Abstract

Chronic wounds can take long periods of time to heal, degrading the patient’s quality of life and adding to the burden of the global health care system. Proper management of a chronic wound requires maintenance of a moist environment as well as control of microbial growth in the wound. A dressing that contributes to both may improve outcomes, promote patient comfort, and lower the cost of care. The Kendall™ AMD antimicrobial foam dressing is impregnated with PHMB, which works as an antimicrobial agent. The foam dressing is highly absorbent and provides both weight support and pressure relief. The dressing is equally effective with varying amounts and flow rates of wound exudate. PHMB exhibits broad spectrum activity against bacteria and fungi, acting by disrupting the cytoplasmic membrane of the microorganism. PHMB attacks bacteria in the exudate as it is being absorbed by the foam, protecting against microbial colonization of the dressing. The dressing has been tested against a variety of organisms in challenge assays and a porcine wound model. The Kendall™ AMD antimicrobial foam dressing creates a moist environment and simultaneously inhibits pathogenic organisms from growing in or penetrating the dressing.

Introduction

A chronic wound does not progress through the usual stages of healing in a predictable time frame, and may take weeks or months to heal, seriously affecting the patient’s quality of life. Most chronic wounds can be categorized as diabetic foot ulcers, pressure ulcers or venous ulcers. About 15-20% of people with diabetes develop foot ulcers, about 40% of patients in intensive care units develop pressure ulcers, and an estimated 1% of the general population will suffer from a venous leg ulcer in their lifetime. Chronic wound management represents a large burden to the nursing staff of hospitals and long-term care facilities, as well as home and community healthcare organizations. Management of microbial burden and moisture from exudate in chronic wounds are two of the most important aspects of wound bed preparation. Simultaneous management of these issues may conflict as clinicians strive to create a moist environment conducive to wound healing without promoting excessive bacterial growth that may interfere with normal healing. Wound exudate is a protein- and cell-rich mixture that seeps from the blood as a result of inflammation, and is a source of neutrophils and macrophages that promote wound healing. Since chronic wounds remain open for an extended period, most wounds may be contaminated with bacteria on the surface. If these bacteria proliferate, progression to wound infection that overwhelms the host defenses may occur. Wound infection may delay healing and even cause wound deterioration by prolonging the inflammatory stage, competing for nutrients and oxygen, and leading to tissue hypoxia with subsequent increased fragility of granulation tissue, reduction of fibroblasts and collagen, can lead to the damage to reepithelialization. Dressings that provide better moisture and bacterial load management may not only improve the wound environment but also might increase patient comfort, improve quality of life and lower the cost of nursing care. A new dressing, Kendall™ AMD Antimicrobial Foam Dressing (Covidien, Mansfield, MA), has been developed with the aim to support clinicians in their efforts to manage both moisture and bacterial balance. The dressing is an open-cell polyurethane foam with superior fluid absorption and retention capability. The dressing is impregnated with 0.5% Polyhexamethylene biguanide (PHMB) as an bactericidal agent. PHMB is effective at inhibiting growth within the dressing of a wide range of microorganisms, including Methicillin-resistant Staphylococcus aureus (MRSA), Vancomycin-resistant enterococci (VRE), yeast and fungi. Additionally, antimicrobial resistance development to PHMB is highly unlikely. In this paper, we describe in-vitro and in-vivo testing performed to evaluate the efficacy of this product. A mode of action of PHMB within the dressings is also illustrated.
Properties of foam dressing

The Kendall™ AMD antimicrobial foam dressing is a dense (0.144 g/cm³) open cell polyurethane foam dressing that is comprised of a network of tiny cells. The cells are made up of cell walls (struts) and open windows (voids). The foam is made through a unique engineering process that yields an open-cell microstructured foam (figure 1). The process leads to a unique structure that allows the Kendall™ AMD antimicrobial foam dressing to have a high absorptive capacity with vertical wicking action, excellent exudate retention properties, and superior softness, with both weight support and pressure relief characteristics. Figure 2 shows the absorptive capacity of the Kendall™ AMD antimicrobial foam dressing compared with other foam dressings currently on the market, in units of mL of fluid absorbed per square inch of dressing. Figure 3 compares softness of the Kendall™ AMD antimicrobial foam dressing with other foam dressings, in units of Newtons (N) per centimeter thickness of dressing. The Kendall™ AMD antimicrobial foam dressing is shown to be the softest and most absorbent of all of the dressings tested, absorbing 28% more than the next most absorbent dressing.

