MilSept
Microbicidal Antiseptic Solution
1% v/v PHMB (Polyhexamethylenebiguanide)
Spray

No Known Resistance

Advanced Wound Cleanser
First to Break the Biofilm Barrier

Role of polyhexamethylene biguanide

PHMB is a synthetic compound that has been in use for more than 60 years in various forms, including contact lens cleaners, mouth-washes, and more recently in wound management products, to reduce surface bioburden. It has demonstrated good clinical safely with no evidence of resistance and minimal toxicity

It has been suggested that PHMB is structurally similar to naturally occurring antimicrobial peptides (AMPs) are produced by most living organisms and have a broad spectrum of activity against bacteria, viruses and fungi They are positively charged molecules that bind to bacterial cell membranes and induce cell lysis by destroying membrane integrity. PHMB is thought to work by breaking down the lipopolysaccharide layer (LPS) of the bacteria cell wall to kill bacteria. This action is quick and so bacteria are unlikely to develop resistance to PHMB

Role of betaine

On a molecular level, betaine has a water-loving 'head' that is attracted to water molecules, and a hydrophobic water-hating 'tail' that repels water and attracts dirt and debris. The hydrophilic head remains in the solution, pulling the dirt and debris away from the wound and causing it to become suspended in the irrigating fluid enabling it to be flushed away.

As a result of its betaine (surfactant) component, has a lower surface tension than that of water, making it a more efficient cleanser. Many wounds are coated with denatured proteins, lipoproteins and lipids from cell membranes and carbohydrates. As these compounds denature (break down) they lose their solubility and coat the wound surface. The resulting low surface tension induced by the surfactant supports the physical removal of debris and bacteria (Figure 1).

Betaine also interferes with the production of homoserine lactone, a signalling molecule used in the cell-to-cell communication of biofilms (known as quorum sensing), which play a role in biofilm pathogenicity. The ability of betaine to disrupt biofilms is particularly beneficial as biofilms are now known to be resistant to cleansing with normal saline, which simply glides over the biofilm without removing it.

