Catch or Kill?

How DACC technology redefines antimicrobial management

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Foreword

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Infection is a major factor in delayed wound healing. All open wounds are contaminated and although not all wounds become infected, this state of contamination is an obvious risk factor that increases when the immune system is compromised. Some doubt regarding the precise mechanisms by which microorganisms cause infection remains (Bowler, Durden and Armstrong, 2001), however, it is generally accepted that the expression of microbial toxins and enzymes destroys tissue cells and interferes with healing. Polymorphonuclear leucocytes (PMNs), which arrive on the scene soon after wounding takes place, express enzymes which can also be detrimental to healthy tissue cells. These two factors help to explain the delay in healing so often observed.

Increasing concern in respect of antimicrobial resistance has led clinicians to reappraise the role of topical agents (antiseptics). It is possible that not all wounds require intervention (systemic or topical) with such active agents. The clinical objective in preventing or managing infection is to ensure the host's defences are able to out-compete microbial pathogens, leaving microbes unable to thrive and proliferate. One means of providing host support is through the introduction of 'passive' antimicrobial mechanisms which may have a role to play in managing wound bioburden.

Evidence already exists supporting the role that non-medicated dressings have to play in managing wound bioburden. In vitro and in vivo studies show that alginates, hydrocolloids and Hydrofibers promote reduction in the wound surface bioburden. Alginates for example can retain bacteria within the dressing matrix (Walker et al, 2003; Tachi et al, 2004).

A more recent development, hydrophobic interaction, has at its heart the fatty acid dialkylcarbamoylchloride (DACC) that coats dressing fibres and interacts with the surface bioburden. Microbes, including fungi, are irreversibly bound through the physical mechanism of hydrophobic interaction to DACC coating on the dressing surface. These are then disposed of at dressing change. The risk of bacterial resistance or sensitization is avoided as there are no active agents involved. Potentially damaging endotoxin release in the wound bed is also prevented as microorganisms are removed whole rather than destroyed.

A strategy to support healing lies in maintaining host immunological control of the wound environment. This novel option of bacterial binding is available to clinicians and has the potential to decrease reliance on 'traditional antimicrobials' as the primary mode of intervention

Efficacy of hydrophobic interaction in reducing the wound bioburden and facilitating healing has been demonstrated *in vitro* and *in vivo*. The value of 'Catch' is still being evaluated and in due course we should learn that it is not always necessary or desirable to 'Kill' when microbial resistance and expression of bacterial toxins can dramatically upset the benefit/risk balance of specific clinical interventions. As always, more research would be welcomed to demonstrate the full benefits of hydrophobic interaction as an alternative to the more aggressive methods, but at the moment this method of managing wound bioburden is worth full consideration.

Catch or Kill? How DACC technology redefines antimicrobial management

The prevention and management of local wound infection relies largely on the use of topical antimicrobial dressings. These treatments achieve their effects by killing bacteria, but this can result in the presence of bacterial cell debris in the wound and the release of endotoxins, which may prolong inflammation. An alternative approach, where bacteria and fungi bind irreversibly to the wound dressing as a result of a hydrophobic interaction and are then removed at dressing change, avoids the risk of prolonged inflammation and the potential for resistance. The fact that there is no risk of toxicity to healthy tissue or systemic absorption is a further benefit.

wound infection • hydrophobic interaction • bacteria • binding • DACC • antimicrobial

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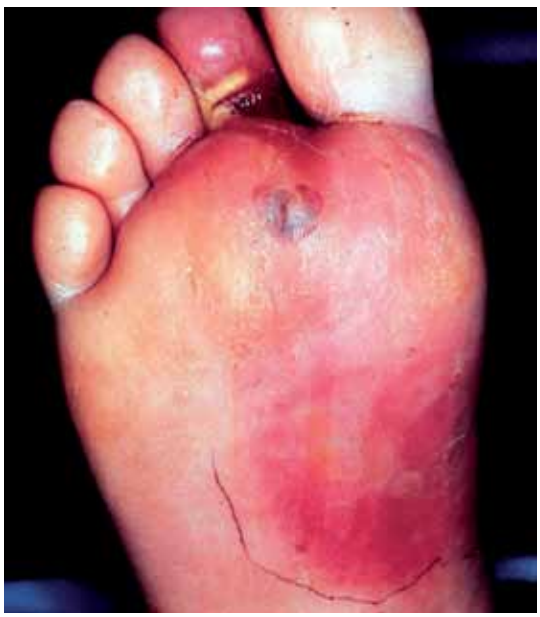
Wound infection is one of the main challenges in wound management; clinicians must take action to control bacteria and reduce the impact of infection on healing outcomes. Traditionally this has relied on a chemical approach with systemic treatments such as antibiotics and antimicrobial dressings aimed at eliminating bacterial colonies. However, with greater understanding of the relationship between the wound environment and colonizing microbes, and in particular the role that endotoxins released by dead and damaged bacteria may have in prolonging the inflammatory response, it is becoming clear that these methods may have less desirable implications for wound healing outcomes. It may therefore be time to re-evaluate and refine this approach. This supplement looks at some of the issues in the current approaches to the problem and identifies how dialkylcarbamoylchloride (DACC) technology can be used to control bioburden through the irreversible binding and deactivation of bacteria and fungi in the wound, without releasing cell debris and endotoxins into the wound bed or the need to use potentially toxic and resistance-inducing chemicals. *Box 1* provides some DACC facts which explains why the technology the technology is so effective.

What is the problem?

Wound infection complicates treatment and impedes the healing process by damaging tissue, reducing wound strength and inducing an undesirable inflammatory response (Wright et al, 1998; Yin et al, 1999; Percival and Bowler, 2004). Increased bacteria within the wound increase the requirements for oxygen and nutrients. In addition, bacteria can secrete harmful chemicals, which can lead to vasoconstriction, decreased blood flow to the wound (Warriner and Burrell, 2005) and cause systemic toxicity (White et al, 2001). Even at lower levels, the development of a critically colo-

Fig 1: Spreading infection in a diabetic foot



nized wound state is a significant factor in delayed wound healing (Warriner and Burrell, 2005), increasing health-care costs and results in poor patient outcomes and quality of life (Derbyshire, 2010b). Therefore, controlling or preventing infections and optimizing the potential for healing by maintaining an ideal wound environment remains central to good wound care (Schultz et al, 2003; World Union of Wound Healing Societies (WUWHS), 2008) and can yield significant cost savings (Zhan and Miller, 2003).

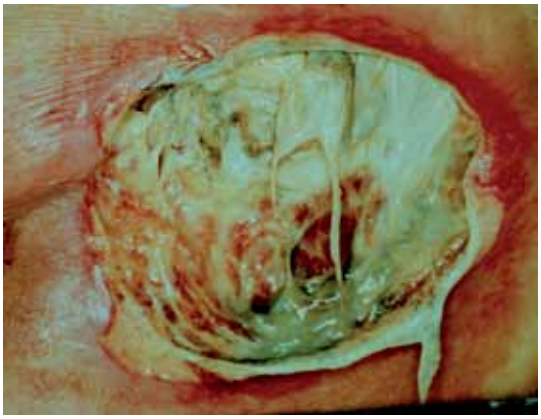
Traditional approaches to bacterial control: antibiotics

The presence of spreading infection is potentially life and/or limb threatening and so requires aggressive treatment. Individuals demonstrating clinical signs of systemic infection (*Figure 1*) should have blood cultures taken and appropriate systemic antibiotic therapy should be implemented immediately (Bowler et al, 2001; European Wound Management Association (EWMA), 2006; WUWHS, 2008).

