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– Infected Wounds –

A new antibacterial wound dressing without chemically active agent for the care of infected wounds

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A new antibacterial wound dressing without chemically active agent for the care of infected wounds

Wound infections are known to delay healing. They are caused by pathogenic organisms that penetrate into the wound where they multiply and produce toxins which act both on the wound tissue and the body as a whole. Common approaches to management include systemic antibiotic therapy and topical antiseptic treatment. The active agents used for this purpose, however, can also adversely affect endogenous cells. Cutisorb® Sorbact® wound dressing, in contrast, utilizes the principle of hydrophobic interaction and cleanses the wound on a purely physical basis without side effects. This article explains the functional principle and influencing factors.

Wound infections and wound treatment

After colonizing tissue, wound microbes multiply, cause local tissue damage due to release of toxins and enzymes and even spread to the blood stream. The human body has multiple defence mechanisms, such as the complement system, phagocytosis, antimicrobial peptides (defensins) and other structures of the innate immune system. Specific antibodies directed against the colonizing microorganisms may also be mobilized to reduce the number of invaders. Numerous studies have shown that high tissue counts of microorganisms delay wound healing. The infectious dose is significantly decreased in patients with diabetes mellitus, corticosteroid or immunosuppressive therapy or impaired peripheral blood supply. The presence of foreign material such as surgical sutures also lowers the infectious dose.[1] Bacterial counts above 10^5/g tissue in an otherwise healthy tissue have been correlated with poor wound healing and impaired skin graft survival.[2] On the other hand, small numbers of bacteria have been shown to enhance the wound healing process in rodents by stimulating the production of collagen hydroxyproline.[3,4]

Initial wound treatment usually comprises mechanical cleansing with water, buffer solutions or disinfectants to remove bacteria and debris.[5,6] This is of paramount importance since debris impedes wound healing. Systemic administration of antibiotics is indicated if signs of infection are present or if bacteria have spread to the blood stream. Decades of experience have shown that it is often advisable to avoid the use of local antibiotics because of the risk of antibiotic resistance. Significant problems are now being encountered with multiple antibiotic resistant wound pathogens such as *Staphylococcus aureus, Entero-coccus* species, *Pseudomonas aeruginosa* but also coagulase-negative staphylococci and streptococci.[7-9] Besides restricting the use of antibiotics to situations in which they are clearly indicated, there is a need for a new and effective way to treat wound infections. The hydrophobic principle offers an interesting alternative approach to the treatment of infected wounds.

The hydrophobic principle and bacterial hydrophobicity

The laws of nature dictate that a system will always tend towards the lowest energy state possible. When two water repellent (hydrophobic) molecules meet, the surrounding water molecules force them together by forming hydrogen bonds between each other. Although there is no force of attraction between the hydrophobic molecules themselves, they associate by a process called hydrophobic interaction. The expelled water molecules enclose the hydrophobic molecules like a coat and hold them together (Figure 1).[10]

Numerous studies have shown that bacteria, such as *Staphylococcus aureus* and Group A streptococci - both common wound pathogens - and the yeast *Candida albicans,* generally express profound cell surface hydrophobicity (CSH).[11-14] This property is of vital importance for microorganisms since, for instance, it enables them to bind to nutrient substrate surfaces. Several structures which render the cell surface hydrophobic have been identified such as the hair-like protein appendages, fimbriae, of *Escherichia coli* which mediate adhesion to the intestinal wall.[15,16] Further hydrophobic structures are lipoteichoic acid in the cell wall of gram-positive bacteria[13] and proteins on *C. albicans* which have been called „hydrophobins".[17]

Cell surface hydrophobicity (CSH) as a virulence trait

The initial phase of infections of the skin and mucosal surfaces is characterized by microbial adhesion to traumatized tissues mediated by hydrophobic interactions between microbes and host tissue structures or by charge interactions. A simple method of determining CSH is the Salt Aggregation Test, SAT.[18,19] Using the SAT it was shown that growth conditions influence the expression of CSH: culture conditions mimicking a wound, i.e. the presence of serum and incubation in 5 % CO_2 enhanced expression of CSH of *S. aureus,* coagulase-negative staphylococci, *E.*

