cfu/ml
1	1 gm	-		-	9 ml	1 ml
2	-	10 disks		-	9 ml	1 ml
3	1 gm	-		9 ml	-	1 ml
4	1 gm	-	9 ml	-	-	1 ml
5	1 gm	10 disks			9 ml	1 ml
6	1 gm	10 disks		9 ml	-	1 ml

Challenge Assay (SSD and AMD dressings)

Combinations of SSD and KERLIX AMD dressings were inoculated with *S. aureus* in D/E broth or Phosphate buffer as shown Table 2. These solutions were incubated at 37° C for 24 hours and quantified for a change in bacterial counts as discussed in previous section.

Challenge Assay (Zone of inhibition)

Three test samples – SSD only, SSD applied on KERLIX and SSD applied on KERLIX AMD – were placed on agar plates seeded with challenge organism at 10⁶ cfu/mL levels. After 24 h incubation at 37° C, the antimicrobial activity of test samples was assessed visually as Zone of Inhibition surrounding the test samples.

SSD (T), PHMB (P) and Combination(T/P) vs. Log Reduction

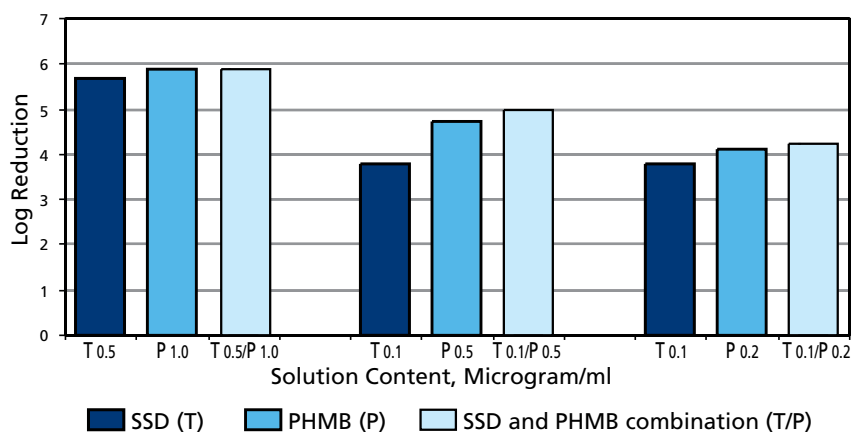


Table 3: SSD and PHMB activity against *S. aureus*

Test sample group	Test sample	Test sample designation	Initial log count	Final log count	Log reduction
A	SSD (0.5 µg/ml)	T0.5	6.85	1.18	5.67
	PHMB (1.0 µg/ml)	P1.0	6.85	0.95	5.9
	SSD/PHMB (0.5 and 1.0 µg/ml)	T0.5/P1.0	6.85	0.95	5.9
B	SSD (0.1 µg/ml)	T0.1	6.85	3.05	3.8
	PHMB (0.5 µg/ml)	P0.5	6.85	2.1	4.75
	SSD/PHMB (0.1 and 0.5 µg/ml)	T0.1/P0.5	6.85	1.85	5.0
C	SSD (0.1 µg/ml)	T0.1	6.85	3.05	3.8
	PHMB (0.2 µg/ml)	P0.2	6.85	2.75	4.1
	SSD/PHMB (0.1 and 0.2 µg/ml)	T0.1/P0.2	6.85	2.59	4.26

RESULTS AND DISCUSSION

SSD and PHMB activity against *S. aureus*

The antimicrobial activity of SSD and PHMB solution, separately and in combination is illustrated in the chart below. The results of three cases (A, B and C) are also presented in Table 3.

It can be concluded that the combination product of SSD and PHMB exhibits antimicrobial activity that is not much different from the activity exhibited by each compound alone.

SSD and AMD dressing activity against *S. aureus*:

The antimicrobial activity of SSD and AMD dressings, separately and in combination is illustrated in Table 4.

The results indicate that a combination of SSD and AMD dressings continue to exhibit antimicrobial activity similar to the antimicrobial activity exhibited by each product separately.