Antibiotics are administered orally, parenterally and in some cases, topically. Most reduce bacterial numbers by targeting bacterial functions or growth processes (Calderon and Sabundayo, 2007). They have a relatively narrow band of effectiveness, with particular antibiotics being needed to treat specific species or strains of bacteria. However, there are problems with their use:

- Systemic antibiotics treat the whole patient, not just the wound. Therefore, they can affect normal flora, leading to unpleasant side effects and systemic complications such as *Clostridium difficile* (*C.difficile*) infections
- They require an adequate blood supply to reach the point of infection and so may be ineffective in treating wounds with high amounts of debris or in patients with underlying arterial disease (*Figure 2*)
- Antibiotic resistance is a serious problem (White et al, 2001). Widespread, indiscriminate use of antibiotics is a major factor in the emergence of drug-resistant bacteria (Easterbrook, 1998; WUWHS, 2008) which has reduced the treatment options for many systemic infections. New antibiotic options are urgently needed, but no new antibiotic preparations are in development; this is a potential time-bomb for both emerging nations and the developed world (Tacconelli et al, 2009)
- Topical antibiotics can provoke delayed hypersensitivity reactions (Zaki et al, 1994)

Figure 2: Large necrotic pressure ulcer



- Systemic antibiotics have limited effect on biofilm colonies (Marr et al, 1997; Moss et al, 1990; Costerton and Stewart, 2001).

Topical antimicrobials

Antibiotics are not normally recommended for wounds that only show signs of local infection (Bowler et al, 2001). Instead, recent guidelines on the management of wound infection (EWMA, 2006; WUWHS, 2008) have suggested that topical antimicrobial dressings may help reduce bacterial load (bioburden) and may be indicated as an adjunct to antibiotic use. Products incorporating iodine, silver, honey and polyhexamethylene biguanide (PHMB) are considered by many to be the first line of treatment in the management of local bioburden, particularly in chronic wound care. They have advantages over systemic antibiotics in many situations (Lawrence, 1998; Sibbald et al, 2001; White et al, 2001; Cooper, 2004). However, their use needs to be targeted to wounds displaying signs of high bacterial load and they should be used for limited time periods (Bowler et al, 2001; EWMA, 2006; Best Practice Statement, 2010). These recommendations have been

Box 1. DACC FACTS

- DACC binds hydrophobic micro-organisms quickly including MRSA, *P. aeruginosa* and *C. Difficile*, reducing harmful microbial load
- Binds bacterial toxins preventing further damage to the wound bed
- Bacteria are irreversibly bound to the dressing
- There is no upper binding capacity so single dressings are effective until nursing protocols require they are changed
- The regime is safe to use for prolonged periods as no chemicals are donated into the wound
- DACC can be used on babies, children, during pregnancy and breast feeding and patients sensitized to silver, iodine or other chemical agents

developed following concerns over their widespread misuse and the significant pressure this places on healthcare budgets. Further concern has been raised over the role that bacterial debris in the wound may have in producing a chronic inflammatory state detrimental to wound repair. The significance of this will be discussed later. There are a number of different forms of traditional topical antimicrobials products available.

Silver dressings

Silver-based products have been shown to have multiple effects on bacterial function and replication (Thurman and Gerba, 1989; Russell and Hugo, 1994) and have been successfully used in burns and in general wound care (Klasen 2000a, 2000b, Demling and De Santi, 2001; Armstrong, 2002; Clarke, 2003), with skin discolouration (argyria) and irritation being the only visible side effects (White, 2002). However, the various antimicrobial properties of silver ultimately lead to bacterial cell death and breakdown. In addition, questions have been raised over the long-term use of these dressings, especially in infants (Denyer, 2009) with concern about silver toxicity and the systemic uptake and deposition of silver in organs such as the liver and kidney (Wan et al, 1991; Parsons et al, 2005; Burd et al, 2007; Denyer, 2009; Wang et al, 2009). Currently, little is known of the long-term consequences of this for patient safety. In addition, there are fears over the emergence of silver resistance, (Percival et al, 2005; Loh et al, 2009) and cost-effectiveness (Bergin and Wraight, 2006; Michaels et al, 2009; Chaby et al, 2007). Yet in the UK, silver dressings represent one in seven of all wound dressing prescriptions (Iheanado, 2010), with high cost implications.

Iodine

Iodine-based products have been used in wound care for many years. Like all antiseptics, iodine simultaneously affects multiple sites in microbial cells. These changes affect the structure and function of both bacterial enzymes and structural proteins. Following exposure to iodine, changes in the bacterial cell walls, membranes and cytoplasm result in cell disruption, rapid death, (Gottardi, 1983) and the exposure of debris in the tissues (Schreier et al, 1997; Cooper, 2007).

Cooper (2007) indicates that not all iodine-based products are the same and the chemical interaction between the carrier and the wound environment alters the availability of the element and therefore its effect. Some forms of iodine are unstable and there have been questions regarding toxicity to host tissues and the ensuing effect on patient comfort (Kramer, 1999; Wilson et al, 2005). Providone-iodine is not as effective as some other biocides in eradicating *S. epidermis* within clinically-occurring biofilms, (Presterl et al, 2007) but cadexomer iodine provides enough iodine for biofilm suppression without causing significant host damage (Akiyama et al, 2004; Rhoads et al, 2008).

Polyhexamethylene biguanide (PHMB)

PHMB is a synthetic polymer that is structurally similar to the body's own antimicrobial peptides (AMPs). These similarities mean that PHMB can enter bacterial cell membranes and kill bacteria in a similar way to AMPs (Moore and Gray, 2007). PHMB is thought to adhere to and disrupt target cell membranes, causing them to leak potassium and other cellular components (Davies et al, 1968; Davies and Field, 1969; Broxton et al, 1984; Yasuda et al, 2003), resulting in bacterial cell death. There is also evidence that PHMB binds to bacterial DNA (Allen et al, 2004), damaging or inactivating them. PHMB therefore disrupts the bacteria causing their death and can result in the release of cell content and debris into the wound.

Honey

Honey has been used in wound care for thousands of years, but in recent times there has been resurgence in interest in honey-based wound care products for the management of wound infection (White, 2002), though the exact effect of honey on bacteria remains unclear. Honey does restrict the access of water to bacteria and other organisms (Molan, 2001), however, this effect is lessened as the honey becomes diluted by wound exudate (Molan, 1999). One other antimicrobial property is the generation of hydrogen peroxide which is slowly released as the honey is diluted by exudate (Molan and Betts, 2004). Some honeys, particularly Leptospermum (Manuka honey), retain their bactericidal properties even without the presence of hydrogen peroxide (Cooper et al, 2002a; 2002b). Research has identified that in Manuka honey this is attributable to the compound methylglyoxal (Adams et al, 2008; Mavric et al, 2008) which appears to interrupt the cell division of *S. aureus* and damages the cell membrane of gram-negative bacteria (Henriques et al, 2009). The antibacterial proper-

