

Suprasorb® X + PHMB: antimicrobial and HydroBalance action in a new wound dressing

When a reduction in microbial load of a wound is required, antiseptic dressings can be used. Dressings should be selected for their ability to promote an optimal environment for healing, their lack of cytotoxic effects on human cells and to reduce the selection of resistant bacterial strains. Suprasorb X + PHMB is a new antiseptic dressing that has these properties, combining Suprasorb X, a unique HydroBalance dressing that is able to both absorb and donate moisture, with PHMB, an antiseptic compound with no known cytotoxicity or resistance.

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KEY WORDS

Wound infection
Antibiotics
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Currently, there is a great deal of interest in the rising prevalence of resistant bacterial strains such as Methicillin-resistant *Staphylococcus aureus* (MRSA). There is also much criticism surrounding the indiscriminate use of antibiotics, which is now widely considered to be a crucial factor contributing to the rise of these resistant micro-organisms (Kingsley et al, 2006; Moffatt, 2006).

The clinical challenge that resistant bacteria such as MRSA pose to wound management is well known (Guyot and Layer, 2006). Guidelines for the management of MRSA include the avoidance of inappropriate or unnecessary use of antibiotics to reduce the likelihood of emergence and spread of resistant strains (Coia et al, 2006). As a result, there has been a renewed interest in the use of antiseptics in wound care. Antiseptics offer many benefits as they can be relatively easy to use, are widely available, frequently cost less than antibiotics, and can be administered without prescription (Principles of Best Practice, 2008).

However, they too should not be used indiscriminately or indefinitely, as there is also evidence for bacterial resistance to some antiseptics, such as silver (Maillard and Denyer, 2006), and there is a lack of clinical evidence surrounding the cytotoxicity of some antiseptic products (Principles of Best Practice, 2008). Clinicians working in wound care, therefore, have a professional responsibility to promptly and accurately recognise episodes of infection and to treat them wisely using the most appropriate products for each individual clinical situation.

When should antiseptics be used?

It is almost inevitable that the majority of wounds, whether acute, chronic,

surgical or healing by secondary intention, will become contaminated with bacteria to some extent. However, contamination, which describes the presence of organisms in a wound, with no active growth and no host response, is of no relevance to clinical practice (Kingsley et al, 2006). However, when wound bioburden increases, clinical effects may be noted and may require intervention. The Wound Infection Continuum is a useful aid to identifying treatment objectives. It should, however, only be used as part of a holistic assessment of the patient and their wound (Gray et al, 2005). The continuum describes the effects of increasing bacterial numbers in wound tissue, using conceptual names for increasingly severe forms of wound bioburden. It can also be used in reverse, to mark the wound's progress towards healing (Figure 1). The different stages are:

- ▶▶ Colonised
- ▶▶ Critically colonised
- ▶▶ Local infection
- ▶▶ Spreading infection (Kingsley, 2006).

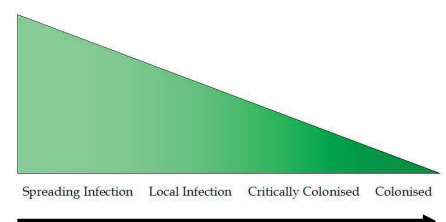


Figure 1. The Wound Infection Continuum.

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Colonised wounds contain multiplying bacteria, however, the host does not have an overt clinical response or clinical symptoms, meaning that the need for topical antimicrobial intervention is unnecessary. Only when there are concerns regarding the patient's immune response or overall medical condition should topical antimicrobials be used prophylactically to prevent an increase in wound bioburden. Indiscriminate prophylactic use of antimicrobials, including both antiseptics and antibiotics, is not encouraged (Kingsley, 2006; Moore and Gray, 2007).

Critically colonised wounds require a reduction in the level of bacteria present, if the wound is to progress towards healing. In chronic wounds, critical colonisation may cause delayed healing in the absence of any indicators of infection, thus the clinician should be alert to this and microbial involvement must be suspected when other causes of indolence have been eliminated. The topical application of an antimicrobial is probably the most effective way in which to reduce the critically colonised wound's bioburden to levels that allow the wound to heal (Sibbald et al, 2001; Fumal et al, 2002). Antibiotics are usually unnecessary in the first line of treatment for critically colonised wounds.

