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Brief report

Efficacy of a novel skin antiseptic against carbapenem-resistant Enterobacteriaceae

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Infections caused by carbapenem-resistant Enterobacteriaceae (CRE) are increasing on a global scale. Because of the need for CRE transmission prevention and control, we sought to evaluate the efficacy of a silver-based skin antiseptic against these organisms. Using a human skin analog, a third party laboratory conducted efficacy testing. The results suggest that this product provides antimicrobial activity against CRE on human skin. Because of the unique properties, this antiseptic may be useful for daily bathing of hospitalized patients to assist in the control of CRE.

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Infections caused by carbapenem-resistant Enterobacteriaceae (CRE) are increasing on a global scale and represent a significant public health concern.^{1,2} Prevention and control of the spread of CRE can be difficult because Enterobacteriaceae are enteric organisms and are consistently shed to the environment and to the hands of health care workers from colonized or infected hosts. Reduction in skin and environmental bioburden are important prevention interventions for organisms transmitted via this route.

The highest quantities of CRE are likely to be on colonized or infected patients, making source control important. Although primarily present in the gastrointestinal tract, these organisms are identified on inguinal and axillary surfaces nearly as often as in the rectum.³ These data support the concept that daily bathing with antiseptic solutions may decrease the CRE skin bioburden⁴ and therefore reduce transmission.

To provide a safe health care environment for patients, it is critical to continue to identify products that are nontoxic and effective for daily bathing while maintaining activity against epidemiologically important organisms, such as these multidrug-

resistant Enterobacteriaceae. The current study describes the efficacy of a novel skin antiseptic against 2 different CRE.

METHODS

Study design

This was a laboratory-based efficacy study evaluating a nontoxic, silver-based skin antiseptic (Theraworx, Avadim Technologies, Asheville, NC) against carbapenem-resistant *Escherichia coli* and carbapenem-resistant *Klebsiella pneumoniae*. To evaluate the potential efficacy of this product for antisepsis on human skin, the VITRO-SKIN model (IMS, Portland, ME) was used. This model consists of a substrate that simulates human skin, with similar topography, pH, surface tension, and ionic strength.

Organisms

E coli and *K pneumoniae* isolates were obtained from the American Type Culture Collection, numbers 81,371 and BAA-1705, respectively. The modified Hodge test was used to document carbapenem resistance in each isolate.

Laboratory methods

A third party, ATS Laboratories (Eagan, MN), conducted all tests and reported results back to the investigators. Controls for purity,

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Conflicts of interest: Dr Wiemken is a consultant for Avadim Technologies and Clorox Healthcare.

Table 1

Efficacy of a novel silver-based skin antiseptic against carbapenem-resistant *Escherichia coli* using a skin model in the presence of 5% bovine serum

Dilution volume	Survivors			
	Replicate 1	Replicate 2	Replicate 1	Replicate 2
	15-min exposure		60-min exposure	
10 ⁰ (1.00 mL)	60	40	185	41
10 ⁰ (1.00 mL)	8	6	20	6
10 ⁻¹ (1.00 mL)	1	0	2	0
10 ⁻² (1.00 mL)	0	0	0	0
10 ⁻³ (1.00 mL)	0	0	0	0
CFU/carrier	1.2 × 10 ³	8.2 × 10 ²	3.7 × 10 ³	8.2 × 10 ²
Log ₁₀ CFU/carrier	3.08	2.91	3.57	2.91
Average log ₁₀	3.00		3.24	
Geometric mean (CFU/carrier)	1.00 × 10 ³		1.74 × 10 ³	
Log ₁₀ reduction	3.84		3.60	
Percent reduction	>99.9		>99.9	

NOTE. Data represent CFU unless otherwise noted. CFU, colony forming units.

