The Effectiveness of a New Antimicrobial Dressing

with Microbinding Action for the Management of Chronic Wounds

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Abstract

The primary aim of this study was to evaluate the effectiveness of a new antimicrobial dressing. This dressing has a broad spectrum of action, no measurable host cytotoxicity, no currently identified allergenicity and no demonstrated risk of bacterial resistance. The study involved a sample of 14 subjects (8 with diabetic foot ulcers, 6 with venous leg ulcers). Dressings were changed up to 3 times a week for the 4-week study duration. The results were promising with respect to wound surface area reduction and pain improvement. This new antimicrobial dressing stalled chronic wounds with signs of increased bacterial burden.

Introduction

Chronic wounds constitute a major financial burden to society, and have a profound effect on quality of life.[1] The underlying causes of wounds need to be addressed as according to Table 1 but, arguably, localized wound infection (often referred to as critical colonization, increased bacterial burden or covert infection) is 1 of the most common challenges in the treatment of healable wounds.[2,3]

With the emergence of bacteria that are resistant to commonly used antibiotics or topical antibiotics, the use of topical non-antibiotic antimicrobial agents has become a sensible option for local wound care and surface bacterial damage.[3,4]

Preferred topical agents should have a broad spectrum of activity, relatively low tissue toxicity, low allergenicity and generally not be used systematically. However, with the advent of a plethora of newer topical antimicrobial agents, clinicians are often confused about when and what antimicrobial agents should be used. Many dressings are impregnated with active ingredients (e.g. silver, iodine, chlorhexidine, honey, gentian violet/methylene blue) that are released into the wound in the presence of wound fluid or exudate. Alternatively, a microbinding dressing can entrap and sequester bacteria in its microarchitecture and ultimately inactivate them.

This trial tested an antimicrobial dressing with microbinding action (Cutimed® Sorbact®; Cutimed,

TABLE 1

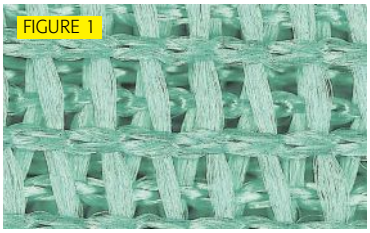
Causes of common chronic ulcers and recommendations for care

Type of chronic ulcer	Cause/aggravating factor	Recommendations for care
Venous leg ulcer	Dermal edema Lipodermatosclerosis associated with venous insufficiency	Compression bandages for healing Compression stockings for maintenance Compression for life (in the absence of arterial disease or other contraindications)
Pressure ulcer	Deep ulcers: Abnormal pressure and shear Superficial ulcers: Friction and moisture Aggravating factors: inactivity, poor nutrition	Relieve, reduce and redistribute pressure Increase activity and mobility Manage incontinence and moisture Reduce shear and friction Optimize nutrition
Diabetic foot ulcer (callus = pressure; blister = friction and shear)	Loss of protective sensation Aggravating factors: infection, ischemia, deformity	Ensure an adequate vascular supply Control infection Redistribute plantar pressure

Boucherville, QC). The dressing is composed of meshed cellulose acetate that reduces the risk of tissue ingrowth and minimizes trauma and pain upon dressing removal. It is available with dressing components, including 1 with an absorbent core to handle moderate to heavy exudation. As a unique feature, the surface of the dressing is coated with a natural fatty acid: dialkyl carbamoyl chloride, which has hydrophobic properties (Figure 1). In the moist environment of an infected wound, microorganisms are attracted to the dressing, where they become immediately and irreversibly bound to it by the hydrophobic interaction (Figures 2 and 3). This antimicrobial dressing can be used in conjunction with other topical agents, providing they do not contain fatty substances (e.g. ointment dressings).