The unique surface structure of the Kendall™ AMD antimicrobial foam dressing is equally as effective with various amounts and flow rates of wound exudate. The dressing swells as it absorbs in response to a high exudate level and flow rate, facilitating commensurate fluid uptake and minimizing pooling and maceration. If the amount and flow rate of exudate decreases, the foam shrinks so that the rate of exudate uptake through the surface is reduced to maintain moisture balance and avoid excessive drying of the wound surface. Localized swelling of the dressing occurs where the dressing is in contact with the wound as it absorbs wound fluid. This helps to reduce any space that may exist between the dressing and the wound, which in theory should insulate and maintain an optimum wound temperature.
Efficacy and mode of action of PHMB

PHMB is a linear polymer comprised of a hydrophobic backbone with attached chains that make it highly water soluble (figure 3). It is active against both gram-negative and gram-positive bacteria, as well as fungi. This activity is not affected by production of beta-lactamase by microorganisms, or by organic matter such as serum, blood, or wound fluid. Broad spectrum activity of PHMB has been demonstrated in studies with gauze dressings containing PHMB.

PHMB is a membrane-active agent whose antimicrobial effect depends on disruption of the microbial cytoplasmic membrane and leakage of macromolecular components. The molecule binds to the surface of the bacterial cell membrane and causes reorganization of the membrane in a manner that prevents removal of the antimicrobial agent. This mode of action makes it highly unlikely that microorganisms can develop resistance. It has been used as an antiseptic in various products ranging from wound dressings to contact lens solutions for more than 75 years with no evidence of resistance.

PHMB is incorporated into the foam dressing during processing while the dense open-cell foam matrix develops. This method allows uniform dispersion of PHMB within the matrix. When wound exudate is absorbed into the dressing and structural changes occur, PHMB attacks bacteria in the wound fluid and minimizes microbial burden levels. As more exudate is absorbed, the foam continues to provide a moist environment while PHMB provides protection against bacterial colonization in, and penetration through, the dressing.

Antimicrobial efficacy of PHMB-impregnated foam dressing

Antimicrobial efficacy of PHMB-impregnated Kendall™ AMD antimicrobial foam dressing was assessed in a challenge assay. Test organisms included S. aureus, including MRSA, P. aeruginosa, VRE, C. albicans, S. epidermidis, E. faecalis, and E. coli. The dressing was immersed in phosphate-buffered saline (PBS) inoculated with 10^6 cfu/mL of the test organism and incubated for 24 hours. Microbial growth was quantified and the PBS solution with the dressing was re-inoculated with 10^6 cfu/mL of the test organism. This was repeated daily over a 7 day period. The foam dressing had excellent antimicrobial efficacy over the entire 7 days for all of the test organisms. Results are shown in figure 4. The presence of PHMB-impregnated foam dressing in the inoculated PBS reduced microbial count more than 99.9% when compared to foam dressing with no PHMB.

In vivo effectiveness of PHMB was tested using a porcine wound model. Full thickness wounds were created on pigs; nine wounds were assigned to each of the following treatment groups: 1) foam with 0.35% PHMB, 2) foam with 0.44% PHMB, or 3) foam without PHMB. Wounds were covered with one of the three dressings within 20 minutes of creation. Three dressings from each group were inoculated with 100 μl of P. aeruginosa on each of days 0, 3 and 6 and then covered with polyurethane dressing for 24 hrs. The dressings and wounds were assessed on days 1, 4 and 7 for P. aeruginosa and total bacterial count using a spiral plater system. Wound tissue biopsies were also taken to determine bacterial counts as cfu/gram. P. aeruginosa was cultured on selective media and...
### Figure 4. Action of PHMB-impregnated dressing and dressing without PHMB against various organisms *in vitro.*

