

# Clinical efficacy of dressings for treatment of heavily exuding chronic wounds

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**Abstract:** The treatment of chronic ulcers is a complex issue and presents an increasing problem for caregivers everywhere. This is especially true in Germany, where more than 4 million chronic wounds are treated each year. Therapeutic decisions must be patient-centered and reflect wound etiology, localization, and healing status. The practice of using the same wound dressing during the entire healing period is no longer reasonable. Instead, multiple types of dressings may be needed for a single wound over its healing trajectory. Selection of the most appropriate dressing should be based on wound phase, depth, signs of infection, and level of exudate. Moisture balance is critical in wound care; dryness will hamper epithelial cell migration while excessive generation of fluid causes maceration at the wound margins. Hence, exudate management is a key issue in chronic wound therapy, particularly given that exudate from chronic wounds has a composition different from that of acute wound fluid. Several studies have shown that exudates from non-healing wounds contain significantly elevated levels of protease activity, increased formation of free radicals, and abundant amounts of proinflammatory cytokines, while concentrations of growth factors and protease inhibitors are markedly decreased. Application of dressings that remove and sequester excess amounts of wound fluid may not only help in restoring the correct balance of moisture, but also support the wound healing process by preventing tissue deterioration caused by abundant protease activity. Several types of dressings, such as hydrogels, hydrocolloids, alginates, hydrofibers, foams, and superabsorbent dressings, are reviewed here and evaluated with regard to their efficacy for highly exuding wounds.

**Keywords:** chronic wounds, exuding, dressings, clinical efficacy

## Introduction

More than 4 million chronic wounds are treated in Germany every year.<sup>1</sup> These include venous ulcers, ischemic wounds (mainly of atherosclerotic origin) diabetic foot ulcers, and decubitus ulcers.<sup>2</sup> This clearly indicates that most chronic wounds are the expression of an underlying physiological condition or systemic disease, such as chronic venous insufficiency, increased mechanical pressure, and vascular, nervous, or metabolic tissue damage.<sup>1</sup> Malignancy, persistent infection, poor primary treatment, and immunologic disease might also delay wound healing.<sup>1,3</sup> Hence, a thorough medical history and physical examination are essential to every patient evaluation.<sup>4</sup> Therefore, the patient history should include: a description of how the wound occurred; any past history of wounds, including previous diagnoses and response to treatment; family history of chronic wounds and/or poor healing; any dermatologic condition that predisposes to ulceration; assessment of edema; consideration of pain; evaluation of systemic conditions that may predispose to wound development or poor healing, including

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human immunodeficiency virus/acquired immune deficiency syndrome, sickle cell anemia, Raynaud's syndrome, rheumatologic disease, chemotherapy, anemia, weight loss, viral hepatitis, illicit drug use, transfusions, or neurologic disorders; previous hospitalizations and surgeries; and all systemic and topical medications used by the patient.<sup>4</sup> Consequently, the treatment of chronic ulcers is complex. After thorough wound diagnostics, therapy of the underlying disease (eg, metabolic control of diabetes, prevention of chronic venous insufficiency, slowing the progression of atherosclerosis) and general systemic treatment (eg, anticoagulant treatment, systemic antibiotic therapy, anti-inflammatory therapy, treatment inhibiting immunologic reactions, vasodilator treatment, rheology-improving drugs, and protein, vitamin, and microelement supplements) have to be initiated before local therapy can be effective.<sup>2</sup>

## Preparation of the wound bed

Therapeutic decision-making must be patient-centered, and treatment goals need to reflect this,<sup>5</sup> such as achieving a clean wound for skin grafting, containing odor or exudates, and reducing pain to improve the patient's social life, or maintaining a clean wound bed to place the patient in another setting to continue care. Of course, the clinician's overall aim is wound healing and prevention of relapses. Therefore, local wound treatment includes adequate preparation of the wound bed to accelerate endogenous healing and/or to increase the efficacy of other therapeutic interventions. Supported by the European Wound Management Association, Schultz et al developed a strategy called TIME, which suggests methods for reinforcing the natural healing process while eliminating aggressive and proliferation-inhibiting activities.<sup>6</sup> The acronym stands for Tissue management (wound cleansing), Infection or inflammation (reduction of infection/inflammation), Moisture imbalance (humidification), and Edge of the wound (epithelialization support). According to this concept, non-viable or deficient tissue needs to be debrided (by autolytic, surgical, enzymatic, mechanical, or biological means) to remove the defective matrix and cell debris that is impairing healing. This restores the wound base as well as functional extracellular matrix proteins and clinically leads to a viable wound base. Chronic wounds are characterized by prolonged inflammation and often high bacterial counts. The subsequent increase in inflammatory cytokines and abundant protease activity markedly reduces growth factor activity and tissue regeneration. Hence, infected foci have to be removed, and antimicrobials, anti-inflammatory agents, and protease inhibitors need to be administered to reduce bacterial counts and control