Localised infection is often characterised by the classic signs and symptoms of inflammation, including redness, heat and pain (Cutting and Harding, 1994). If local infection is identified, in most instances, it can be managed with topical antimicrobials, providing the practitioner is satisfied that the patient's overall condition does not suggest that there is a risk of the infection spreading. However, the clinician should remain alert to the possibility of spreading infection, and be prepared to alter treatment as required (Kingsley et al, 2006). If, however, infection has invaded soft tissues or is spreading, then treatment with both local and systemic measures is indicated. Wound dressing choice will have little impact on the spreading infection, but can help to reduce the level of bacteria at the wound surface and thus help prevent re-infection.

Once the need for topical antiseptic intervention has been identified, it is important to select a product that will provide optimum conditions to support rapid healing. The ability of the agent to reduce or eradicate micro-organisms, must also be considered, along with its specificity, cytotoxicity to human cells, its potential to select resistant strains and its allergenicity (Vowden and Cooper, 2006).

The ability of the carrier dressing to handle exudate and remove necrotic tissue from the wound is beneficial, since purulent exudate, necrotic tissue and slough are all growth mediums for bacteria (Cutting, 2008). The dressing's ability to reduce malodour, conform to the site and shape of the wound, perform wound bed preparation functions, satisfy patients' expectations and to meet treatment goals also need careful consideration (Vowden and Cooper, 2006).

Antiseptic agents

Antiseptics have been in use for much longer than antibiotics yet resistance to antiseptics presents much less of a problem. This may be because antiseptics differ from antibiotics in that they are generally active against a broader-spectrum of organisms including common pathogenic anaerobic and aerobic bacteria, and fungi. Unlike antibiotics, antiseptics also tend to have multiple target sites, including the bacterial cell wall or membranes, in the organisms on which they exert their effects. This means that the micro-organisms are less likely to mount an effective defence and survive as resistant strains (Gilbert, 2006).

The range of topical antiseptic agents currently in common use in wound dressings in the UK include silver, iodine, and honey. Polyhexamethylene biguanide (PHMB) is a relatively new entrant to the UK wound care market although it is in common use in Europe and US.

Polyhexamethylene biguanide

PHMB is a synthetic compound which is structurally similar to naturally occurring antimicrobial peptides (AMPs). AMPs

are produced by the majority of living organisms and have a broad spectrum of activity against bacteria, viruses and fungi (Moore and Gray, 2007). AMPs are positively-charged molecules that bind to bacterial cell membranes and induce cell lysis by destroying membrane integrity, in a similar way to penicillin and cephalosporin antibiotics. AMPs are produced by many cells within the wound, such as keratinocytes and inflammatory neutrophils, where they are thought to play a role in protection against infection (Sorensen et al, 2003).

The structural similarities between AMPs and PHMB mean that the latter can insert into bacterial cell membranes and kill bacteria in a similar way to AMPs (Moore and Gray, 2007).

Some bacterial cells use an efflux pump to protect themselves from the effects of some antiseptics. However, the effect of PHMB on the bacterial cell membrane mean that the pump is unable to remove antiseptic, so bactericidal concentrations are maintained in the cell. This mechanism of action is quick and means that bacteria are unlikely to develop resistance to PHMB (Seipp and Korber, 2008).

PHMB in wound management

Polyhexamethylene biguanide (PHMB) is a commonly used antiseptic which appears in a variety of products including contact lens cleaning solutions, perioperative cleansing solutions and swimming pool cleaners. Its safety and effectiveness as an antiseptic both in vitro and in vivo in these different applications is well documented (Motta, 2004; Motta, 2005; Larkin et al, 1992). It exerts little toxicity and has been in general use for approximately 60 years with no evidence of the development of resistance (Moore and Gray, 2007). In wound care, specifically, PHMB has previously been demonstrated to block *Pseudomonas aeruginosa*-induced infection (Cazzaniga et al, 2000) and prevent its degradation of wound fluid and skin proteins in vitro (Werthen et al, 2004). It can also kill a diverse range of bacteria and fungi (Lee et al, 2004).

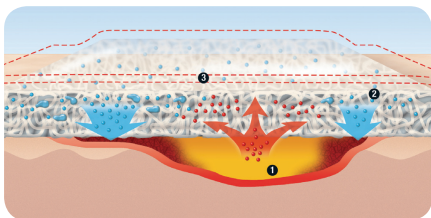


Figure 2. The unique HydroBalance of Suprasorb X. 1. Surplus exudate from the wound is absorbed, and 2. Moisture is released from the dressing to lightly exuding wound areas. 3. Safely removes debris and traps it within the dressing.