Table 2

Efficacy of a novel silver-based skin antiseptic against carbapenem-resistant *Klebsiella pneumoniae* using a skin model in the presence of 5% bovine serum

Dilution volume	Survivors			
	Replicate 1	Replicate 2	Replicate 1	Replicate 2
	15-min exposure		60-min exposure	
10 ⁰ (1.00 mL)	>300	>300	>300	>300
10 ⁰ (1.00 mL)	132	>300	109	107
10 ⁻¹ (1.00 mL)	24	40	22	22
10 ⁻² (1.00 mL)	3	2	2	3
10 ⁻³ (1.00 mL)	1	1	0	1
CFU/carrier	2.64 × 10 ⁴	8.0 × 10 ⁴	2.18 × 10 ⁴	2.14 × 10 ⁴
Log ₁₀ CFU/carrier	4.42	4.90	4.34	4.33
Average log ₁₀	4.66		4.34	
Geometric mean (CFU/carrier)	4.57 × 10 ⁴		2.19 × 10 ⁴	
Log ₁₀ reduction	1.86		2.18	
Percent reduction	98.6		99.3	

NOTE. Data represent CFU unless otherwise noted. CFU, colony forming units.

organic soil (5% fetal bovine serum) sterility, neutralizer sterility (Lethen Broth, VWR-America, Radnor, PA), and carrier (silver-based antiseptic) sterility were also performed for each test and are available on request.

Initially, a standard suspension of approximately 3 log₁₀ of the organism under study was prepared. Then, 1 mL of the suspension was dried on a 2.54 cm² area of a 3.81 cm² rehydrated VITRO-SKIN carrier at ambient air temperature. The surface was then wiped with a silver-based antiseptic impregnated towelette over and back twice (4 passes total) for all tests. After the appropriate time under study (15 and 60 minutes elapsed time since antiseptic contact), the product was neutralized, and the organisms were plated at 35–37°C for 48 hours on Tryptic Soy Agar with 5% Sheep Blood (BAP, Remel, Lenexa, KS).

Both organisms were tested in the presence of organic material (5% fetal bovine serum). Each test was performed on the undiluted sample and on 4 serial dilutions.

RESULTS

All American Type Culture Collection organisms evaluated were documented to be carbapenem resistant via the modified Hodge test. Tables 1 and 2 outline the average efficacy of the silver-based antiseptic against carbapenem-resistant *E coli* and *K pneumoniae* at 15 and 60 minutes after antiseptic contact, in the presence of 5%

fetal bovine serum. All control results for culture purity, organic soil load sterility, neutralizer sterility, and population and neutralization confirmation were considered acceptable by the third party laboratory.

CONCLUSIONS

Our study documents that this particular silver-based antiseptic may be useful for skin antiseptics in patients colonized or infected with CRE because of its confirmed activity against 2 of these organisms on a human skin analog. Being silver based, it may have excellent activity against a broad range of organisms other than CRE.⁵ Furthermore, this antiseptic provides many benefits over soap and water, including (compared with data available for hand hygiene)⁶ antibacterial activity, skin nourishment, pH maintenance, and promotion of cell growth and skin barrier protection. Each ingredient is considered nontoxic and has been tested in whole for biocompatibility and toxicity (testing results and safety data sheet available from Avadim Technologies). These properties make it an attractive option for skin antiseptics in hospitalized patients, and the enhanced antibacterial activity should reduce transmission of pathogens similarly to other available skin antiseptics.⁷

Development of resistance is always a concern with any antimicrobial agent. Although silver resistance is possible through *sil*-mediated binding and efflux pumps,⁸ clinically documented resistance even in the presence of silver resistance genes remains limited and controversial.^{9,10} It will be critical to maintain surveillance for clinically resistant isolates as silver becomes an important agent in the infection prevention arsenal.

This study has some limitations. First, we did not evaluate all Enterobacteriaceae, and other genus and species may have varied susceptibilities. Therefore, these results cannot be extrapolated directly to other organisms. We also used a human skin analog as opposed to actual skin. It is possible that activity on human skin may be different than on the analog because of the skin microbiome and other properties that may not have been accounted for in the skin analog. Finally, we did not have a direct comparison with an active and inactive control antiseptic, limiting the generalizability. The strengths of this study include the use of a third party certified laboratory with significant experience conducting efficacy testing and the multiple tests conducted.

In conclusion, this study documented antimicrobial activity of a novel, nontoxic, silver-based skin antiseptic against 2 CRE in a human skin model. It will be important to evaluate the effectiveness of this product in the clinical setting to ensure activity in practice. Nevertheless, this antiseptic may be useful for daily bathing of hospitalized patients to assist in the control of CRE transmission.

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