inflammation. Moisture balance is critical in wound care, ie, while excessive fluid generation causes maceration at the wound margins, dryness will hamper the migration of epithelial cells. Application of moisture-balancing dressings, negative pressure wound therapy (NPWT), or other fluid removal methods, as well as compression, will control disproportionate release of exudate, avoid maceration, reduce edema, and prevent wound desiccation to enable optimal conditions for cell migration and proliferation. Clinically, the wound edge may be non-advancing or "undermined" as a result of non-responsive wound cells or abnormal protease activity. Debridement, skin grafting, biological agents, and other adjunctive treatment options have been suggested as corrective therapies to increase cellular migration and restoration of an appropriate protease profile. It is imperative that clinicians reassess wound status during dressing changes so that appropriate interventions can be implemented.<sup>5</sup>

## Moist wound healing and exudate management

Wound exudate, which is essentially blood depleted of most of its red cells and platelets, is a key component in all stages of wound healing, irrigating the wound and keeping it moist, supplying nutrients, and providing favorable conditions for cell migration and proliferation.<sup>3</sup> The wound tissue should be neither too dry nor too wet but physiologically humid.<sup>7</sup> Since the work by Winter showing increased healing rates of wounds covered with occlusive dressings,<sup>8</sup> the use of dressings that keep the wound moist has also been associated with improved cosmetic outcomes, less pain, lower infection rates, and decreased overall health care costs.<sup>7</sup> If the wound tissues are adequately moist with minimal exudate production, then the applied dressing should maintain the tissue hydration status without too much absorption as this would desiccate the wound. Such moisture-retentive dressings retain moisture or have a low enough moisture vapor transmission rate (less than 35 g/m<sup>2</sup>/hour in partial thickness wounds), permitting moist wound healing.<sup>9</sup> However, to clinically translate moist wound healing into practice remains difficult due to the lack of unified operational definitions.<sup>10</sup> For instance, achieving or maintaining a moist environment does not mean that a wound should be covered in fluid. In certain conditions, such as venous leg ulcers or wounds associated with lymphedema, excessive amounts of exudate are present and may lead to complications, such as maceration of the surrounding skin, skin breakdown, wound enlargement, and increased pain.<sup>11,12</sup> Increased exudate levels may further be the result of liquefying hard and eschar-like necrotic tissue producing a wet and sloughy mass.<sup>3</sup>

Exudate from chronic wounds has a composition that is considerably different from that of acute wound fluid. Several studies have shown that exudates from non-healing wounds contain significantly elevated levels of proteases, such as matrix metalloproteinases (MMPs) and polymorphonuclear (PMN) elastase.<sup>13–16</sup> The continuous excessive production of proteases in chronic wounds and their persistently elevated activity lead to considerably reduced amounts of growth factors and proteinase inhibitors<sup>17</sup> as well as successive degradation of extracellular matrix.<sup>18</sup> So far, neutrophil-derived protease elastase and MMPs have received most of the attention in studies of chronic wounds. Acting in concert, they are capable of degrading every known constituent of soft connective tissue.<sup>19</sup> MMPs mainly destroy extracellular matrix, and several studies showed that high levels of active MMP-9 are associated with lower wound closure rates.<sup>20–22</sup> In addition, several MMPs are able to deactivate  $\alpha_1$ -protease inhibitor and  $\alpha_2$ -macroglobulin, which are two important inhibitors of the serine protease elastase. High MMP levels in wounds can therefore indirectly lead to increased amounts of this protease. Elastase, which mainly degrades elastin (a major constituent of elastic fibers), has been held responsible for degrading essential growth factors, such as platelet-derived growth factor and transforming growth factor-beta.<sup>15</sup> In turn, elastase also leads to degradation of fibronectin, and the degradation products of fibronectin stimulate the release of MMPs.<sup>23,24</sup> Effective management of exudate is therefore of crucial importance in chronic wound care. Application of dressings that remove and sequester excess amounts of wound fluid may not only help in restoring the right balance of moisture, but may also prevent the destruction of tissue by abundant protease activity to support the wound healing process.