The results with D/E broth are presented in this table for reference only. D/E broth is a known neutralizer of antimicrobial agents such as PHMB and SSD. Thermazene or AMD dressings alone or as combination exhibit antimicrobial activity indicating compatibility between the two agents. The activity neutralized only in the presence D/E broth.

Table 4: Antimicrobial activity of SSD and AMD dressings, separately and in combination

Test sample	Initial challenge	Bacterial count after 24 hours	Result
SSD	6.04	0	6 log reduction
SSD + D/E Broth	6.04	7.90	Growth
AMD dressing	Historic data AMD dressings - 6 log reduction		
AMD dressing + D/E broth	6.04	8.28	Growth
SSD + 0.2% PHMB	6.04	0	6 log reduction
SSD + AMD dressing	6.04	0	6 log reduction
SSD + AMD dressing + D/E broth	6.04	7.78	Growth

Zone of Inhibition Study

The results of ZOI study are presented below.

Average ZOI:

A: SSD	4.9 mm
B: SSD + KERLIX	5.5 mm
C. SSD + KERLIX AMD	5.7 mm

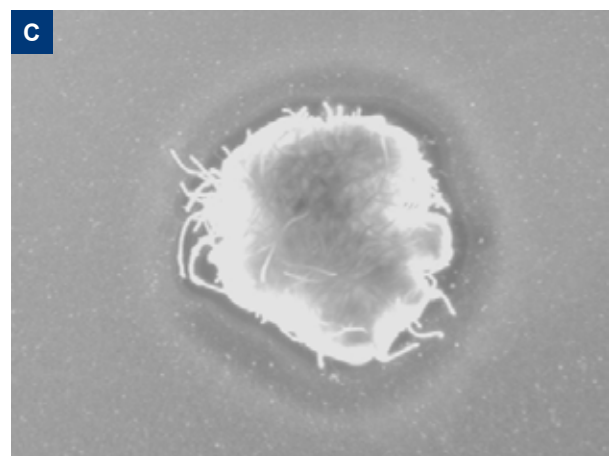
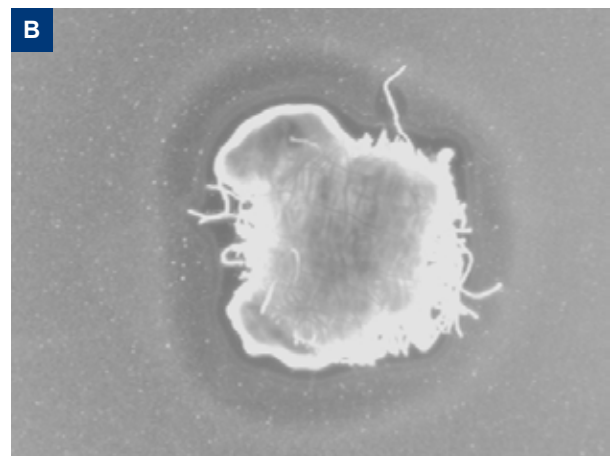
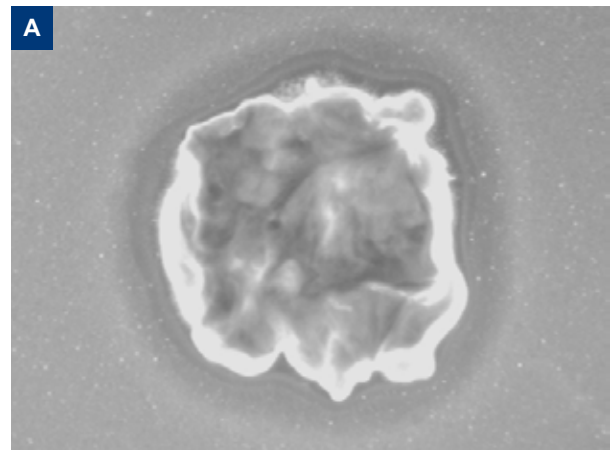
CONCLUSIONS

Based on the results of experiments described, it can be concluded that the application of SSD on KERLIX AMD dressings does not negatively impact the antimicrobial efficacy of the resulting combination product. The combination product is not expected to provide significantly better antimicrobial efficacy compared to the use of each product separately.

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