Furthermore, to date PHMB has been used successfully in wound dressings, including non-adherent products, gauze, drains and intravenous sponges (Motta and Trigilia, 2005; Moore and Gray, 2007). The long-term use of PHMB in other indications without cytotoxicity or the development of resistance suggests this is unlikely to happen when the antiseptic is used in wound management (Gilbert, 2006).

PHMB has been incorporated into a new wound management product, Suprasorb® X +PHMB (Activa Healthcare, Burton-upon-Trent) which gives antimicrobial activity to the unique HydroBalance dressing, Suprasorb X.

The Suprasorb X dressing range

Suprasorb X

Suprasorb X dressings have a unique structure made up of biosynthetic HydroBalance fibres. These fibres are the products of a cellulose fermentation process using a proprietary strain of *Acetobacter xylinum*. The bacteria produce fibrils of cellulose which are 200 times finer than cotton, giving the material an exceptionally high surface area. The same microbes 'weave' a mesh structure of fibrils that enhances both its moisture handling capabilities and its tensile strength.

As a result of the biosynthetic HydroBalance fibres, Suprasorb X is able to regulate the absorption and donation of moisture at the wound-dressing interface (Figure 2). Depending on the status of the wound, surplus exudate can be absorbed by the dressing, or donated in the case of lightly exuding wounds. This moisture absorbing and donating



Figure 3. An 86-year-old female with a wound following excision of an infected haematoma using versajet, followed by two weeks of topical negative pressure therapy. (a) The patient had a history of severe wound and urinary tract infection. She also has *C. Difficile* infection, is severely malnourished and thus is at very high risk of re-infection. (b) Suprasorb X + PHMB dressing was applied to the wound to ensure that the wound bioburden remains at a level conducive to healing.

capacity can also be exerted within the same wound, removing exudate and donating moisture to drier areas.

It also protects the wound against abrasion, desiccation and external contamination. These unique fluid-handling capabilities of the dressing mean that Suprasorb X can be used on moderately exuding, non-exuding and dry wounds. The moist environment also has a cooling effect that has demonstrated a significant reduction in pain (Alvarez, 2004; Davis, 2006).

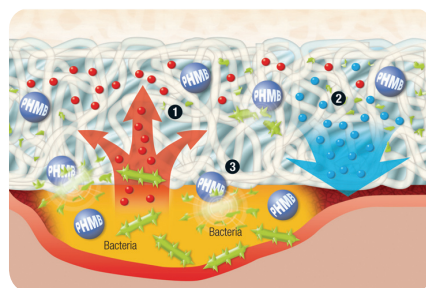


Figure 4. Mechanism of action of Suprasorb X + PHMB. Surplus exudate from the wound is absorbed by the dressing, and 2. Moisture is released from the dressing to lightly exuding wound areas. 3. Killing of micro-organisms by the PHMB that is released.

In a 24-patient, multicentre randomised controlled study carried out by Alvarez et al (2004) to determine effectiveness of Suprasorb X compared with care already being received in patients venous leg ulcers, Suprasorb X was found to significantly promote autolytic debridement and significantly reduce wound pain at weeks three, six and eight of the 12-week study. An improved rate of wound closure, in terms of increased epithelialisation and granulation tissue was also noted (Alvarez, 2004). Results of decreased pain, increased granulation and epithelialisation and an improved rate of wound closure were also observed by Vijverberg et al (2007) and Eberlein et al (2007).

The new dressing, Suprasorb X +PHMB, combines the proven efficacy of Suprasorb X with the antimicrobial action of PHMB (0.3%), and is indicated for use on lightly to moderately exuding, superficial and deep, infected wounds in all phases of wound healing (Figure 3). The PHMB component exerts its antimicrobial effects both within the dressing, but also at the wound-dressing interface (Figure 4). As the PHMB is not bound to the HydroBalance fibres of the dressing, it is released into the surrounding fluid along a concentration gradient.

The presence of fluid in the dressing means that antimicrobial activity is possible even on dry wounds, unlike silver-containing dressings which require the mechanical action of wound fluid to initiate antimicrobial activity.

Suprasorb X + PHMB in clinical practice

A clinical case series performed by Mulder (2007) to determine the antimicrobial effects of Suprasorb X + PHMB showed that PHMB effectively reduced wound bioburden and had a positive effect on wound healing. Twelve patients with a total of 26 wounds were evaluated, 11 of whom had previously been unresponsive to silver- or iodine-containing dressings.