Table 1. Antimicrobial interventions

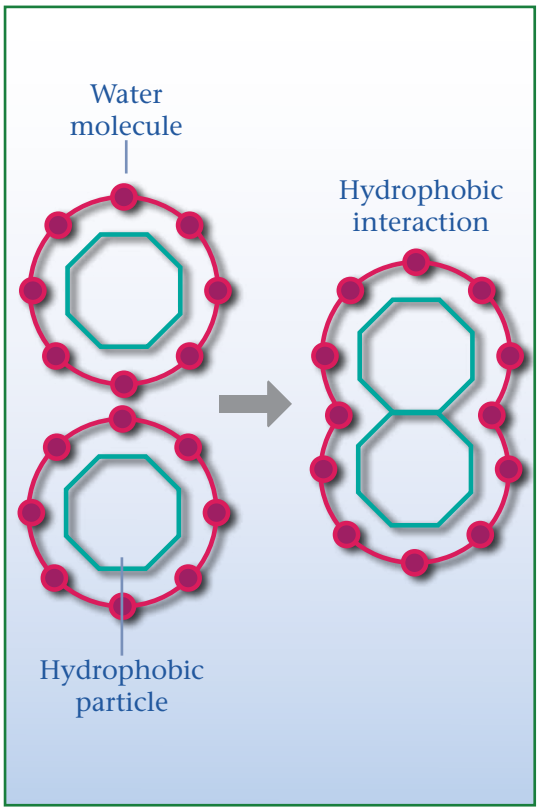
	Systemic antibiotics	Topical antibiotics	Topical antimicrobial solutions	Topical traditional 'antimicrobial' dressings	DACC antimicrobial dressings
Action	Administered orally, intramuscularly or intravenously and delivered via the bloodstream to the whole body Target bacterial cell wall or membrane interfering with essential bacterial enzymes (bactericidal) Or, target protein synthesis (bacteriostatic)	Applied directly to the wound bed Target bacterial cell wall or membrane interfering with essential bacterial enzymes (bactericidal) Or, target protein synthesis (bacteriostatic)	Applied directly to the wound and surrounding tissues (bactericidal)	Applied directly to the wound bed. Action varies according to specific active ingredient. Some affect cell wall function, others disrupts nucleic function and DNA replication (bactericidal)	Applied directly to the wound bed Irreversibly binds bacteria by the process of hydrophobic interaction Bound microorganisms are unable to replicate Prevents the release of toxins
Advantages	Do not require changes to wound care regimes Effective in controlling specific bacterial strains	Effective in controlling specific bacterial strains Only target the wound area avoiding systemic side effects	Wide range of action against bacteria, bacterial spores, fungi and some viruses Easily available (several listed on Drug Tariff)	Have a wide range of action against bacteria, bacterial spores, fungi and some viruses Available in a variety of formats - products may have multiple dressing actions and indications	Available in a variety of formats to suit most wounds Contains no toxic chemicals No systemic absorption Does not kill bacteria or leave debris in the wound Bound bacteria removed at each dressing change May be safely used for wound prophylaxis Binds wide variety of microorganisms including fungi
Disadvantages	Species-specific action No effect on fungi or viruses Affects normal flora as well as wound bioburden May adversely affect bacterial balance in colonized but stable wounds leading to pathogenic species proliferation May induce allergic reaction May induce side effects and systemic complications. May be ineffective in wounds with high necrotic burden or arterial insufficiency Can select for strains with resistance Limited effect on biofilm colonies Leave bacterial debris and endotoxins in the wound	Species-specific action No effect on fungi or viruses May adversely affect bacterial balance in colonized but stable wounds leading to pathogenic species proliferation Can select for strains with resistance Can provoke delayed hypersensitivity reactions Limited effect on biofilm colonies Leave bacterial debris and endotoxins in the wound	Can provoke delayed hypersensitivity reactions Very short-term effect Require repeated applications to invoke any benefit Some have potential for systemic absorption Leave bacterial debris and endotoxins in the wound	Some can provoke delayed hypersensitivity reactions May interfere with thyroid activity (Iodine) May be absorbed systemically and be deposited in organs with unknown long-term effect Leaves bacterial debris in the wound	Binding may be compromised if the dressing comes into contact with oil-based emollients
Overall effect	Bacteriocidal with debris left in wound	Bacteriocidal with debris left in wound	Bacteriocidal with debris left in wound	Bacteriocidal with debris left in wound	Bacteriostatic with removal of bacteria at dressing change No cell debris

ties of honey therefore appear to affect the cellular activity of bacteria but these properties vary according to its source. Ultimately, all honey-based products leave bacterial debris within the wound.

The problem of bioburden

As can be seen, the traditional interpretation of 'antimicrobial' is to assume biocidal action; that is the ability of a chemical to kill bacteria. But what negative effect might the death of bacteria within the wound have on the wound healing cascade? The destruction of bacteria reduces the level of toxins they produce. However, their death results in the release of endotoxins from within each cell and the dumping of cell debris leading to further inflammatory events. Neutrophils and macrophages are essential to health; they target and destroy bacteria by engulfing them (phagocytosis) and breaking them down with lyosomal enzymes. They also play a key role in growth factor production. However, neutrophils can also have a negative effect on wound healing; high levels become highly destructive (Hallett, 2003; Sansonerri, 2006; Friedl and Weigelin, 2008) with breakdown of growth factors, damage to extracellular matrix proteins (Diegelmann and Evans, 2004; Dovi et al, 2004) and production of a hypoxic wound environment (Hopf and Rollins, 2007). This chemically signals further neutrophil recruitment. This spiralling inflammatory state can cause tissue breakdown and the production of a chronic wound. It can also herald systemic damage, even septic shock (Cooper, 2002). Therefore, effective wound management should seek to avoid causing a prolonged inflammatory state. Treatment modalities that reduce wound bacterial numbers and proliferation rates without inducing bacterial death and the release of these toxins may be beneficial to long-term wound health. Wysocki (2002) claims that the capacity of a dressing to absorb and retain (i.e. sequester) bacteria is an important function, particularly in chronic wound management. However, few dressings — mainly Hydrofiber and alginates — sequester bacteria into the dressing material, and then only as a mechanical by-product of their mode of action. However, if the binding of bacteria could be more effectively facilitated as a primary dressing function by using naturally-occurring processes, it would offer clinicians a safer method of managing bioburden.

Figure 3: The principle of hydrophobic interaction



What is the solution?

The principle of hydrophobic interaction is a key mechanism for bacterial attachment. In order for invading pathogens to initiate an infection, they need to adhere to underlying damaged tissues (Wadström et al, 1990; Ofek and Doyle, 1994). Doyle (2000) showed there is a clear relationship between hydrophobicity and infection. Microbes attach to exposed proteins in a wound by hydrophobic and charge interactions and with receptor-like cell surface proteins called hydrophobins (Wessels, 1997). Hydrophobic (lacking an affinity for water molecules) interactions take place when cells expressing cell-surface hydrophobicity (CSH) come into contact with each other in an aqueous environment. This causes the molecules to 'stick' (Hjertén and Wadström, 1990) and expel the water molecules (Hjertén and Wadström, 1990; Curtis et al, 2002) between them. In this way, they clump together, held by the surrounding water molecules (*Figure 3*).

Common wound pathogens, including anaerobes have been shown to express hydrophobicity, with the majority expressing high or moderate CSH (Ljungh and Wadström, 1995; Doyle, 2000; Ljungh et al, 1985; Ljungh et al, 1986; Cowan et al,

1992). This enables them to 'stick' to hydrophobic proteins in the wound. Binding to the wound bed appears to protect them from host defence mechanisms. They then produce enzymes and toxins, enabling them to spread rapidly within and degrade the tissues to obtain nutrients (initiating the signs of infection) or to inactivate host defence mechanisms. The expression of hydrophobicity is therefore an important mechanism of microbial attachment (Doyle, 2000). However, strains of the same species may vary in their CSH (Eriksson et al, 1989). The expression of increased hydrophobicity by bacteria is often a reaction to stress conditions such as starvation and adverse environmental factors. These conditions may exist in many chronic wounds where there may be a shortage of nutrients and oxygen (Ljungh and Wadström, 1995) owing to poor tissue perfusion or competition from other bacterial species. These conditions may also affect the bacterial growth phase, leading to some bacteria forming spores. These spores may express a higher CSH than dormant cells (Ahimou et al, 2001). This is probably a general property of bacterial spores, which are much more resilient than planktonic bacterial forms to environmental challenges such as lack of moisture and chemical attack (including many antiseptics), making their control and eradication more problematic.

As wound bacteria have hydrophobic characteristics, a dressing that is highly hydrophobic is able to physically bind bacteria to the dressing fibres enabling them to be removed from the wound when the dressing is changed (*Figure 4*). This bacterial binding effect is already well established (Ljungh et al, 2006) and is therefore of particular interest in wound care but is not usually referred to as 'antimicrobial' as the microorganisms are not killed by this interaction. This is an important change of perspective in antimicrobial care thinking and practice; it is now clear that the wound does not need to be charged with chemically-active agents to reduce its microbial load. The clear benefit to this is that there are no risks of cytotoxic reactions, systemic uptake or development of bacterial resistance (Kammerlander et al, 2008).

