PuraPly™ Antimicrobial for a comprehensive biofilm-based wound management approach

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*In 2016, we participated in a working group on wound biofilm with colleagues from academic settings, teaching hospitals, and wound care clinics. Together we published recommendations for optimizing outcomes in the management of biofilm (*Wounds*. 2016;28[6 suppl]:S1-S20). Rising to the forefront of our discussion was the need for increased awareness of biofilm biology, prevalence, and clinical significance, and the need for educational resources on the optimal approach to managing wound biofilm. This perspective paper is based on the previously published recommendations and provides a concise overview of BBWM™, an approach that incorporates sharp debridement and a broad-spectrum antimicrobial such as PuraPly Antimicrobial.*

Studies have shown that biofilm can impair healing and lead to infection in wounds.[1,2] Therefore, many experts believe that wound treatment strategies should adjust to directly address biofilm. A biofilm-based wound management approach is a proactive approach in which all wounds are considered at risk for biofilm. Here we discuss a novel technology, PuraPly Antimicrobial, an essential component of comprehensive BBWM™. In combination with debridement, PuraPly Antimicrobial helps control biofilm re-formation while supporting healing.[3,4]

Biofilm is prevalent and impairs healing

All wound types are at risk for developing biofilm. Many experts believe that most chronic wounds are likely to contain biofilm.[5,6] While acute wounds are less likely to have biofilm, these wounds are still at risk if bioburden is neglected.[7] Diagnosing biofilm is a significant challenge for wound care specialists, because biofilm is not typically visible on the wound surface and classic signs of infection are often absent.[8]

Biofilm is a direct cause of delayed wound healing and is responsible for 80% of human infections.[1] Biofilm impairs healing by stalling wounds in the inflammatory phase.[1] For all wounds, a proactive approach to biofilm reduction and prevention is warranted.

There are 2 elements that are thought to be essential to a comprehensive BBWM™ approach: sharp debridement of the wound bed and application of a broad-spectrum, noncytotoxic, antimicrobial product. Treating and preventing biofilm re-formation allows the wound to utilize natural healing mechanisms.

Debridement is a critical element for BBWM™

Debridement has been standard protocol in chronic wound care for decades. Aggressive and frequent debridement is necessary to remove surface biofilm and, importantly, colonies of biofilm residing below the wound surface.[8] However, it is clear that debridement alone is not sufficient for managing biofilm due to rapid re-formation beginning within 24 hours.[1] In fact, biofilm can fully mature within 3 days following debridement.[8] Thus, debridement is necessary but not sufficient for managing the re-formation of wound biofilm.[8]

Managing biofilm requires an effective antimicrobial

A broad-spectrum, noncytotoxic, antimicrobial product is essential following debridement for comprehensive BBWM™.[8] However, not all antimicrobials are equally effective; in fact, some antibiotics are nearly ineffective against an established biofilm. The polymicrobial nature of biofilm ensures that a single antibiotic is unlikely to kill all microbes, and it is common to develop antibiotic-resistant or antibiotic-tolerant microbes.[8]

Another consideration is impact on healing; some antibiotics and antimicrobials are detrimental to wound healing.[9] For example, some silver dressings demonstrate nonspecific cytotoxicity to both pathogenic bacteria and host cells required for healing, resulting in delayed epithelialization.[10]

An ideal treatment is one that can counter each of these biofilm defenses. It should be effective against a range of microbes (broad spectrum), able to penetrate extracellular polymeric substance (EPS), have a nonspecific mechanism of action to prevent mutation and resistance of the bacteria, and have a neutral impact on healthy cells. The need for technology that balances antimicrobial potency with high tissue compatibility led to the development of PuraPly Antimicrobial.[3]

PuraPly Antimicrobial enables comprehensive BBWM™

PuraPly Antimicrobial is a novel technology for frontline proactive management of bioburden and the prevention of biofilm re-formation following debridement.[3,4] PuraPly Antimicrobial combines the broad-spectrum, noncytotoxic antimicrobial PHMB (polyhexamethylene biguanide) with a purified native collagen matrix.[3] The synergistic action of PHMB with native collagen makes PuraPly Antimicrobial an ideal technology for a proactive and comprehensive BBWM™ approach.

Indications

PuraPly Antimicrobial is approved for the management of wounds as an effective barrier to resist microbial colonization within the dressing and reduce microbe penetration through the dressing. It is indicated for multiple types of wounds:

- Partial- and full-thickness wounds
- Pressure ulcers
- Venous ulcers
- Diabetic ulcers
- Chronic vascular ulcers
- Tunneled or undermined wounds
- Surgical wounds (eg, donor sites/grafts, post-Mohs surgery, post-laser surgery, podiatric, wound dehiscence)
- Trauma wounds (eg, abrasions, lacerations, second-degree burns, skin tears)
- Draining wounds

Contraindications are a known sensitivity to porcine material or PHMB, and use of the product for third-degree burns.