Wound swabs were taken before and after treatment with Suprasorb X

+PHMB. Before treatment, organisms were identified in the wounds of eight patients, most commonly *Pseudomonas aeruginosa* and *Staphylococcus* (including MRSA). At the end of the evaluation, levels of bacteria were decreased in five of the eight patients (two patients were lost to follow up, and one patient experienced no change in bioburden). For the eight patients, there was a mean reduction in wound size from 6.79cm² to 4.57cm² in a mean of 25 days. Two wounds healed during the study and 13 showed improvement.

An evaluation of Suprasorb X + PHMB in the treatment of four patients with wounds which had previously been treated unsuccessfully with various silver-containing dressings was undertaken by Davis (2006). Although two wounds were locally infected, application of Suprasorb X + PHMB healed three of the four wounds, protected peri-wound tissue and resulted in a decrease in wound pain (Davis, 2006).



Figure 5. The wound at first assessment.



Figure 6. Following one week of treatment with Suprasorb X+PHMB.

Similarly, an evaluation of Suprasorb X + PHMB in the treatment of 79 wounds of varying aetiology by Cavorsi (2006) revealed that healing or clinical improvement was achieved in >80% of the cases receiving treatment with Suprasorb X and PHMB. In a subset of wounds that had not been responsive to prior treatment with silver dressings, a decrease in wound size of 33% was observed after three weeks.

A reduction in wound bioburden and progress towards healing was also observed in the following case report.

Case report

The patient was an 83-year-old woman with a history of chronic renal disease, hypertension and venous ulceration of the left leg of long duration. On initial presentation, the wound was sloughy and painful with high exudate levels. These symptoms and the associated malodour led to a diagnosis of critical colonisation.

To identify any reduction in bacterial load within the wound bed, a swab was taken on day one and another on day seven. Photographs were taken at every visit.

On first application of Suprasorb X + PHMB the wound measured approximately 13cm² with the wound bed consisting of 90% devitalised tissue and 10% granulation tissue. The peri-wound region was fragile but had evidence of epithelialisation (Figure 5). Microbiological finding showed +++ mixed skin flora.

A secondary foam dressing was applied over the Suprasorb X+PHMB and secured with stockinet, wool bandage and double setocrepe for support as the patient had not tolerated compression on previous applications.

The dressing was removed and the wound reviewed after three days. The dressing had remained hydrated under the bandaging and foam and was atraumatic on removal. The wound bed had improved with a reduction in the amount of devitalised tissue and an

increase in the granulation tissue to a ratio of approximately 60/40, however, there was some maceration to the peri-wound area. There had also been a reduction in the overall size of the wound to 9.4cm² (Figure 6). The wound swab results now showed a reduction in skin flora to just + mixed skin flora.

The patient responded extremely well to Suprasorb X+PHMB with the wound improving and the bacteria being reduced considerably during the two-week treatment. The dressing is moist on application and therefore, fitted the criteria for promoting wound healing in this patient's wound.

Conclusion

The ideal antiseptic dressing will reduce wound bioburden while providing a moist wound environment that promotes wound healing. Such a dressing, however, must be used wisely to minimise the cytotoxic effects on the cells needed for wound healing, and to reduce the selection of resistant bacterial strains (Vowden and Cooper, 2006). Suprasorb X + PHMB is able to effectively reduce the number of pathogens in the wound. Currently, PHMB does not have a history of resistance or cytotoxicity, making it a good alternative to antiseptics for which the development of bacterial resistance and toxicity is an issue.

Suprasorb X's unique ability to absorb and/or donate moisture depending on the needs of the individual wound provides a moist environment that will allow the wound to progress towards healing and leads to a reduction in pain.

These unique properties of Suprasorb X + PHMB make it an attractive alternative to the antiseptic dressings that are currently available. **WUK**

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Key Points

- ▶▶ The clinical challenge that resistant bacteria such as MRSA presents to wound management is well known.
- ▶▶ As a result there is renewed interest in the use of topical antiseptics.
- ▶▶ Antiseptics should not be used indiscriminately or indefinitely due to potential cytotoxic effects on healthy wound cells, or the selection of resistant bacteria.
- ▶▶ The ideal antiseptic dressing should have the ability to reduce bioburden in the wound, while providing optimal conditions for wound healing.
- ▶▶ Suprasorb X + PHMB dressing combines the unique HydroBalance properties of Suprasorb with the non-cytotoxic antiseptic PHMB.
- ▶▶ Studies have shown that Suprasorb X + PHMB dressing effectively reduces wound bioburden, promotes autolytic debridement, improves the rate of wound closure, through increase in granulation and epithelialisation, and effectively reduces wound-related pain.