DACC

DACC is a synthetic, manufactured derivative of a naturally occurring fatty acid which is also found in cobwebs. Historically, cobwebs have been used to treat wound infection (Forrest, 1982). A visual indication is seen as water droplets forming on

Figure 4: Binding of microorganisms to DACC-coated dressings

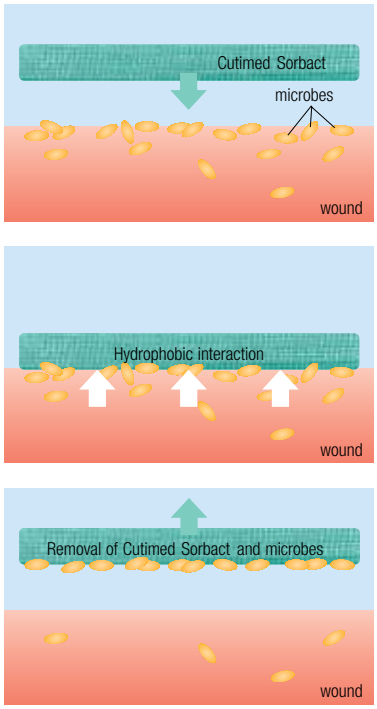


Figure 5: Cutimed Sorbact dressing range

Figure 6: Cutimed Sorbact gel

Figure 7: Binding action of Cutimed Sorbact: Staphylococcus aureus (yellow), Pseudomonas aeruginosa (purple), Enterococcus faecalis (blue), Klebsiella spp (green) bound to the dressing at 4000 times magnification

cobwebs due to their hydrophobic nature. This hydrophobic fatty acid derivative is coated to a dressing material during its manufacture, resulting in a dressing with highly hydrophobic properties. Rather than being physically trapped within the dressing material, microorganisms which also have hydrophobic cell surfaces, when exposed to the material are irreversibly bound to the dressing by hydrophobic interaction. Once bound to the dressing, bacteria and fungi are rendered inert and so are prevented from multiplying or releasing harmful toxins. At each dressing change, microorganisms are then removed from the wound bed along with the dressing, thereby consistently reducing the bacterial load.

Cutimed Sorbact dressings

DACC is a primary component of the bacterial binding wound dressing, Cutimed Sorbact (BSN medical Ltd, Hull). Designed as primary wound contact dressings, these are effective when in close contact with the wound bed in a moist environment. The product is most commonly used as a green acetate swab and a green coloured cotton ribbon (*Figure 5*). Swabs are available in a folded flat sheet format or a 3D ball suitable for packing wounds. For wounds with little or no exudate, an amorphous hydrogel-coated swab is available (Cutimed Sorbact gel) (*Figure 6*) and for wounds with higher levels of exudate, Cutimed Sorbact dressing pads and Cutimed Sorbact Hydroactive with a gel sheet matrix are available. Both have a coated acetate wound contact layer and highly absorbent cores. If required, Cutimed Sorbact swabs may be used in conjunction with secondary absorbent products and devices such as compression bandages. However, care should be taken to avoid contact with oily emollients as this can reduce the effectiveness of the hydrophobic action.

DACC, and specifically the Cutimed Sorbact product range as the pioneer of this technology, offers a real alternative to traditional approaches to bioburden management by using the natural binding characteristics of bacteria and avoiding many of the limitations and drawbacks associated with the alternative antimicrobial interventions (see *Table 1*). Such binding means it is safe to use the dressing for longer than the 2-week period advocated for active topical antimicrobials in the Wounds UK Best Practice Statement. It can also, therefore, safely be used as a prophylaxis. To assess how this is transferable to the clinical situation, it is important to evaluate the product's effectiveness in bacterial binding in the laboratory situation.

Supporting evidence for DACC from laboratory studies

Over more than 30 years, multiple laboratory studies have demonstrated the effective binding of microorganisms to DACC-coated wound dressings. In one of the earliest, Wadström et al (1985) undertook a series of tests which studied the ability of a variety of dressing materials to influence bacterial colonization with three commonly-encountered wound pathogens. The team found that the DACC-coated sample showed greater bacterial uptake than the other products tested (Wadström et al, 1985). In their subsequent *in vivo* experiments, wounds treated with the DACC dressing showed no signs of infection while all the comparators displayed continuous formation of pus.

Bowler et al (1999) showed that there is a correlation between a high hydrophobicity and efficacy of binding. Dressing materials were exposed to different bacterial species over a 4-hour period. Even in this relatively short period the DACC dressing retained significantly more *S. aureus* and *P. aeruginosa* than both the alginate comparators ($p<0.05$). In particular, it was highly effective in binding *P. aeruginosa* (78.6%); this is thought to be related to

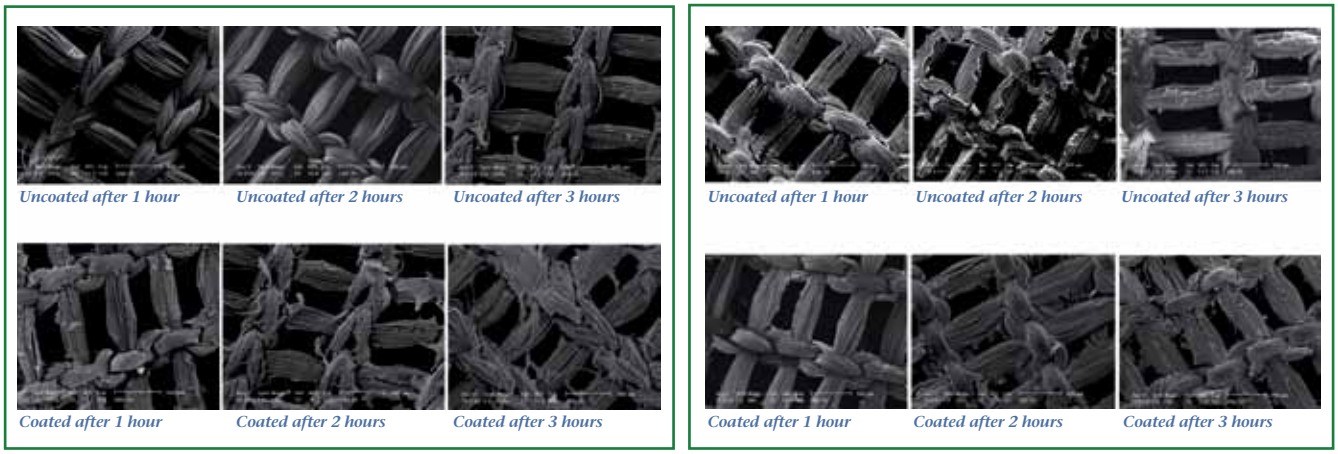


Figure 8: Binding of MRSA and P. aeruginosa biofilms: DACC-coated dressings versus a control

the chemical nature of the bacteria and their relative hydrophobicity. Binding was also measured by Hastings (2009) who reported on laboratory experiment. He clearly demonstrated the ability of bacteria and *C. difficile* spores to bind to the DACC dressing material. Some bacterial binding occurred immediately but increased significantly over prolonged exposure to the material. These findings were supported in a study by Ljungh et al (2006) who demonstrated that a variety of different bacteria and fungi bind to the DACC-coated dressings. The numbers of bound organisms increased over time and in a mixed culture of bacterial and fungal species, microbes co-aggregate and bind to each other as well as to the dressing. They concluded that DACC-coated Cutimed Sorbact dressings can be used on clinical infections because its binding action (*Figure 7*) reduces the microbial load in a wound without the need for antibiotics.

Efficacy against biofilms

The presence and activity of biofilms (colonies of bacteria from different species living together under a microbe-manufactured protective slime film) in chronic wounds have recently been thought to be of clinical significance in wound healing. These biofilms have decreased sensitivity to antimicrobial agents and antibiotic therapy, making them particularly difficult to manage and control (Ceri, et al, 1999; Wolcott and Rhoads, 2008). Cooper and Jenkins (2009) described tests undertaken to determine whether DACC has a potential role to play in biofilm management. Samples of Methicillin-resistant *Staphylococcus aureus* (MRSA) and pseudomonas biofilms were tested with Cutimed Sorbact dressing material. Samples of the DACC-coated product were compared with uncoated dressings. These were examined under an electron microscope after 1, 2 and 3 hours of exposure. The images gave clear evidence that biofilms of MRSA and *P. aeruginosa* bound more extensively to DACC-coated dressings than uncoated product (*Figure 8*). These images were then assessed by blinded volunteers to ensure reliability. This test demonstrated that *in vitro* DACC enhances biofilm binding.