The wound care market is consistently growing and new products seem to be introduced daily. Traditional classification into passive, inactive, and active dressings<sup>25</sup> has therefore become difficult. Dressings can be categorized according to the materials used and important product groups according to the S3 guideline of the German Wound Healing Society as follows: pads (gauze/synthetic fibers), films, alginates, hydrogels, hydrocolloids, foams, microfibers, hydrofibers, and polyacrylates. Additionally, the guideline differentiates combinatory products (eg, foam dressings with hydrofibers).<sup>26</sup>

## Products suitable for exuding wounds

There is no one dressing that is suitable for all wound types, so one of the most challenging aspects of wound

care is choosing the right dressing, and that choice remains controversial. However, clear requirements for an optimal wound dressing exist, ie, it should: keep the wound moist; absorb excess exudate without leakage; eliminate dead space (a nidus for infection); protect against infection and external factors; provide optimal pH, thermoregulation, gas exchange, and humidity; cooperate with the wound healing process; avoid trauma and pain during dressing changes; minimize formation of scar tissue; have minimal toxicity to the surrounding skin/wound base and not be allergenic; be easy to use and comfortable for the patient; and have extended wear time, which directly translates into cost-effectiveness.<sup>2,27</sup>

Daily clinical routine shows that selection of dressing is based on local practice and empirical experience. That is not surprising, given that there are no large randomized controlled trials with definite conclusions (level A trials) for any type of dressing. Available systematic reviews on dressings for management of chronic wounds yield only weak levels of evidence for clinical efficacy,<sup>28</sup> and no dressing can be recommended over another based on the results of these studies.<sup>1,26</sup> In the absence of “hard” scientific evidence, selection of dressing should be guided by the type of wound, its appearance, the amount of exudate, the patient’s pain levels, and/or signs of infection.<sup>1,29</sup>

Dressings can be classified in different ways, according to their physical form (eg, gel, film, foam), chemical composition (eg, carboxymethylcellulose, alginate, collagen), material description (eg, hydrogel, hydrofiber, hydrocolloid), or function (debriding, antibacterial, absorbent). Unfortunately, these terms are often used interchangeably when it comes to sorting dressings into categories, eg, hydrogels and hydrocolloids (material description) are put alongside alginates (chemical composition), foams (physical form), and absorbent dressings (displaying function). However, it is difficult to avoid such pitfalls, given that some of these terms, eg, hydrogel, have become so popular that they are inseparable from daily practice. Who cares that most (but not all) of the hydrogels are polyacrylamide derivatives? Others, like hydrocolloids, may only be suitably rated according to their material description because their chemical composition would be too complex to describe and make them difficult to place. Where should they be put if one considers that they are a blend of polyurethane and swellable particles made from carboxymethylcellulose, pectin, or gelatin? All in all, different aspects and approaches have to be considered when classifying dressings. With regard to wound bed preparation and managing moisture imbalances, a suitable way would be sorting them according to their ability to manage exudate,

employing the most commonly used and easiest product descriptions (Figure 1).