PHMB in PuraPly Antimicrobial is an ideal antimicrobial for wound biofilm

PHMB is a positively charged polymer with a well-characterized mechanism of action elucidated by more than 25 years of study.[9] PHMB kills microbes through direct physical contact rather than chemical reactions, which is the mechanism for silver and most antibiotics. The positively charged polymer interacts with negatively charged phospholipids in microbial membranes, forming "punched holes" within the membrane (Figure 1).[11] This results in loss of cellular integrity leading to bacterial cell death. Critically, PHMB exerts low cytotoxicity to surrounding mammalian cells due to their positively charged membranes.[12]

This mechanism has additional advantages. Unlike antibiotics, which only kill metabolically active microbes, PHMB is effective against quiescent cells within biofilm. Local application of

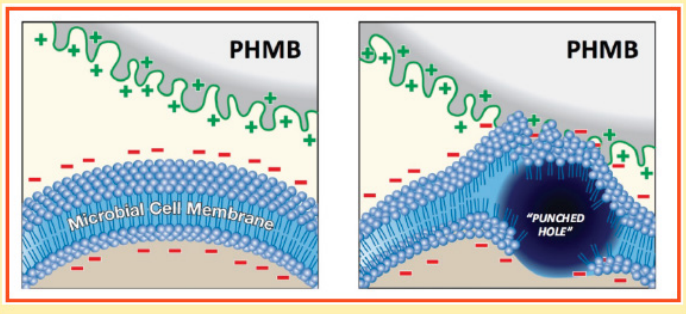

Figure 1: The mechanism of action of PHMB on the microbial cell membrane. There is a progressive interaction of positively charged PHMB with the negatively charged microbial cell membrane, leading to membrane dissolution and microbe death.

Source: Adapted from Gilbert and Moore, 2005.[11]

PHMB allows it to kill both free-floating and biofilm-associated microbes. Since the mechanism is a direct effect on microbial membranes, there is no known microbial resistance.[11] Given that virtually all microbes have negatively charged phospholipids in their cell membranes, PHMB has a broad antimicrobial spectrum that includes gram-positive bacteria, gram-negative bacteria, anaerobic bacteria, spore-forming bacteria, intracellular bacteria, and fungi.[9]

Specific cytotoxicity for microbes over host cells is critical for an effective antimicrobial. The biocompatibility index of PHMB (along with octenidine dihydrochloride) was found to be higher than other tested agents including povidone iodine solution, povidone iodine ointment, chlorhexidine digluconate, and a variety of silver preparations. Thus, PHMB was potent against the tested bacteria, but not against host fibroblasts.[12]

Despite extensive study, PHMB may be underutilized in wound care settings. The unique mechanism of action of PHMB makes it an ideal antimicrobial to address biofilm in wounds.[9]

Native purified collagen in PuraPly Antimicrobial supports healing

PuraPly Antimicrobial is composed of 2 layers of collagen, which are cross-linked to enhance the handling characteristics, to resist proteolytic degradation, and to provide a sustained antimicrobial effect in the wound.[3,4] Intact collagen plays an active role in all phases of wound healing: hemostasis, inflammation, proliferation,

An ideal antimicrobial for biofilm

- Broad antimicrobial spectrum
- No microbial resistance
- High tissue compatibility
- Sustained barrier effect

and remodeling. As a wound heals, a network of collagen fibers is formed, serving as a framework for fibroblasts to migrate along and close the wound. Collagen controls many cellular functions, including cell shape and differentiation, migration, and protein synthesis.[13]

In chronic wounds, the repair phase can be thwarted by excessive chronic inflammation caused by biofilm. Proteinases such as matrix metalloproteinases (MMPs), which are released by inflammatory cells, target denatured and damaged proteins but can also damage intact proteins. An imbalance in proteases plays a critical role in the disordered remodeling of extracellular matrix (ECM) during delayed wound healing.[14]

One approach to combat the proteolytic environment has been the topical application of collagen-based dressings, which have been shown to sequester proteolytic enzymes including MMPs.[14] The collagen matrix in PuraPly Antimicrobial was chosen specifically because it retains the native collagen structure that is believed to play a critical role in determining biomechanical behavior. A laboratory study demonstrated that ECMs that retain the native tissue structure inhibited a wider range of MMPs, including collagenases, gelatinase, and neutrophil elastase. Therefore, many experts believe that collagen with native structure is likely more effective at addressing the proteolytic environment than collagens that are reconstituted.[14]

Combination of PHMB and collagen enables comprehensive BBWM™

Although intact native collagen is proven to facilitate wound healing, adequate bioburden control is a prerequisite to reap the benefits of collagen. PHMB binds, disrupts, and blocks re-formation of biofilm; the native collagen matrix forms a durable biocompatible scaffold that supports healing. Thus, PHMB and native collagen in PuraPly Antimicrobial work in combination to block biofilm and create a wound environment that supports healing.

Debridement and proactive biofilm prevention with broad-spectrum, noncytotoxic, antimicrobial product are the foundation of BBWM™. PuraPly Antimicrobial is a unique technology that epitomizes BBWM™ by combining PHMB and a native collagen matrix to control biofilm re-formation and support healing. Although additional studies are needed, the application of PuraPly Antimicrobial following debridement may provide the support required for a wound to proceed to closure.[3] PuraPly Antimicrobial enables proactive and comprehensive BBWM™ for a broad range of wound types.

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This paper features select topics and content adopted from a previously published, co-authored supplement to Wounds *June 2016 titled: Expert Recommendations for Optimizing Outcomes in the Management of Biofilm to Promote Healing of Chronic Wounds. This focused paper draws from the authors' previous contributions to the published supplement and provides expanded discussion.*

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