DACC in real-world situations

The laboratory data on the effectiveness of DACC appears compelling. However, laboratory conditions are very different to the relatively uncontrolled environments found in the clinical environment. Since its introduction, DACC-coated Cutimed Sorbact dressings have been successfully used in the management of patients with wound bioburden. The findings of a variety of published comparative and non-comparative clinical trials, along with multiple case-study series, have supported the findings of laboratory studies.

In a study of contaminated, colonized and infected wounds, Von Hallern and Lang (2005) reviewed 418 patients treated with DACC dressings over a 22-month period. The study aimed to determine whether the dressing could reduce the microbial count without adversely affecting the wound healing process and whether it could be removed atraumatically and painlessly. The DACC-coated dressings were applied between a few hours to 48 months after injury and the product was used for between 2–53 days. Bacteriological analyses were

performed on deep-brush wound biopsy swab specimens from 38 patients with chronic and secondary healing wounds which showed decreases in common wound pathogens. In some cases, organisms were identified from the removed dressing materials that were no longer found in the direct deep wound swabs. The investigators concluded that DACC-coated dressing resulted in microbial elimination. This was supported by clinical observations which noted that after 2-8 days there was often a marked decrease in signs of infection. In such cases, the DACC-coated dressings were replaced by simple wound dressings. In patients with arterial insufficiency, to keep the wounds moist, the dressing was used in combination with a hydrogel and an absorbent dressing compress, often up to the end of treatment, otherwise it was discontinued after an average of 10-12 days. DACC therapy was found to be an effective bioburden control method and did not prolong the total duration of healing (Von Hallern and Lang, 2005).

Multicentre study

The efficacy of DACC in managing bacterial burden is further supported in another large clinical study. Kammerlander et al (2008) presented the findings of a 116-patient multicentre study undertaken in four centres across Europe. A wide variety of wounds healing by secondary intention were treated using the wound management protocols of the participating clinics. A standardized evaluation form was used to monitor and record wound progression towards healing and the condition of the surrounding skin. The tolerability of the dressing was determined using a visual analogue scale (VAS) pain assessment tool and documented at every dressing change. Subjects were asked about their subjective impression of the feel of the dressing. Clinicians were also asked to comment on the handling and application of the trial product at each dressing change. These could be rated as 'very good', 'good', 'satisfactory' or 'unsatisfactory'. Additional comments were also encouraged.

Patients with a systemic infection (which showed symptoms in addition to the local wound infection) were treated with antibiotics and clinicians chose the secondary dressing used (e.g hydrogels, alginates, hydrocolloids) depending on the characteristics of the wound.

The patients included in the study had an average age of 63 years (range 27-95 yrs) and had an average wound duration of 6 months (range 1 day-54 months). They were treated for 37 days on average (range 4-134 days) and had an average of 2.5 dressing changes a week. The subjects had a variety of underlying health problems (see *Figure 9*). Wound infection was diagnosed at the start of treatment in 84% of the patients enrolled. One patient developed a wound infection during the course of treatment. There were no incidents of a recurrence of a successfully treated wound infection. Less than 10% of the patients with a wound infection received additional antibiotic treatment. Of the 98 infected wounds at commencement, 79 (81%) were successfully treated at the study end. In seven cases (6%) the wounds remained stagnant, one case (1%) deteriorated, 84 cases (72%) improved and 24 cases (21%) were healed (*Figure 10*).

Figure 9. Underlying health problems in study subjects

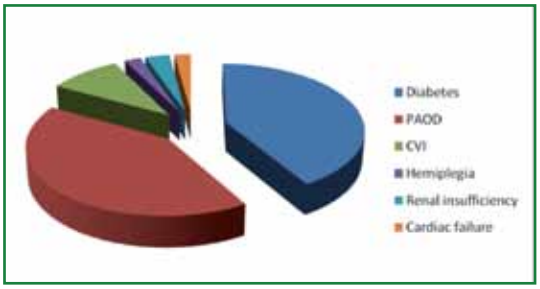


Figure 10. Clinical efficacy of a DACC-coated dressing

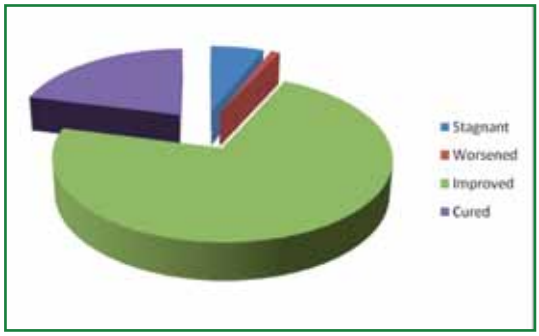


Table 2. Improvement of pain symptoms

Pain score (VAS)	Baseline	End of study
0 (no pain)	52.2%	83.5%
1–3 (mild pain)	33.0%	14.8%
4–6 (moderate pain)	4.3%	0.9%
7–10 (severe pain)	10.4%	0.9%

A comparison of the pain data generated at the beginning and end of treatment revealed a marked improvement in pain symptoms during the course of therapy as shown in *Table 2*.

Patients identified the dressing as pleasant or very pleasant with no pain, burning, skin irritation or negative sensations in 71% of cases, and in only 2% of cases was the dressing identified as 'unpleasant'. Patients did not report any undesirable side effects of the various dressing combinations. Furthermore, the DACC-coated dressing did not cause discolouration in any of the wounds and no product-specific odour was reported. During the study, different presentations of the DACC-coated dressing were selected by clinicians according to individual wound presentation (location, depth, topography, area). In 97% of cases, the dressing change was rated as 'good' or 'very good'. Clinicians were extremely satisfied with the handling characteristics of the dressings.

In this study, the DACC-coated Cutimed Sorbact dressing was tested under the conditions normally found in the participating clinics. It achieved a good level of efficacy in bacterial reduction and management within a programme of wound care. In the study, 81% of wounds showing signs of infection at the start of treatment healed and in 93% of cases there was an improvement in wound healing or a complete cure. The study demonstrated that Cutimed Sorbact can reduce signs of inflammation, reduce or eliminate local infection, achieve subjective tolerability by patients, has a broad compatibility with other wound management products and provides easy product handling during dressing changes. In particular, the consistently easy handling convinced health professionals of the versatility and value of this alternative to current antimicrobial dressings.

Fungal infections

The treatment of foot conditions is a major focus in managing patients with diabetes. Inter-digital skin can provide the ideal environment for bacterial and fungal growth, (Romano et al, 2001; Mayser et al, 2004) and provides a source of infection which can have disastrous consequences to the individual. Traditional management of inter-digital fungal infections has relied on systemic or topical administration of pharmaceutical antifungal agents. This has had varying success and can cause potential adverse reactions (toxicity or allergy) plus the risk of the development of resistance (Martinez-Rossi et al, 2008). Johansson et al (2009) undertook a non-comparative study of the ability of a DACC dressing to manage inter-digital infections in 20 diabetic subjects with confirmed fungal foot infections. All the subjects received 10 daily treatments with the DACC-coated dressing. Following treatment, 75% of the subjects improved or healed, 20% remained unchanged, and only one patient had deteriorated - in this case the fungal skin reaction improved but the ulceration present on the fourth toes had worsened, possibly owing to the use of inappropriate footwear. When asked, 83% of patients said they found the treatment easy or very easy to apply. Laboratory investigations revealed that a variety of fungi were present prior to commencement of the dressing. However, in 55% of subjects no fungi were cultured at the end of the study (Johansson et al, 2009).

Case reports

A number of authors have presented a variety of case studies to demonstrate the outcomes of the use of DACC-coated Cutimed Sorbact dressings in the clinical environment. Although these reports lack the structure and rigour of formalized trials, they are much closer to the clinical scenarios seen by most clinicians and describe effectiveness in clinical practice in treating wounds of differing aetiologies.

Hampton (2007) reports a case series of 21 patients treated with DACC-coated dressings. These patients, with a mean age of 83 years (range 67–96 years), had chronic non-responding wounds of at least 3 months duration with a variety of underlying aetiologies. All the patients were treated for at least 4 weeks; those healing but not yet closed were treated for up to 10 weeks. Dressing change was undertaken as often as considered necessary by the care team. Frequency was determined by individual clinical presentation and patient need.

