Alcohol-Based Handrubs: Understanding the Variables That Drive Antimicrobial Efficacy

Lead Author:
James Bingham, MS, Research Microbiologist

Contributing Authors:
Dave Macinga, PhD, Principal Microbiologist
Jane Kirk, MSN, RN, CIC, Clinical Manager

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Executive Summary

Alcohol-based handrubs are complex formulations, balancing antimicrobial efficacy with product aesthetics and skin performance to ensure healthcare worker acceptance and use. Results from in vivo Healthcare Personnel Handwash (HCPHW, ASTM E1174) studies show that product formulation and product application volume, not alcohol concentration or product form are key determinants of the in vivo antimicrobial efficacy of ABHR. Therefore, critical examination of HCPHW data along with the quantity of product applied to hands in the test should be conducted when comparing antimicrobial efficacy of products.

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Introduction:

Hand hygiene has been used as a measure of personal hygiene since the 19th century.[1] The first written handwashing guidelines for healthcare workers in the United States were published in 1975 by the Centers for Disease Control and Prevention (CDC). These guidelines have evolved over the last 36 years and currently recommend handwashing when hands are visibly dirty or contaminated, and alcohol-based handrubs (ABHR) for routine decontamination when hands are not soiled.[1] ABHR offer several advantages over handwashing, including superior antimicrobial efficacy, better skin tolerability under high-frequency use, greater convenience and time savings, all of which contribute to better end-user acceptability and higher compliance.[1–3] The purpose of this publication is to review the variables that influence the antimicrobial efficacy of ABHR.

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The U.S. Food and Drug Administration (FDA) has determined that alcohol across the concentration range of 60% to 95% is safe and effective for use in ABHR.[4] ABHR must meet minimum FDA efficacy requirements to be sold into the United States healthcare market. While ABHR may meet the FDA minimum efficacy requirements, the antimicrobial performance of individual formulations are not all equal. ABHR are complex formulations, balancing antimicrobial efficacy with product aesthetics and skin performance to ensure healthcare worker acceptance and use. Variables such as alcohol concentration, product formulation, product form and product quantity may influence the antimicrobial efficacy of ABHR. Studies using two standardized test methods, *in vitro* time-kill (ASTM 2315) and Healthcare Personnel Handwash (HCPHW, ASTM E1174) will be used to examine the variables that may influence the antimicrobial efficacy of ABHR.

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Time-Kill Studies:

In vitro time-kill studies performed by Price and others have demonstrated that the concentration at which alcohol in water kills bacteria varies depending on the organism, but is typically well below the concentrations used in marketed ABHR products.[5–7] Figure 1 shows the relationship between alcohol concentration and bactericidal activity for representative gram-negative (*Serratia marcescens*) and gram-positive bacteria (*Staphylococcus aureus*).[8] As the figure illustrates, a "threshold concentration" exists for each organism, below which little to no activity is observed and above which the activity is maximal. For *S. marcescens*, this transition takes place between 35% and 40%, whereas for *S. aureus*, the transition takes place between 45% and 50%. Across the FDA's required concentration range (60%–95%), bactericidal activity is maximal and there are no detectable differences. These studies are primarily used to assess broad-spectrum activity of ABHR. Because the threshold for the efficacious activity of alcohol is below the minimal FDA active concentration (60%) time-kill assays cannot easily discriminate the influence of product formulation, product form and product quantity on *in vivo* antimicrobial efficacy of ABHR.

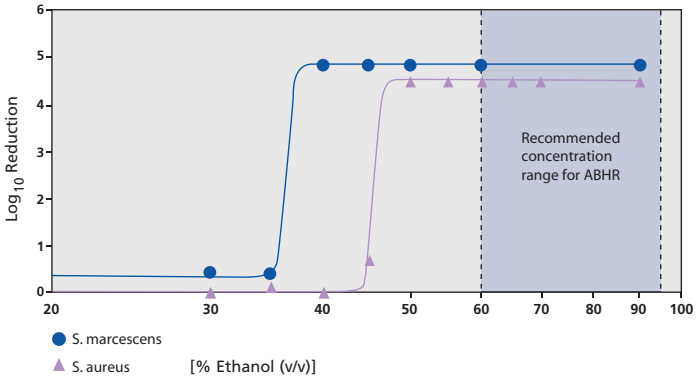

Figure 1. Concentration dependence of the bactericidal activity of alcohol. Various concentrations of alcohol (v/v) were evaluated by 15-second time-kill experiments according to ASTM E2315 against *S. marcescens* (ATCC 14756) and *S. aureus* (ATCC 6538). Data was visualized using GraphPad Prism and curves were fit using a sigmoidal dose-response (variable slope).