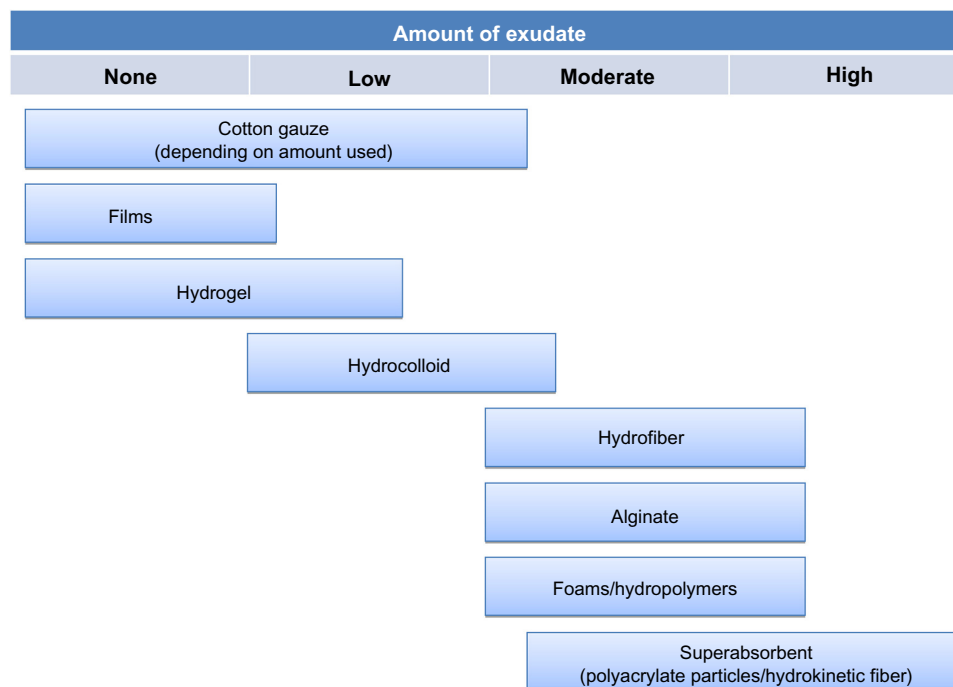
Gauze is often used in the clinical setting because it is inexpensive and easily accessible. However, there are also several limitations to its use, including its easy dehydration, its adherence, and often painful removal, as well as fiber shedding and poor barrier qualities.<sup>30,31</sup> In the light of modern, active, and more suitable wound dressings, gauze is not recommended for management of chronic wounds. In these settings, films also may rather serve as secondary dressings than being placed directly on a chronic wound. Films are excellent for superficial lacerations and wounds producing small amounts of exudate like thin burn wounds, venous catheter sites, or split-thickness skin graft donor sites.<sup>32</sup> However, fluid will accumulate underneath the film, and skin stripping could occur due to tight adherence and exertion of shearing forces.

Hydrogels consist of approximately 95% water inside a cross-linked hydrophilic polymer network comprised of polyacrylamides, polyethylene, polyvinyl alcohol, or others.<sup>32</sup> Therefore, hydrogels are able to rehydrate a dry desiccated wound, promoting healing by creating a moist wound environment.<sup>5</sup> These dressings are very comfortable to wear and provide a cool and soothing feeling to the patient accompanied by a certain amount of pain relief.<sup>4,32</sup> However, although being slightly absorbent, use of hydrogels on wounds that are already highly moist may result in overhydration and cause maceration of the surrounding skin.

Hydrocolloids contain hydrophilic colloidal particles made from carboxymethyl cellulose, pectin, or gelatin in an adhesive polyurethane matrix.<sup>5</sup> They provide an occlusive environment as well as absorption and maintain a moist milieu.<sup>4</sup> It is thought that they promote debridement of slough and necrosis and can reduce pain through hydration of nerve endings, similar to hydrogels.<sup>27</sup> Hydrocolloids are best used in low to moderately exuding wounds because large amounts of exudate may cause peri-wound maceration and off-floating of the dressing. An offensive odor, skin stripping,<sup>4,32</sup> and allergic reactions<sup>12,33,34</sup> have also been reported.

Whenever the wound is generating moderate to high levels of exudate, an absorbent dressing is required. Absorbent dressings include alginates, hydrofibers, foams, and hydropolymers, as well as superabsorbent materials, which have a high capacity to capture and hold fluid. They require fewer dressing changes within a set period compared with dressings that are not as absorbent, so enable undisturbed wound healing and less time spent on the part of the caregiver (eg, nurse or clinician).<sup>7</sup>

Alginates are derived from seaweed and can be manufactured into highly absorptive, fibrous dressings that can hold up 10–20 times their own dry weight and in and have hemostatic properties.<sup>35</sup> They form a soft gel upon contact with wound fluid, thereby effectively filling dead space and maintaining a moist wound environment.<sup>35</sup> Because alginates require moisture to function, they are not indicated for dry



**Figure 1** Recommendations for types of wound dressing according to amount of exudate present.

wounds or wounds covered with hard necrotic tissue unless they are first moistened with saline.<sup>4</sup> Furthermore, care has to be taken to cut alginates into the shape of the wound bed and avoid overlaps with normal skin, as peri-wound maceration may occur because of the distribution of fluid over the entire surface of the alginate dressing (“lateral wicking”).<sup>4</sup>

Hydrofiber dressings are moisture retention dressings that consist of sodium carboxymethyl cellulose fibers. Like alginates, they gel on contact with wound fluid, which promotes a moist wound healing environment yet retains wound exudates by vertical absorption. This has been found to be beneficial for both caregivers and patients in terms of ease of application and removal, as well as reduction of pain at dressing changes.<sup>28,36</sup>