After 4 weeks treatment, six wounds had healed and 14 were progressing towards healing as characterized by an improvement within the Wound Healing Continuum (Gray et al, 2004). Malodour was identified in 56% of the wounds at the start of treatment, with 28% of wounds being recorded as extremely malodorous and 28% as having some malodour. This was reduced to 0% at the end of the 4-week evaluation. During this time improvements in patients' peri-wound skin condition was observed with the proportion of patients with healthy skin increasing from 38% to 68% by day 28. The Cutimed Sorbact pads absorbed exudate well with no visible maceration or excoriation, and in all patients exu-

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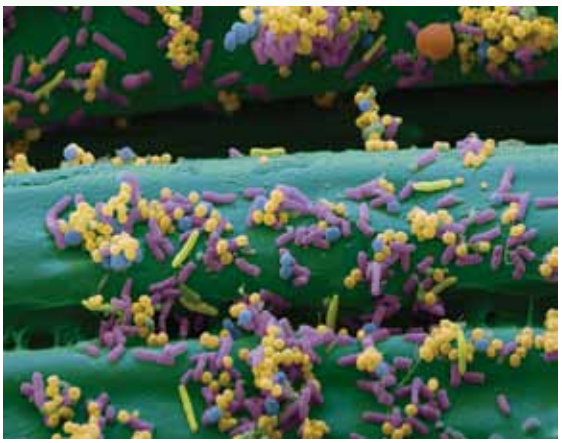
Cutimed® Sorbact®

Infection Management in a New Light



Wound bacteria and fungi binding to Cutimed Sorbact

CUTIMED SORBACT is the only range of dressings coated with **DACC** that can reduce the bacterial load.[1,2]

In a moist environment, bacteria and fungi irreversibly **BINDS** to the dressing helping to kick start the healing process.[1,2]

Dressings can be used **SAFELY** on all patients and on all moist wounds with none of the drawbacks of conventional antimicrobial dressings[1,2]:

- no cytotoxicity
- no bacterial toxin release
- no contraindications

Cutimed Sorbact - a SAFE and innovative antimicrobial dressings range for your Formulary.

For further information please go to:
www.cutimed.com or contact us at
advancedwoundcare.uk@bsnmedical.com

BSN medical

1) Ljungh et al (2006) Using the principle of hydrophobic interaction to bind and remove wound bacteria. Journal of Wound Care, 15 (4): 175 80 2) Powell G (2009) Evaluating Cutimed Sorbact: using a Case Study Approach. British Journal of Nursing 18 (15): S30. S32-S36

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date levels reduced with product use. Consequently, dressing change intervals were also extended from three dressing changes per week (on average) to one or two per week (on average), making the dressing increasingly cost effective. Pain scale scores, which were assessed weekly throughout the study, were significantly reduced possibly owing to a reduction in wound bioburden and inflammation. Clinicians reported that the product was easy to use, with the Cutimed Sorbact dressings staying in place over the wounds between dressing changes and being easy to remove without inducing wound bed trauma.

Powell (2009) reported on a series of case studies using DACC-coated dressings. Three patients with indolent, highly exuding chronic leg ulcers were treated with DACC in combination with compression therapy and absorbent dressings. In each case, odour, exudate and pain reduced significantly shortly after the introduction of the product. In one of these cases, the DACC-coated dressings were safely used for approximately 4 months and kick started healing in a previously recalcitrant wound. Two patients were treated with Cutimed Sorbact following the breakdown of wide excision and surgical closure wounds to correct pilonidal sinus. These wounds are notoriously painful (Stephen-Haynes, 2008) and because of the anatomical position rapidly become heavily colonized with bacteria. In both cases, the application of Cutimed Sorbact ribbon brought about a rapid improvement in wound healing with rapid closure by secondary intention. Finally, Powell reported on the treatment of a patient with multiple fungating lesions to the breast and abdomen. Prior to treatment, these wounds were heavily exuding, sloughy and extremely malodorous. A palliative regime was implemented using daily DACC-coated ribbon and absorbent dressing pads. This was highly successful and within 3 days the offensive odour was no longer a problem. Two weeks of treatment witnessed marked reduction in exudate and an improvement in the surrounding skin condition. By this time, the dressing only needed to be changed twice a week. Powell (2009) concluded that DACC-coated Cutimed Sorbact was an effective treatment when critical colonization and signs of infection are observed and should be considered for wounds at risk of infection because of location and aetiology. The product is now included within the trust's wound care formulary (Bristol Community Health, 2011).

Riley (2010) adopted a case study approach to the treatment of two patients with diabetes and foot wounds. Both patients had serious arterial occlusion and exposed bone in their wounds. Patient 1 was advised that amputation of his lower limb was required and patient 2 had already undergone a forefoot amputation. DACC-coated dressings were introduced to manage the bacterial burden in both patients. Despite the poor vascularization and extent of the two wounds (patient 1 measured 4.5x3.5cm at presentation, and patient 2 was 13.5cm in length) both healed following 20 weeks of treatment with Cutimed Sorbact. During therapy no other form of antimicrobial was required.

Case studies

Haycocks and Chadwick reported the use of Cutimed Sorbact on a diabetic patient with a foot wound (*Figure 11*) and a previous history of recurrent foot ulceration and osteomyelitis (Haycocks et al, 2011). He had developed further ulceration with underlying osteomyelitis in the head and distal three quarters of the first metatarsal. This had been resistant to therapy, so he was taken to theatre for resection of the infected bone. The patient was

Figure 11: Start of Cutimed Sorbact

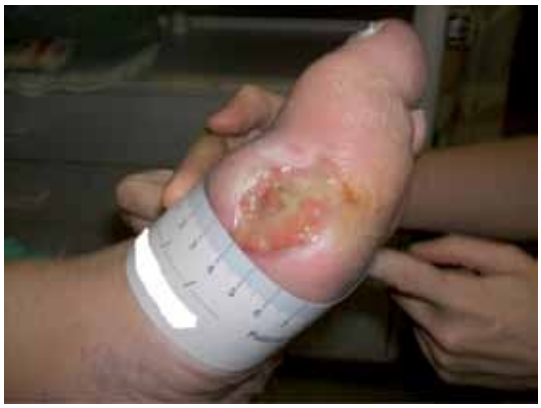


Figure 12: Two weeks after commencing DACC

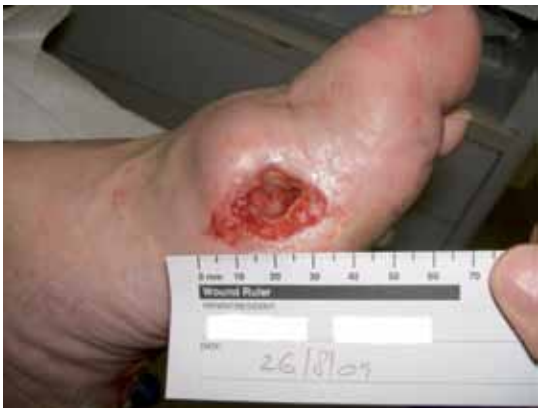
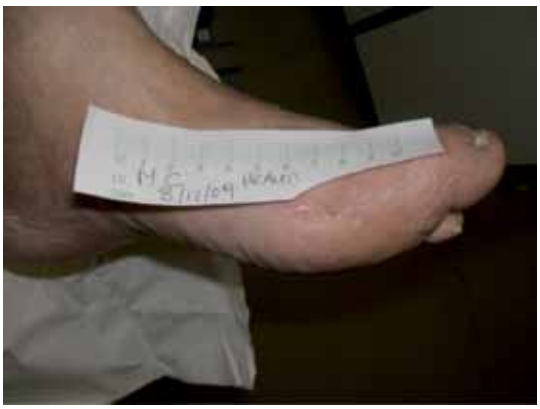


Figure 13: Fifteen weeks later: healed



home treated with intravenous antibiotics and had gentamicin beads inserted into the wound bed.