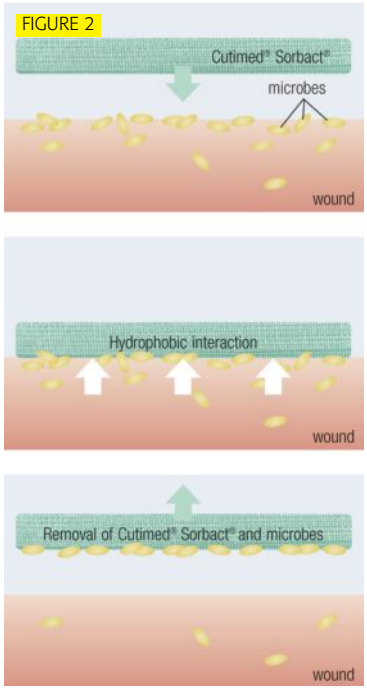
The effectiveness of the antimicrobial dressing with microbinding action has been demonstrated in a number of studies, including a multicentre investigation that involved 116 patients.[5] In addition, its binding capacity has been tested in an in vitro study;[6] within the first 30 seconds the dressing started to bind with *Staphylococcus aureus* and *Pseudomonas aeruginosa*, with increased binding after 10 minutes. Maximal binding was observed at 120 minutes, when 107 out of 108 inoculums had bound to the dressing.

FIGURE 1



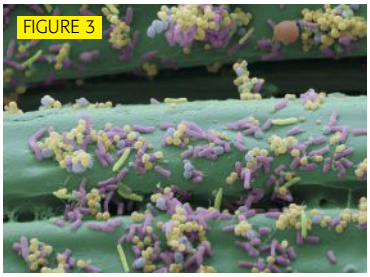
The hydrophobic dressing coating.

FIGURE 2



Hydrophobic interaction: Sequestering bacteria, preventing them from causing further localized tissue damage.

FIGURE 3



Staphylococcus aureus and *Pseudomonas aeruginosa* bound to the dressing.

Description

This clinical study enrolled a total of 16 patients, with 14 completing the study. One patient withdrew consent prior to dressing application and another patient developed an uncontrolled systemic inflammatory process after study entry (necrobiosis lipoidica of the deep dermis), which was unrelated to the local dressing application. The process subsequently evolved into an aggressive deep infection requiring intravenous antibiotics and study discontinuation.

The evaluable subjects were 18–85 years of age (mean 60.8 years), with 13 men and 1 woman. All wounds were chronic (>1 month) and the patients had received treatment of the underlying cause (Table 1), along with local wound care as outlined in the paper by Sibbald and colleagues.[3] Eligibility criteria included an adequate blood supply to heal (ankle brachial pressure index >0.5), no uncontrolled systemic disease and the absence of medication that would prevent healing. Written informed consent was obtained from all participants.

The dressings were changed up to 3 times a week for period of 4 weeks. All subjects were evaluated at weeks 0, 2 and 4 (at the end of the study). Where appropriate, debris within the ulcer was debrided with curette, scissors or scalpel blade. Wound surface areas were estimated by the longest wound length and wound width that were perpendicular to each other. Wound-related pain was evaluated by using an 11-point numeric rating scale. The characteristics of the wound base and surrounding skin were evaluated.

Results

Improved healing was demonstrated in all subjects (Figure 4), except for 4 who had several factors for delayed healing, including complex coexisting diseases and poor adherence to a pressure-offloading device. The cumulative patient total average surface area reduced from 1.74 at visit 1 to 1.15 cm^2 at visit 4 (t=0.998; df 14; p=0.337) (Figure 5). The mean pain level improved from 3 to 2.07, respectively, on a scale of 1–10 (t=1.54; df 14; p=0.145) (Figure 6).

There was no significant difference in the NERDS and STONEES checklist criteria for signs of superficial or deep infection.[7] The dressing was easy to apply and remove. No serious adverse events were reported.