<table>
<thead>
<tr>
<th>Standard Foam v.</th>
<th>Day 1</th>
<th>Day 2</th>
<th>Day 3</th>
<th>Day 4</th>
<th>Day 5</th>
<th>Day 6</th>
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<tbody>
<tr>
<td>MRSA</td>
<td>1.9</td>
<td>1.2</td>
<td>1.4</td>
<td>1.4</td>
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<tr>
<td>VRE</td>
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<tr>
<td>Epidermis</td>
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<td>3.7</td>
<td>2.8</td>
<td>2.2</td>
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<td><em>S. aureus</em></td>
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<td>0.6</td>
<td>0.6</td>
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<td><em>P. aeruginosa</em></td>
<td>-0.7</td>
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<td><em>E. coli</em></td>
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<td><em>C. albicans</em></td>
<td>0.9</td>
<td>0.8</td>
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<td>0.4</td>
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<tr>
<td><em>E. faecalis</em></td>
<td>1.2</td>
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<td>1.0</td>
<td>1.2</td>
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<tr>
<td>Avg Log Reduction of all Bacteria</td>
<td>1.5</td>
<td>1.0</td>
<td>0.9</td>
<td>0.8</td>
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**Avg Log Reduction vs. 8 Bacteria Species**

- Standard Foam
- Kendall™ AMD Antimicrobial Foam
total bacteria on tryptic soy/blood agar. Results showed that the PHMB-impregnated dressings and wounds protected by PHMB-impregnated dressings had lower bacterial counts at all assessment times (Figure 5). These results suggest that the foam with PHMB acts as a barrier to P. aeruginosa and may have important implications clinically for the prevention of wound infections. Similar results were obtained in a porcine wound model using gauze dressings impregnated with PHMB.17

Discussion

Moisture and bacterial management in chronic wounds are two of the most important aspects of wound bed preparation. Research and clinical experience have shown that a moist wound environment hastens the healing of acute and chronic wounds, promoting the growth of new tissue.4 Management of infection and moisture are key elements in chronic wound healing, however, creation of a moist environment that does not promote excessive bacterial growth is a constant challenge to the wound clinician.

Various antimicrobial substances have been added to wound dressings to facilitate management of infection and moisture. A consensus panel sponsored by the French National Authority for Health published recommendations for chronic and acute wound dressings in 2007. They concluded that the most suitable dressings for chronic wounds at the granulation stage were foam and low-adherent dressings. However, no consensus was reached on the use of antimicrobial agents in wound dressings.18 A review article published recently by Fonder and colleagues considered dressings that incorporate cadexomer iodine, silver ions, nanocrystalline silver, or metallic silver. They found that most of these dressings promoted wound healing, but adverse effects to the patient were observed.19 Vermeulen and colleagues, in a Cochrane review, point out that silver does not act specifically against bacteria, but against proteins nonspecifically, and may actually slow healing if relatively few bacteria are present.20 Silver resistant bacteria have also been reported.21 Silver ions that are incorporated into a dressing migrate into the wound bed as the dressing absorbs fluid. This may cause irritation and discoloration of surrounding tissues, and may exert toxic effects on keratinocytes and fibroblasts that are active in the healing process.19, 22, 23 PHMB mostly remains in the foam dressing, exerting its microbiocidal activity in the dressing itself.24 This prevents migration of pathogenic microorganisms from the environment through the dressing into the wound, allowing the natural defenses of the body to function in the moist wound environment. It also prevents microbial contamination from the patient's wound into the environment, thereby helping to prevent cross-contamination among patients and or caregivers. A further advantage to PHMB usage in wound dressings is the low likelihood that pathogenic organisms will develop resistance, due to its nonspecific mechanisms of action.
Conclusions
The balance of moisture maintenance and prevention of infection in chronic wound management presents a difficult challenge to the health care provider. A dressing that addresses both issues may aid in healing of chronic wounds and enhance the patient’s quality of life. The Kendall™ AMD antimicrobial foam dressing creates a moist environment. Incorporation of PHMB into the dressing inhibits pathogenic organisms from penetrating the dressing and helps protect the wound from infection due to exogenous factors. PHMB has been shown to kill pathogens, yet it exhibits none of the adverse effects of other microbiocidal compounds that have been incorporated into wound dressings.

Key points
• Wound care requires a balance of moisture maintenance and infection prevention for optimal healing.
• Incorporation of PHMB into dressing material inhibits pathogenic organisms from penetrating the dressing and contaminating the wound.
• Foam dressings absorb wound exudate, insulate the wound and provide a moist wound healing environment.
• Reduced bacterial burden in the dressing helps to promote a better wound environment.
• A dressing that simultaneously manages moisture and bacteria is an intriguing concept in advanced woundcare.
REFERENCES