DACC-coated dressings were initiated 2 weeks postoperatively when the gentamicin beads were removed. The dressing was changed three times a week and he was reviewed at the podiatry clinic weekly. The dressing was found to be easy to use and was said to be comfortable by the patient. Throughout treatment, the wound remained clean and infection free (*Figure 12*), with complete closure being achieved in 15 weeks (*Figure 13*). Haycocks and Chadwick reported that bioburden management is a vitally important consideration in high-risk patients. There were no side effects and no risks of cytotoxic or irritative reactions. The ability of DACC in Cutimed Sorbact to bind effectively to the hydrophobic, pathogenic bacteria and fungi found in many diabetic wounds makes Cutimed Sorbact 'an important, safe and innovative newcomer to the antimicrobial dressing toolkit' (Haycocks et al, 2011).

Derbyshire reported on a series of three case studies (Deryshire, 2010a; b). Two of these involved highly exuding and painful leg ulcers, which had been present for a number of years and one involved a gentleman with extensive solar skin damage to his scalp. All the patients' wounds had been resistant to conventional therapies and had involved considerable nursing intervention and years of dressing prescriptions. In all cases, the use of DACC-coated dressings resulted in reduced bacterial bioburden with resultant reductions in pain, exudation and maceration (*Figure 14* and *Figure 15)*. Due to the chronic nature of these wounds healing is slow but ongoing; however, the author has identified substantial cost savings in the use of Cutimed Sorbact as well as improved wound healing outcomes.

Figure 14: Head prior to application of Cutimed Sorbact dressings

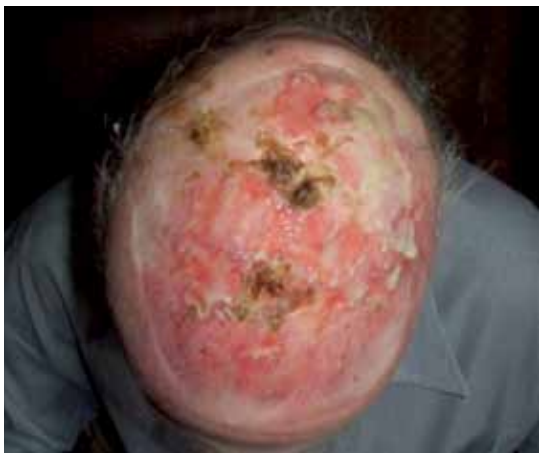
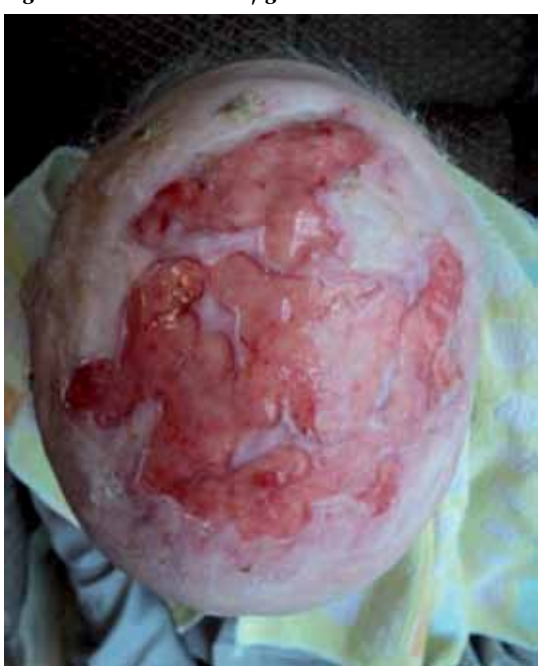


Figure 15: Formation of granulation tissue



New case study evidence

For this supplement, two new case studies are presented which provide further evidence on the efficacy of DACC-coated dressings.

Diabetic foot ulcer

Haycocks and Chadwick present data from a 44-year-old female with type 1 diabetes, renal disease and who had a below-the-knee amputation in 2004 following infection. In 2005, the patient also had a Charcot foot and a kidney/pancreas transplant. The patient developed an ulcer during a holi-

Figure 16: Patient B: On presentation

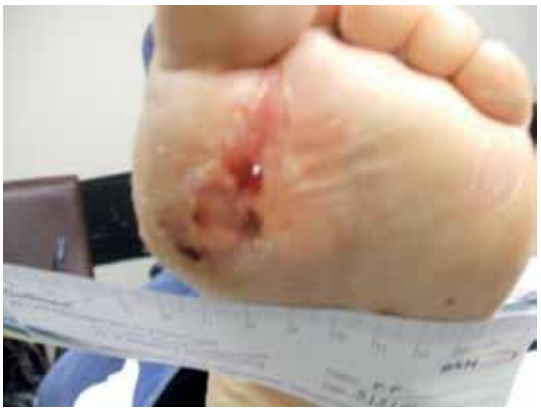


Figure 17: Patient B: 5 day review

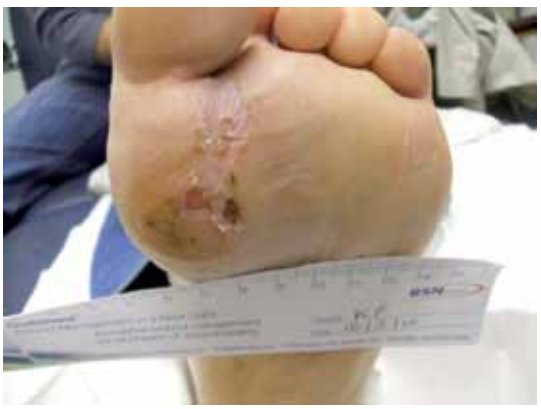
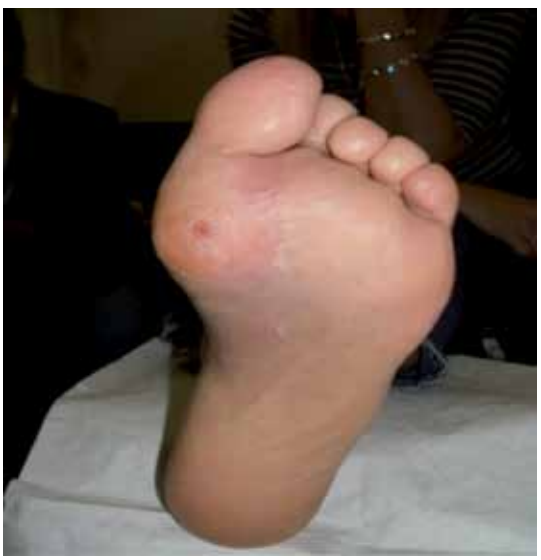


Figure 18: Patient B: Healed



day (*Figure 16*) with antibiotics started. Infection was a concern with this patient as she had a history of infection and was immunosupressed as a result of the transplant and her background diabetes.

On presentation, the wound had been present for a week, it was necrotic with sloughy areas, and measured 40mmx10mmx2mm deep. There were low amounts of exudate and localized cellulitis. On review 5 days after commencement of DACC-coated dressing (*Figure 17*), the cellulitis had resolved and the wound had reduced by 50%. As exudate levels were nil, Cutimed Sorbact gel dressings were commenced. By week 4 there had been a 99% reduction in the wound size. The wound had healed 5 weeks after starting use of DACC-coated dressing (*Figure 18*).

Haycocks and Chadwick's case study shows that DACC is recommended as an alternative antimicrobial option to reduce bacterial load. It is useful for complex, chronic wounds which require longer periods of antimicrobial dressing use than the 2 weeks described in the recent Best Practice Statement (Wounds UK, 2010) as no chemicals are donated into the wound bed from the dressing.

The above case study was provided by Samantha Haycocks, Specialist Podiatrist and Paul Chadwick, Principle Podiatrist, Salford Primary Care Trust, Podiatry and Foot Health, Hope Hospital, Salford

Leg ulcer

Derbyshire presents data from a 93-year-old male who was referred to his district nursing team as he was no longer able to attend the surgery for leg ulcer treatment. Initially, he was seen twice a week by the practice nurse with family members padding the leg daily between visits. Exudate management was poor, with maceration and complaints from family members regarding frequent washing of bedding and clothes. Pain management was uncontrolled, impacting severely on his quality of life. A referral to the hospital to help clear the blockages in his leg and improve circulation was unsuccessful, with the consultant suggesting amputation – an option not favoured by the patient. The patient was accepted onto Derbyshire's caseload for support and to help family members with the dressing regime until surgery was accepted.