Figure 1 Role of Prontosan in the disruption and removal of biofilm

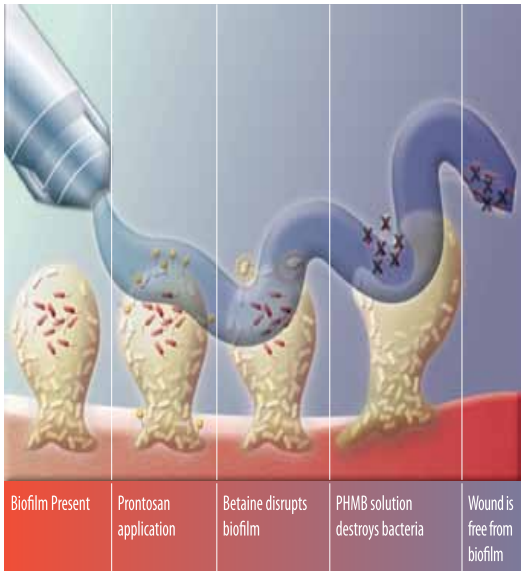

Table 1 Summary of evidence of PHMB

Study reference	Title	Type	Purpose	Outcomes
Perez R et al. *Wund Management* 2010; 4(2): 44-8[47]	Effect of different wound rinsing solutions on MRSA biofilm in a porcine wound model	Animal study	To evaluate activity of Prontosan on MRSA and biofilms in a partial thickness porcine wound model, against untreated control	Significant reduction of MRSA at 48 and 72 hours ($p<0.05$) compared to the other treatment groups. Removal of MRSA biofilm was only demonstrated using Prontosan; both saline solutions failed to reduce MRSA counts
Romanelli M et al. *Skin Pharmacol Physiol* 2010; 23 (Suppl 1): 41-4[43]	Evaluation of the efficacy and tolerability of a solution containing propyl betaine and polihexanide for wound irrigation	Single centre, prospective, controlled, explorative comparison trial (n=40)	To evaluate the efficacy and tolerability of Prontosan in controlling bacterial burden in colonised, critically colonised and infected venous leg ulcers	Prontosan group (n=20) showed a significantly better control of bacterial burden versus those treated with saline at each dressing change. It was well tolerated and useful in the absorption of wound odours
Moller A et al. *Wund Management*, 2008; 3: 112-7[28]	Experiences with the use of polyhexanide-containing wound products in the management of chronic wounds — results of a methodical and retrospective analysis of 953 patients	Retrospective study (n=953)	To assess the efficacy of PHMB-containing wound products in wounds of various aetiologies	Wound infection rate fell from 40% to 3% and 80% of the patients in the group with good cleansing results and improved findings achieved wound closure
Valenzuela AR, Perucho NS. *Rev ROL Enf* 2008; 31(4): 247-52[48]	The effectiveness of a 0.1% polyhexanide gel	Observational study (n=78 Prontosan vs n=64 control)	Evaluation of the use of Prontosan Gel in chronic wounds	Prontosan Gel was found to reduce bioburden (p=0.004) and to aid wound healing, reducing the time to closure
Horrocks A. *Br J Nurs* 2006; 15(22): 1222–8[31]	Prontosan wound irrigation and gel: management of chronic wounds	Observational study (n=10)	To evaluate the use of Prontosan in chronic wounds	Prontosan was found to provide a more efficient method of cleansing hard to heal wounds than normal saline
Andriessen AE, Eberlein T. Assessment of *Wounds* 2008; 20(6): 171-5[17]	Assessment of a wound cleansing solution in the treatment of problem wounds	Retrospective review (n=59 vs n=53 controls)	To assess the clinical efficacy and cost effectiveness of using a wound antiseptic to treat venous leg ulcers	Infection rates wre reduced to 3% in the Prontosan group compared to 13% in control group using normal saline/Ringer's solution. Prontosan group healed quicker (3.31 months) compared to controls (4.42 months)

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ROLE OF PHMB IN COMPARISON TO COMMONLY USED WOUND WASHES

Solutions for cleansing in wound hygiene*	
Solution	**Rationale**
Non-antiseptic	
Water	▪ Ineffective in reducing bacterial load.[2,4] ▪ Taps can be colonised with viable microbes: the presence of *Pseudomonas aeruginosa* in plumbing systems is well documented.[12-14] ▪ Ineffective in reducing bacterial load.[2,4] ▪ Single-use sterile containers are no longer sterile after opening.[2]
Saline	▪ Ineffective in reducing bacterial load.[2,4,9] ▪ Low toxicity.[2,4] ▪ Single-use, as bacterial growth can occur within 24 hours of opening.[2]
Surfactant-containing solution	▪ Due to their surfactant content, some formulations have been shown to disrupt microbial load when less force is applied.[2] ▪ Some formulations have shown antibiofilm capabilities *in vitro* by reducing microbial attachment and biofilm formation.[15] ▪ Gentle to healthy cells and can restore cellular integrity.[2,15]

Topical antimicrobial and antibiofilm agents commonly used in wound dressings*	
Agent	**Evidence for antimicrobial/antibiofilm action**
Polyhexamethylene biguanide (PHMB)	▪ The antimicrobial activities of PHMB were tested against intracellular *Staphylococcus aureus* in infected host cells.[5] Results showed that it: ▪ Killed 99.9% of intracellular *S. aureus*[5] ▪ Might interact with the bacteria inside the host cells [5] ▪ Reduced biofilm mass by 28–37%[5] ▪ Was tolerated by host cells at high concentrations[5] ▪ Was more effective against intracellular *S. aureus* than the antibiotic[5] enrofloxacin.
Povidone iodine	▪ Povidone-iodine exhibits antibiofilm activity against *Staphylococcus epidermidis* and *S. aureus* at sub-inhibitory concentrations.[6] ▪ Inhibition of biofilm by povidone-iodine correlated with gene transcription processes that repressed reproduction of *S. epidermidis*.[6] ▪ No viable *Pseudomonas aeruginosa* biofilm material was recovered after 4 and 24 hours of management with a povidone-iodine ointment at 100% and 10% concentrations.[7] whereas povidone-iodine–based antiseptics require higher concentrations to completely inhibit bacterial growth (3%–7.5%
Silver	▪ Atomic force microscopy studies suggest that the way silver ions bind to the bacteria destabilises sessile (immobile) *S. epidermidis* biofilm matrix.[8] ▪ In experiments comparing silver with a control on plastic and stainless steel surfaces, there were no significant differences in biofilms between silver and a control, although in some cases biofilms formed more rapidly with the control than with silver.[9]
Hypochlorous acid	▪ Rapid, broad-spectrum antimicrobial activity with low cytotoxicity.[18,19] ▪ Can be used to loosen dressings as well as for cleansing.[18,19]