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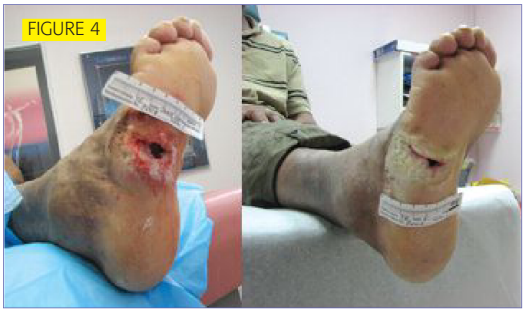
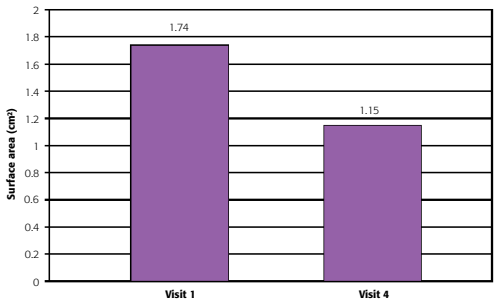
FIGURE 4



Wound improvement between the first visit and week 4.

FIGURE 5



Reduction in surface area between the first visit and week 4.

Conclusions

Persons with chronic wounds often experience stalled wound healing because of local wound-related factors, even after the cause of the wound has been corrected and patient-centred concerns addressed. With adequate debridement and moisture balance achieved, wound healing can stall because of persistent and abnormal inflammation and/or bacterial damage of both the superficial and deep compartments.

One way to neutralize the surface damage is to sequester the bacteria and their related inflammatory mediators. This meshed dressing with bound fatty acids is able to absorb harmful exudate with associated bacteria and inflammatory mediators. In this clinical study there was a trend toward wound surface area reduction over a 4-week period, indicating improvement of the bacterial-related stalled healing response. Pain (which has been associated with wound critical colonization and infection) also improved over time, indicating the dressing neutralized surface inflammation. The ability of the antimicrobial dressing with microbinding action to reduce pain symptoms has also been demonstrated in other studies.[8–10]

The results of this study demonstrate a link between the antimicrobial dressing with microbinding action properties and a tendency to reduced wound surface area and chronic-wound-associated pain.

FIGURE 6

Reduction in surface area between the first visit and week 4.

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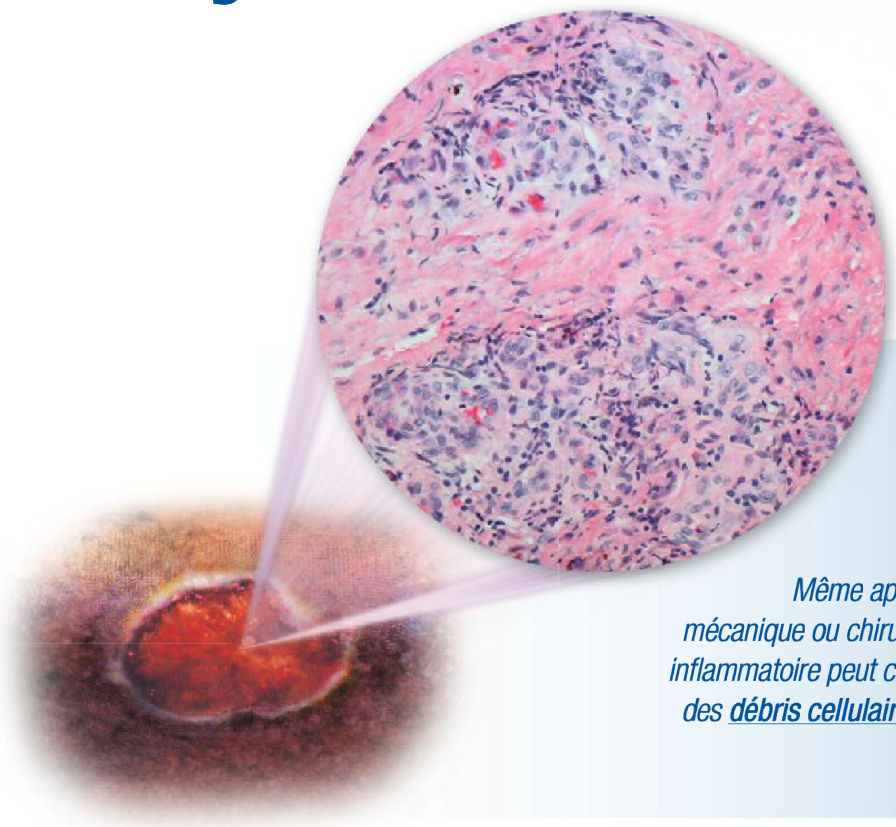

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Occasional slight transient erythema has been noted in surrounding tissue when applied outside the wound. One case of systemic hypersensitivity has been reported after 1 year of treatment with collagenase and cortisone.