The wound was circumferential on the left leg, with extensive areas of slough, some small patches of necrosis and high exudate levels (*Figure 19* and *Figure 20*). Wound swabs showed mixed growth. The previous dressing regime was Aquacel Ag covered with an absorbent secondary dressing. Upon taking the case, the first priority was to manage the exudate levels and eliminate any infection

Figure 19: Initial presentation of wound outer left leg

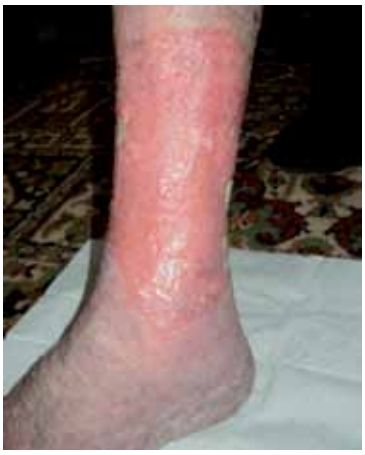


Figure 20: Initial presentation of wound. Rear and inner left leg view

Figure 21: Initial application of Cutimed Sorbact swab

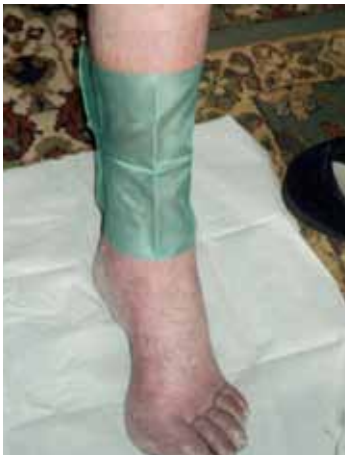


Figure 22: Outer left leg 5 weeks later

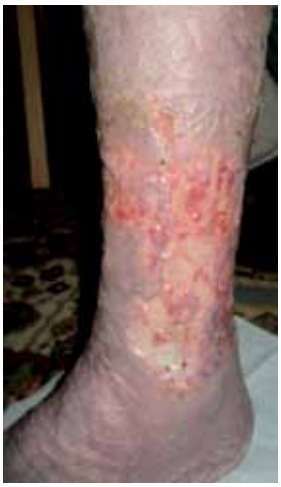


Figure 23: Inner left leg 5 weeks later

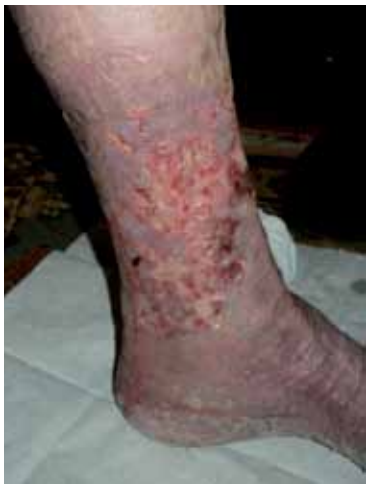


Figure 24: Outer left leg Following 8 weeks of treatment

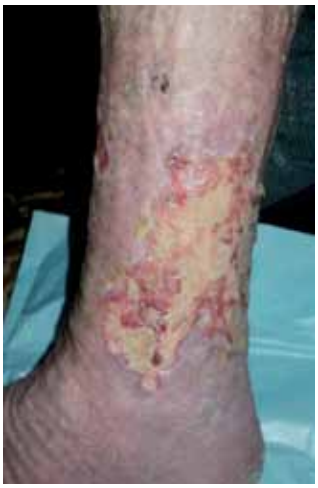
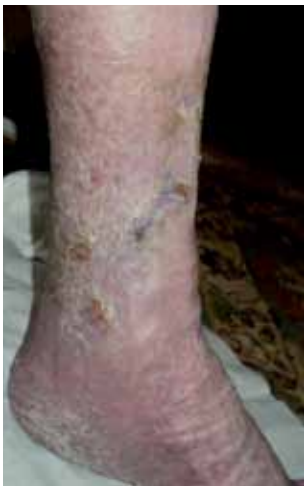


Figure 25: Inner left leg Following 8 weeks of treatment



present. Cutimed Sorbact swabs were commenced (*Figure 21*) with gauze padding and Zetuvit as secondary dressing and secured with a retention bandage. The secondary dressings were changed daily and Cutimed Sorbact every three days.

No emollient was applied as this can reduce the binding efficacy of the dressings.

Five weeks after referral, the wounds were clearly continuing to improve (see *Figure 22* and *Figure 23*), as had pain levels.

The regime of DACC-coated dressings was continued because of the ongoing improvement seen, with the dressings changed twice per week. At this stage, the patient was happy and chose not to proceed with the amputation; a decision that has been vindicated by the visible improvement in his wounds.

Within a further 3 weeks the wounds had substantially improved (*Figure 24* and *Figure 25*). Twice weekly dressing changes continued.

Unfortunately, a month after the photos in *Figure 24* and *Figure 25*, the patient fell from his chair and fractured his hip. He died in hospital 48 hours later. At the post-bereavement visit, the patient's family were keen to share how his quality of life had dramatically improved in recent months owing to the healing progression achieved with DACC-coated dressings.

The above case study was provided by Adam Derbyshire, Senior District Nurse, Advanced Nurse Practitioner and Practice Educator, Albany House Medical Centre, Northampton Primary Care Trust

Conclusion

The effective management of wound bioburden will remain an important feature of wound care for the foreseeable future and the need to find alternative methods of pathogen control via topical antimicrobials, is likely to grow. As clinicians, we need to explore new avenues that work in combination with the body's own defences to bring about optimal wound healing outcomes.

Treatment with a technology that can bind bacteria to it (Catch it) rather than just kill it represents a distinct and new shift from previous held approaches to bioburden management. As has been shown, traditional methods of control that aim to destroy microbes can be problematic as the chemical arsenal developed can turn against the environment it were designed to protect. Patient sensitization, the development of resistant pathogens, cellular and systemic toxicity and the promotion of extended inflammatory response are all very real issues for the wound care clinician. Patient quality of life and cost implications are also significant daily challenges that need to be recognized.

Cutimed Sorbact is the first DACC-coated dressing range that uses the hydrophobic properties inherent in a wide variety of wound pathogens, including multi-resistant organisms and biofilms, to bring about control and the benefit of reduced pain and odour for the patient. By irreversibly binding microbes to its DACC coating, Cutimed Sorbact is able to provide a safe and effective method for clinicians to reduce bacterial load within the wound at every dressing change. By providing bioburden containment and control, DACC technology offers a new treatment for wounds that are either infected or susceptible to the development of infection. This has particular relevance where such infection can be catastrophic, such as in the diabetic foot and pressure ulcer wounds. It enables the balance of wound bioburden to be tipped back in favour of the body's own defence systems without the risk of cytotoxic reactions or development of bacterial resistance. It should therefore always be considered alongside other topical dressings, as a new way of providing antimicrobial care.

Key points

- Most antimicrobial dressings reduce bioburden by killing bacteria
- Effective wound management seeks to avoid eliciting a prolonged inflammatory state, but the chemicals used in most topical antimicrobial dressings can promote inflammation because of the endotoxins released by the ensuing bacterial debris in the wound
- DACC is a hydrophobic fatty acid derivative that is coated to a dressing material during its manufacture, resulting in a dressing with highly hydrophobic properties
- Microorganisms which have naturally hydrophobic surfaces, are irreversibly bound to the dressing's surface by the principle of hydrophobic interaction
- With each dressing change, more bacteria are removed from the wound bed along with the dressing, thereby consistently reducing the bacterial load
- Case studies have shown that a DACC-coated dressing can be used on chronic wounds for prolonged lenths of time with no toxicity to healthy tissue or systemic absorption making them suitable both for episodes of infection and for long-term prophylactic use

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1) Data on file. 2) Laboratory findings on the exudate-handling capabilities of cavity foam and foam-film dressings, Steve Thomas, JWC Vol 19, No 5, May 2010

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