Foam dressings were introduced into clinical practice to facilitate maintenance of a moist wound environment and thermal insulation.<sup>4</sup> These products offered important advantages over traditional gauze dressings because they did not shed particles/fibers or adhere to the wound bed.<sup>5</sup> Foams can manage light to moderate amounts of exudate,<sup>4,12</sup> and might even be recommended for highly exuding wounds if combined with certain hydropolymers.<sup>11,35</sup> The latter are thought to be appropriate for wounds with excess slough and to support autolytic debridement.<sup>35</sup> However, foam dressings cannot prevent surrounding skin maceration in heavily exuding wounds, and formation of a malodorous discharge has been reported.<sup>4</sup>

Polyacrylate-containing wound dressings, also known as superabsorbent polymer (SAP)-containing dressings or just superabsorbent dressings, have been shown to be particularly effective in the treatment of heavily exuding wounds.<sup>37–39</sup> The majority of SAPs is of synthetic/petrochemical origin, and most commonly acrylic acid (and its sodium or potassium salts) and acrylamide are used as the starting monomers. There are also polysaccharide-based and poly(amino acid)-based SAPs available that have different properties when compared with synthetic SAPs.<sup>40</sup> Other dressings feature hydrokinetic fibers produced from hydrophilic cellulose and sodium polyacrylate particles using a special mechanical process without bonding agents or adhesives.<sup>41</sup> Some studies suggest that such dressings also enhance selective autolytic debridement by attracting and retaining proteins from necrotic tissue as well as toxins and bacteria.<sup>38</sup>

Direct and impartial comparison of ultimate performance of these dressing types (Table 1) *in vivo* is difficult. Not only are clinical studies and randomized controlled trials lacking, but trials are also complicated by the fact that no two patients are identical. Hence, standard tests for characterizing wound

dressings are usually employed to determine properties and potential functioning. These tests include fluid handling properties, absorbency, moisture vapor permeability, fluid affinity, water uptake, and gelling properties.<sup>3</sup> Absorbency (the dressing’s ability to absorb and retain wound fluid) and moisture vapor loss (evaporation of water through the outer dressing surface) are crucial mechanisms in the management of exudate. They are measured as the fluid handling capacity of a dressing. Exudate handling properties are also related to the gel-forming characteristics of alginate, hydrofiber, and hydrocolloid dressings.<sup>3</sup> Studies showed that these might differ widely in a product group despite comparable chemical precursors.<sup>42,43</sup> For instance, gelling of alginates depends on the ratio of homopolymeric M-regions (consisting of D-mannuronic acid) and G-blocks (formed by L-guluronic acid) in the polysaccharide.<sup>44,45</sup> Although the tests for water vapor permeability, fluid affinity, and water uptake are a meaningful way of characterizing the different dressings, they are mainly based on the structure rather than the performance of the dressings. As a result, they are limited in their ability to predict the performance of a dressing *in vivo*.<sup>3</sup> Recently, first efforts have been undertaken to visualize the fluid distribution in dressings with and without compression.<sup>46</sup> For the “maceration test”, dressings were applied to an artificial wound in a tissue substitute comprised of 10% (w/v) gelatin and 10% (w/v) milk powder (Figure 2A). Evaluation of fluid uptake and distribution in the dressings was done by video recording. In addition, loss of shape of the dressings, maximal fluid uptake, and time to maceration could be determined. In this study, the alginate dressing showed less fluid uptake when compared with carboxymethyl cellulose and cellulose/cellulose-ethylsulfonate dressings (Figure 2B). Moreover, it was found that these dressings shrank during fluid uptake, while no loss of surface coverage was observed for the alginate (Figure 2C). The results are still limited to a small number of hydroactive dressings, but they may present a valuable tool for evaluation of dressing performance, fluid handling, and maceration risk under conditions mimicking the clinical situation more closely.