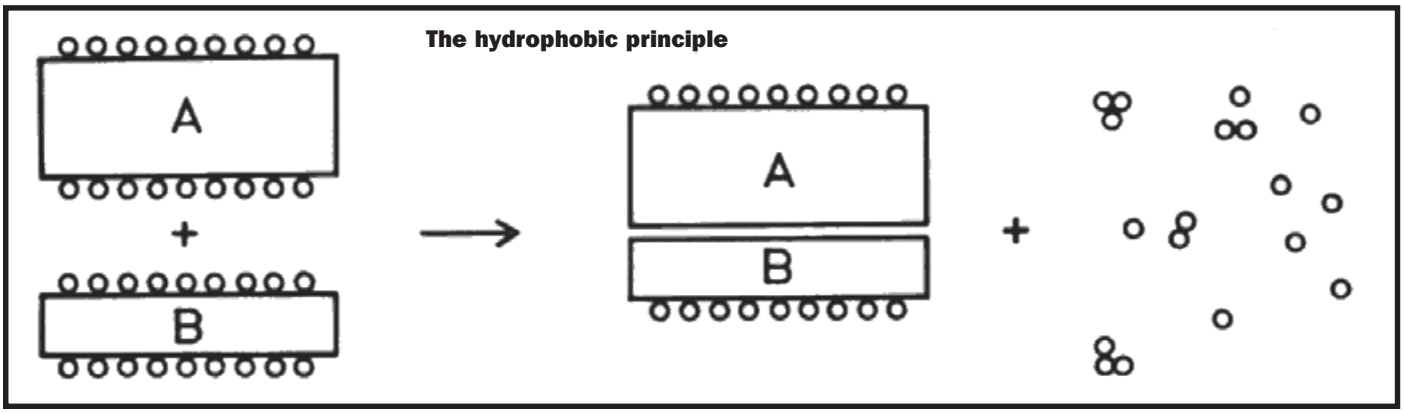

Figure 1
Two hydrophobic molecules, A and B, collide and bind to each other by hydrophobic interaction, causing water molecules (o) to be expelled (modified from[10]).

coli, Enterobacter cloacae, P. aeruginosa, C. albicans and several other bacterial species (Table 1).[21] Growth on nutrient-poor media simulating bacterial „starvation" on the skin promotes expression of molecules which mediate binding of extracellular matrix proteins, ECM, in various microorganisms.[22,23]

The Sorbact® method

Cutisorb® Sorbact® wound dressings make use of the hydrophobic properties of wound pathogens. They are made of acetate or cotton fabric coated with a fatty ester (produced by impregnating with DACC, diacylcarbamoyl chloride), which gives the material strong hydrophobic properties. In the moist environment of an exudating wound, microbes adhere to the dressing fibres by hydrophobic interaction and are removed from the wound when the dressing is changed. During the course of wound treatment, *Cutisorb® Sorbact®* reduces the amount of microorganisms and creates the conditions for the natural healing process to begin.

Figure 2
Microbes binding to *Cutisorb® Sorbact®* at electron microscopic magnification x 2,000: *Staphylococcus aureus* (yellow), *Enterococcus faecalis* (blue), *Pseudomonas aeruginosa* (pink), *Klebsiella* spec. (green), and *Candida albicans* (orange).

Figure 3
Staphylococcus aureus (yellow), *Pseudomonas aeruginosa* (pink) and *Klebsiella* spec. (green) adhering to the hydrophobic surface of *Cutisorb® Sorbact®* fibres (magnification x 15,000).

Table 1
Influence of growth conditions on the expression of cell surface hydrophobicity of three typical wound bacteria measured by the salt aggregation test (SAT) (modified from[21])

Growth conditions	Cell surface hydrophobicity (SAT value)		
	Staphylococcus aureus	*Escherichia coli*	*Pseudomonas aeruginosa*
Blood, O_2	> 2	> 2	> 2
Blood, 5% CO_2	2	2	> 2
Blood + serum, 5% CO_2	1	0,5	1
Hematin, O_2	> 2	2	> 2
Hematin, 5% CO_2	2	2	2
Hematin + serum, 5% CO_2	0,5	0,25	1

A low SAT value corresponds to high cell surface hydrophobicity (CSH). The CSH expression is increased by the presence of serum in the growth medium and by growth in CO_2 atmosphere, which is indicated by lower SAT values.

The effectiveness of this approach has been demonstrated in several studies. This hydrophobic dressing enhanced wound healing in pigs infected with *S. aureus.*[24] A clinical study on infection prevention in newborn umbilical cords showed comparable results to those obtained for disinfection with ethanol/chlorhexidine solution.[25] Wound healing in patients with wound infections caused by various microorganisms as well as the take of skin grafts were also enhanced.[26-28] The use of *Cutisorb® Sorbact®* reduces the number of infective microorganisms to below the level which impairs or prevents the healing process. It does not eliminate all bacteria, but this may in fact be beneficial since small numbers of microorganisms have been shown to stimulate wound healing.[3]

These findings indicate that *Cutisorb® Sorbact®* may represent an alternative to the use of topical antibiotics and antiseptics and consequently reduce the spread of antibiotic resistant organisms.

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