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On a noté un érythème occasionnel et léger sur les tissus environnants lorsque l'application de l'onguent dépasse le pourtour de la plaie. Un cas d'hypersensibilité systémique a été rapporté après un an de traitement à la collagénase et à la cortisone.

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DESCRIPTION: Santyl® (collagenase) ointment is a sterile topical enzymatic debriding agent that contains 250 units of collagenase per gram of white petrolatum USP. The enzyme collagenase is derived from the fermentation of *Clostridium histolyticum*. It possesses the unique ability to selectively digest denatured and undenatured collagen that binds necrotic debris to the wound surface.

CLINICAL PHARMACOLOGY: Santyl® (collagenase) possesses the ability to digest insoluble collagen, undenatured and denatured, by peptide bond cleavage, under physiological conditions of pH and temperature. This ability makes it particularly effective in the removal of detritus from dermal lesions, contributing towards the more rapid formation of granulation tissue and subsequent epithelization of dermal ulcers and severely burned areas. Collagen in healthy tissue or in newly formed granulation tissue is not digested.

INDICATIONS: Santyl® (collagenase) is a sterile ointment indicated for the debridement of dermal ulcers or severely burned areas.

CONTRAINDICATIONS: Application is contraindicated in patients who have shown local or systemic hypersensitivity to collagenase.

WARNINGS: Debilitated patients should be closely monitored for systemic bacterial infections because of the theoretical possibility that debriding enzymes may increase the risk of bacteremia.

PRECAUTIONS: The enzyme's optimal pH range is 6 to 8. Significantly lower pH conditions have a definitive adverse effect on the enzyme's activity, and appropriate precautions should be carefully taken. The enzymatic activity is also adversely affected by detergents, hexachlorophene and heavy metal ions such as mercury and silver that are used in some antiseptics and by cobalt, magnesium and manganese. When it is suspected such materials have been used, the site should be carefully cleansed by repeated washings with normal saline before Santyl® (collagenase) ointment is applied. Soaks containing metal ions or acidic solutions such as Burow's solution should be avoided because of the metal ion and low pH. Cleansing materials such as hydrogen peroxide or Dakin's solution followed by sterile normal saline do not interfere with the activity of the enzyme. The ointment should be confined to the area of the lesion in order to avoid the possible risk of irritation or maceration of normal skin; however, the enzyme does not damage newly forming granulation tissue. A slight erythema has been noted occasionally in the surrounding tissue particularly when the enzyme ointment was not confined to the lesion. This can be readily controlled by protecting the healthy skin with a material such as zinc oxide paste. Since the enzyme is a protein, sensitization may develop with prolonged use.

ADVERSE REACTIONS: Although no allergic sensitivity or toxic reactions have been noted in the recorded clinical investigations to date, one case of systemic manifestations of hypersensitivity has been reported in a patient treated for more than one year with a combination of collagenase and cortisone. Irritation, maceration or erythema has been noted where prolonged contact of normal skin with Santyl® (collagenase) ointment has been allowed, either by application of the ointment to areas of normal skin or by excessive application of ointment to the wound crater with subsequent spread to normal skin when dressings are applied. The reported incidence for this type of reaction was 1.8%.

SYMPTOMS AND TREATMENT OF OVERDOSE: Symptoms: To date, the irritation, maceration or erythema reported on prolonged contact of normal skin with Santyl® (collagenase) ointment constitute the only symptoms of overdosage reported. **Treatment:** Santyl® (collagenase) ointment can be rendered inert by the application of Burow's solution USP (pH 3.6 - 4.4) to the treatment site. If this should be necessary, reapplication should be made only with caution.