***In-vitro* time-kill studies indicate a "threshold concentration" exists for each organism, below which little to no activity is observed and above which the activity is maximal.**

Healthcare Personnel Handwash Studies:

Because *in vitro* time-kill studies do not predict the performance of ABHR on human skin or with repeated use, products are also evaluated by *in vivo* methods to measure reduction of microorganisms on the hands of human.[4,9] The HCPHW method was originally designed in the 1970s to evaluate antimicrobial handwashing agents, which are lathered with the aid of water and then rinsed off. In the absence of a method specifically designed to evaluate ABHR, the HCPHW method has become the default method for *in vivo* ABHR evaluation. HCPHW measures the reduction of a transient marker organism (*S. marcescens*) on the hands of adult subjects after a single product use and after 10 consecutive contaminations and product uses. The FDA requires a 2 $\log_{10}$ reduction (99%) of *S. marcescens* after the first product application and a 3 $\log_{10}$ reduction (99.9%) after the tenth product application.[4]

HCPHW measures the reduction of a transient marker organism (*S. marcescens*) on the hands of adult subjects after a single product use and after 10 consecutive contaminations and product uses.

Impact of Product Volume on Antimicrobial Efficacy:

Studies have shown a direct correlation between the amount of product applied to the hands and antimicrobial efficacy regardless of alcohol concentration or formulation.[10–12] Because product dry time is directly proportional to the amount of product applied to the hands, there is a practical limit to the volume of product that can be used without disrupting healthcare workflow. The ideal product application quantity is one that minimizes workflow disruption while maintaining maximum antimicrobial efficacy.[1] It must be noted that efficacy of ABHR are often tested at unrealistically high product volumes (i.e., 5 mL). Therefore, product literature should be examined to compare the quantity of product used in HCPHW tests to realistic in-use volumes.

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Impact of Product Form on Antimicrobial Efficacy:

ABHR are available in a number of different delivery forms including rinses (i.e., unthickened liquids), gels, foams, sprays and wipes. Studies have suggested that rinses provide higher efficacy than gels and foams; however, the studies contain multiple uncontrolled variables.[13–15] Therefore, no definitive conclusion can be drawn regarding which variables contribute to the perception of higher efficacy from rinses: alcohol concentration, product formulation or product form. A recent study

has demonstrated that a commonly used gel thickening system does not negatively impact ABHR efficacy in HCPHW studies.[16] Furthermore, Figure 2 illustrates that properly formulated gel and foam ABHR met FDA requirements, whereas two rinse formulations failed to meet the requirements at application 10.[17] In addition to these studies, technical product literature from several ABHR manufacturers indicates that a variety of rinse, gel and foam formulations meet FDA HCPHW requirements. Product form is, therefore, not a primary determinant of antimicrobial efficacy.

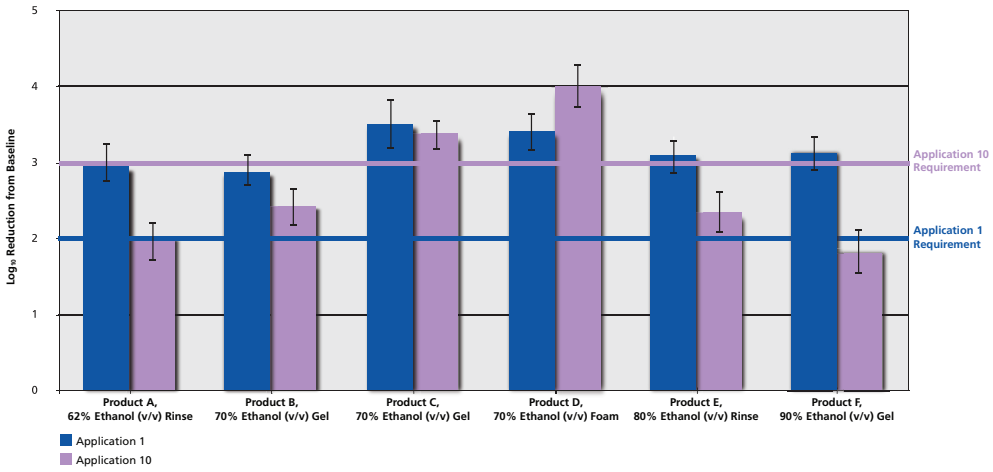

Figure 2. Evaluation of 2 mL applications of various ABHR formulations by HCPHW (ASTM E1174). Error bars = 95% confidence Intervals.

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Impact of Alcohol Concentration on Antimicrobial Efficacy:

Antimicrobial efficacy cannot be assumed based solely on the alcohol concentration of ABHR. Figure 2 clearly shows that antimicrobial efficacy does not correlate with alcohol concentration.[17] Two 70% formulations (Products C and D) perform significantly better at application 1 and 10 than another 70% formulation (Product B) indicating that alcohol concentration does not drive antimicrobial efficacy. Furthermore, some 70% formulations (Products C and D) perform significantly better than higher alcohol formulations (Product E and F) indicating that increasing alcohol concentration does not correlate to increased antimicrobial efficacy. In addition, a study using a newly accepted test method designed specifically to more accurately reflect ABHR use conditions (ASTM E2755) has demonstrated that identical formulations with varying alcohol levels achieved statistically equivalent log reduction of *S. marcescens*.[8] These results further demonstrate that alcohol content does not drive antimicrobial efficacy as long as the alcohol concentrations are within the safe and effective range established by the FDA.

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Impact of Product Formulation on Antimicrobial Efficacy:

Differences in antimicrobial efficacy can often be attributed to variation in product formulation. ABHR are complex formulations, combining alcohol with various ingredients to create specific attributes including skin tolerance, skin moisturization and aesthetic properties. These additional ingredients in some cases either improve or inhibit the formulation's antimicrobial efficacy.[18–23] As further

illustrated in Figure 2, the antimicrobial performance of different formulations varies in the HCPHW test regardless of alcohol content.[17] Two products containing 70% alcohol were statistically superior to a third product containing the identical level of alcohol at the tenth application. The study results demonstrate that there is no ideal concentration of alcohol that ensures formulations meet FDA efficacy requirements and highlight the importance of formulation on antimicrobial efficacy.

There is no ideal concentration of alcohol that ensures formulations meet FDA efficacy requirements.

Conclusion:

Understanding the test methods used to evaluate ABHR efficacy and resulting test data are critical when interpreting manufacturers' claims and when comparing product efficacy. Ideally products should be compared by head-to-head testing in third-party labs under identical and well-established test conditions. Total product formulation and product application volume, not alcohol concentration or product form, are key determinants of the *in vivo* antimicrobial efficacy of ABHR. Because formulation plays an important role in ABHR antimicrobial efficacy, critical examination of HCPHW data along with the quantity of product applied to hands in the test should be conducted when comparing antimicrobial efficacy of products. Finally, hand hygiene compliance is perhaps the most critical element to achieving clinical effectiveness. For this reason, the most effective ABHR are those that balance antimicrobial efficacy with skin performance and healthcare worker acceptability to ensure maximal compliance to hand hygiene practices.

Total product formulation and product application volume, not alcohol concentration or product form, are key determinants of the *in vivo* antimicrobial efficacy of ABHR.

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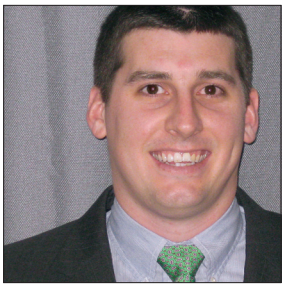
Biographies



James E. Bingham is a Research Microbiologist with GOJO Industries. His current research areas include *Clostridium difficile* spore biology, prevalence of pathogenic microorganisms on skin and environmental surfaces, and antimicrobial mechanisms of action. He holds a Master's degree in Food Microbiology from North Carolina State University and an undergraduate degree in Food Science from Cornell University.

David R. Macinga is a Principal Scientist with GOJO Industries and leads the Microbiology Department within Research and Development. Dr. Macinga holds a Ph.D. in Molecular Biology and Microbiology from Case Western Reserve University and has 14 years of industry experience developing both antibiotics and topical antimicrobials. He has published several research articles and book chapters on these topics and recently led the efforts to develop a new ASTM standard for evaluating alcohol-based hand rubs.

Jane Kirk is the Healthcare Clinical Manger for GOJO Industries, and is responsible for bringing the clinical perspective to our Acute Care and Long-Term Care businesses. Prior to joining GOJO in 2008, she was Director of Infection Control at a 600+ bed hospital in Northeast Ohio where she initiated a robust hand hygiene program. Jane's experience in nursing also includes Public Health, Emergency Nursing, Critical Care, Ambulatory Nursing, and Clinical Instructor at Walsh University in Canton, Ohio. Jane holds a Master's in Science in Nursing from Walden University and an undergraduate from University of Detroit Mercy.

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[1]Based on a comparison with the top 10 nationally distributed healthcare market hand sanitizers, by dollar value sales, as reported by GHX Market Intelligence through March 2011.
[2]Healthcare Personnel Handwash Study #100635-101, September 24, 2010, BioScience Laboratories, Bozeman, MT.