DOSAGE AND ADMINISTRATION: For external use only. Santyl® (collagenase) ointment should be applied once daily, or more frequently if the dressing becomes soiled (as from incontinence) in the following manner: **(1)** Prior to application the lesions should be gently cleansed with a gauze pad saturated with sterile normal saline, to remove any film and digested material. If a stronger cleansing solution is required, hydrogen peroxide or Dakin's solution may be used, followed by sterile normal saline. **(2)** Whenever infection is present, as evidenced by positive cultures, pus, inflammation or odor, it is desirable to use an appropriate antibacterial agent. Should the infection not respond, therapy with Santyl® (collagenase) ointment should be discontinued until remission of the infection. **(3)** Santyl® (collagenase) ointment should be applied (using a tongue depressor or spatula) directly to deep wounds, or when dealing with shallow wounds, to a non-adherent dressing or film dressing which is then applied to the wound. The wound is covered with an appropriate dressing such as a sterile gauze pad and properly secured. **(4)** Use of an occlusive or semi-occlusive dressing may promote softening of eschar, if present. Alternatively, crosshatching thick eschar with a #11 blade is helpful in speeding up debridement then cleanse with sterile saline. It is also desirable to remove as much loosened detritus as can be done readily with forceps and scissors. **(5)** All excess ointment should be removed each time the dressing is changed. **(6)** Use of Santyl® (collagenase) ointment should be terminated when debridement of necrotic tissue is complete and granulation is well under way.

HOW SUPPLIED: Available in 30 gram tubes of ointment. Sterile until opened. Contains no preservative. Do not store above 25°C.

Product monograph available upon request.

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DESCRIPTION : Santyl® (collagénase) onguent est un agent de débridement topique stérile enzymatique qui renferme 250 unités de collagénase par gramme de pétrolatum blanc U.S.P. L'enzyme collagénase est dérivée de la fermentation de *Clostridium histolyticum* possédant le pouvoir unique de digérer de manière sélective le collagène aussi bien naturel que dénaturé qui lie les fibres nécrosées à la surface de la plaie.

PHARMACOLOGIE CLINIQUE : Santyl® (collagénase) a la capacité de digérer le collagène insoluble, non dénaturé et dénaturé, par clivage de la liaison peptidique à un pH et à une température physiologiques. Cette caractéristique le rend particulièrement efficace dans l'élimination des déchets des lésions dermiques favorisant ainsi la formation du tissu de granulation et l'épithélialisation ultérieure des zones dermiques ulcérées et gravement brûlées. Le collagène des tissus sains ou du nouveau tissu de granulation n'est pas digéré.

INDICATIONS : Santyl® (collagénase) est un onguent stérile indiqué pour le débridement des zones dermiques ulcérées ou gravement brûlées.

CONTRE-INDICATIONS : L'application est contre-indiquée chez les patients ayant présenté une hypersensibilité locale ou systémique à la collagénase.

MISE EN GARDE : Les patients atteints de conditions débilitantes doivent être surveillés étroitement pour éviter la généralisation des infections bactériennes. Les enzymes de débridement augmenteraient le risque de bactériémie.

PRÉCAUTIONS : Le pH optimal de l'enzyme est de 6 à 8. Un pH nettement inférieur à un effet nettement adverse sur l'action de l'enzyme et des précautions appropriées doivent alors être prises. L'action de l'enzyme est également contrariée par les détergents, l'hexachlorophène et les ions de métaux lourds, comme le mercure et l'argent, présents dans certains antiseptiques, et par le cobalt, le magnésium et le manganèse. Quand on soupçonne l'utilisation de ces produits, la zone affectée doit être soigneusement nettoyée par des lavages répétés avec une solution saline avant l'application de l'onguent Santyl® (collagénase). Les bains contenant des ions de métaux ou des solutions acides comme la solution de Burow doivent être évités en raison de l'ion métal et du faible pH. Les solutions nettoyantes comme l'eau oxygénée ou la solution de Dakin suivie d'une solution stérile saline n'entravent pas l'action de l'enzyme. L'application de l'onguent doit se limiter à la zone affectée pour éviter le risque possible d'irritation ou de macération de la peau saine. Cependant, l'enzyme n'altère pas le nouveau tissu de granulation. Un érythème bénin dans le tissu avoisinant pourrait se produire. Cela peut facilement être évité en protégeant la peau saine avec un produit comme de la pâte d'oxyde de zinc. Compte tenu de la nature protéique de l'enzyme présent dans le médicament, son emploi prolongé pourrait amener une sensibilisation.

EFFETS SECONDAIRES : Bien qu'aucune sensibilité allergique ni réaction toxique n'aient été notées à ce jour dans les compte rendus d'études, on a signalé un cas de manifestations systémiques d'hypersensibilité chez un patient traité pendant plus d'un an avec une association de collagénase et de cortisone. On a noté de l'irritation, de la macération ou de l'érythème dans le cas de contact prolongé de la peau normale avec l'onguent Santyl® (collagénase), soit par application de l'onguent sur les régions normales de la peau, soit par application excessive de l'onguent dans le cratère de la plaie, permettant à celui-ci de s'étendre à la peau normale lors de l'application des pansements. L'incidence signalée de ce type de réaction était de 1,8%.

SYMPTÔMES ET TRAITEMENT DU SURDOSAGE: Symptômes: Jusqu'ici, l'irritation, la macération ou l'érythème signalés en cas de contact prolongé de la peau saine avec l'onguent Santyl® (collagénase) représentent les seuls symptômes signalés de surdosage. **Traitement :** On peut rendre l'onguent Santyl® (collagénase) inerte en appliquant la solution de Burow U.S.P. (pH 3.6-4.4) sur la plaie. La réapplication du produit, si elle est considérée nécessaire, ne se fera qu'avec prudence.

POSOLOGIE ET ADMINISTRATION : Pour usage externe seulement. L'onguent Santyl® (collagénase) doit être appliqué une fois par jour ou plus fréquemment si le pansement se souille (à cause d'incontinence par exemple) de la façon suivante : **(1)** Avant application, les lésions doivent être nettoyées doucement avec une gaze saturée d'une solution stérile saline normale pour enlever toute pellicule et toute matière digérée. Si l'on a besoin d'une solution nettoyante plus puissante, on peut utiliser de l'eau oxygénée ou de la solution de Dakin suivie de solution stérile saline normale. **(2)** En cas d'infection, révélée par la présence de cultures positives, de pus, d'une inflammation ou d'une odeur, il serait souhaitable d'employer un agent antibactérien approprié. Il faut interrompre le traitement au Santyl® (collagénase) jusqu'à rémission de l'infection, si l'infection ne se résorbe pas. **(3)** Appliquer Santyl® (collagénase) directement sur les blessures profondes à l'aide d'un abaisse-langue ou d'une spatule. Pour les plaies superficielles, appliquer l'onguent sur une compresse non adhérente ou un pansement transparent à être déposée sur la plaie; puis recouvrir d'un pansement approprié tel une compresse de gaze stérile adéquatement retenue. **(4)** L'utilisation d'un pansement occlusif ou semi-occlusif peut favoriser le ramollissement de l'escarre, le cas échéant. Ou, si l'on hachure une escarre épaisse à l'aide d'une lame numéro 11, on peut accélérer le débridement. Nettoyer alors avec une solution saline stérile. Il est également souhaitable d'enlever autant de détritus lâches que possible à l'aide de pinces et de ciseaux. **(5)** Enlever tout excès d'onguent à chaque renouvellement du pansement. **(6)** Arrêter les applications de l'onguent Santyl® (collagénase) dès que le tissu nécrosé est suffisamment débridé et que le bourgeonnement est bien entamé.

PRÉSENTATION : Disponible en tubes de 30 grammes d'onguent. Stérile dans l'emballage non ouvert. Aucun agent de conservation. Ne pas entreposer au-dessus de 25°C.

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