## Antimicrobial treatment

Infected wounds are commonly painful, display hypersensitivity, and produce odor, resulting in increased discomfort and inconvenience for the patient.<sup>47</sup> Further, infected wounds are regularly associated with high exudate levels, increasing the number of dressing changes required, the amount of nursing time involved, and consequently the overall cost to the health care provider. In this regard, chronic wounds, which

**Table 1** Summary of wound dressings for exuding wounds, important characteristics, and available products

Type	Description	Indications	Advantages	Disadvantages	Comments	Examples*
Hydrocolloid	Various forms: powders, pastes, films, even foams made from CMC, gelatin, or pectins in a carrier material; occlusive or semi-occlusive dressings adhere to the wound when dry but become non-adherent as soon as they are swollen	Light to moderate exudate usable for autolytic debridement of necrotic tissue	Occlusive, retains moisture; absorbent painless removal protects wound from contamination when worn long term	May cause allergies; adheres to dry skin; skin stripping insufficient adherence to moist skin (sweating, incontinence); opaque fluid trapping malodorous discharge gel can be confused with slough or pus in wound	Can be left in place up for 7 days or until fluid leaks; not for infected or necrotic wounds; not for highly exuding wounds; not to be used over sinus tracts; gel needs to be completely removed during dressing changes	Alloplaque Askina Biofilm Askina Hydro Comfeel Plus DracoHydro Hydrocoll Nobacolloid Nu-Derm Restore Suprasorb H Tegasorb Traumasive Ultec Pro Varihesive E Aqualcel Aqualcel Extra#
Hydrofiber	CMC as band or sheets is hydrophilic and forms a transparent gel upon contact with wound fluid	Moderate to heavy exudate; bacteria-infected or neglected wounds; deep wounds (packaging)	Highly absorbent; moisture-retentive; observation of the wound through gel; possible minimal lateral wicking	Fibrous debris (seldom); might desiccate wound; requires secondary dressing; rapid fluid uptake might cause pain	Can be left in place for up to 7 days or until fluid leaks; peri-wound skin should be dried before application; sheets should overlap with wound edge; dressing shrinkage possible	Alginate M Curasorb DracoAlign Kaltostat Melisorb NobaAlgin SeaSorb Soft Sorbalgon Sorbsan Suprasorb A# Tegagen Trionic Algosteril Urgosorb Allelyn# Askina Heel Curafoam 3M Foam DracoFoam Mepilex# PermaFoam
Alginate	Polysaccharide derived from brown algae; sodium and calcium salts of alginic acid used in form of sheets and fibers; may be combined with CMC	Suitable for moderate to high exudate; wet ulcers with abundance of fibrin; infected wounds, deep wounds (packaging); bleeding	Highly absorbent; forms gel on wound (moist environment, pain relief); packaging possible; hemostatic; low allergenic potential	Fibrous debris; lateral wicking; no thermoregulation; requires secondary dressing; gel can be confused with slough or pus in wound	Can be left in place until saturated with exudate; must be fitted to the wound bed; not to be placed on the peri-wound skin; not to be used over exposed bone or tendon	Alginate M Curasorb DracoAlign Kaltostat Melisorb NobaAlgin SeaSorb Soft Sorbalgon Sorbsan Suprasorb A# Tegagen Trionic Algosteril Urgosorb Allelyn# Askina Heel Curafoam 3M Foam DracoFoam Mepilex# PermaFoam
Foam/ hydropolymer	Mostly hydrophilic polyurethane; also polymethyl-siloxane; do not expand during fluid uptake; may be coated Expand during fluid uptake; also contains polyacrylates	Light to moderate exudate; support autolytic debridement; can be used at terminal stage of clearing process	Absorbent occlusive thermal insulation; no adherence to wound bed; pain-free removal protects wound padding effect	Opaque exudate may pool; malodorous discharge; traumatic removal after desiccation; does not prevent peri-wound maceration if exudate level is too high; not able to manage viscous exudate (clogs pores)	Change every 1–3 days according exudate level; not for infected wounds; not to be used over dry necrosis	Alginate M Curasorb DracoAlign Kaltostat Melisorb NobaAlgin SeaSorb Soft Sorbalgon Sorbsan Suprasorb A# Tegagen Trionic Algosteril Urgosorb Allelyn# Askina Heel Curafoam 3M Foam DracoFoam Mepilex# PermaFoam

Sterisorb					
Suprasorb P					
Biatain					
Cutinova hydro					
Hydrafoam					
Tielle					
DryMax Extra		Cannot be cut to fit the wound;	High fluid retention also	Moderate to high	Polyacrylate particles
Eclipse	Can be left in place until saturated with exudate	rapid fluid uptake may cause pain	under compression;	exudate; infected	or cellulose fibers with
KerryMax			reduction of odor	wounds; wounds in	incorporated polyacrylate
Mextra Superabsorbent			protection of the peri-	need of cleaning	
Sachet S			wound skin; prevention		
TenderWet <sup>#</sup>			of maceration; long		
Viiwasorb <sup>#</sup>			wear time; reduced		
Zetuvit Plus			dressing changes		

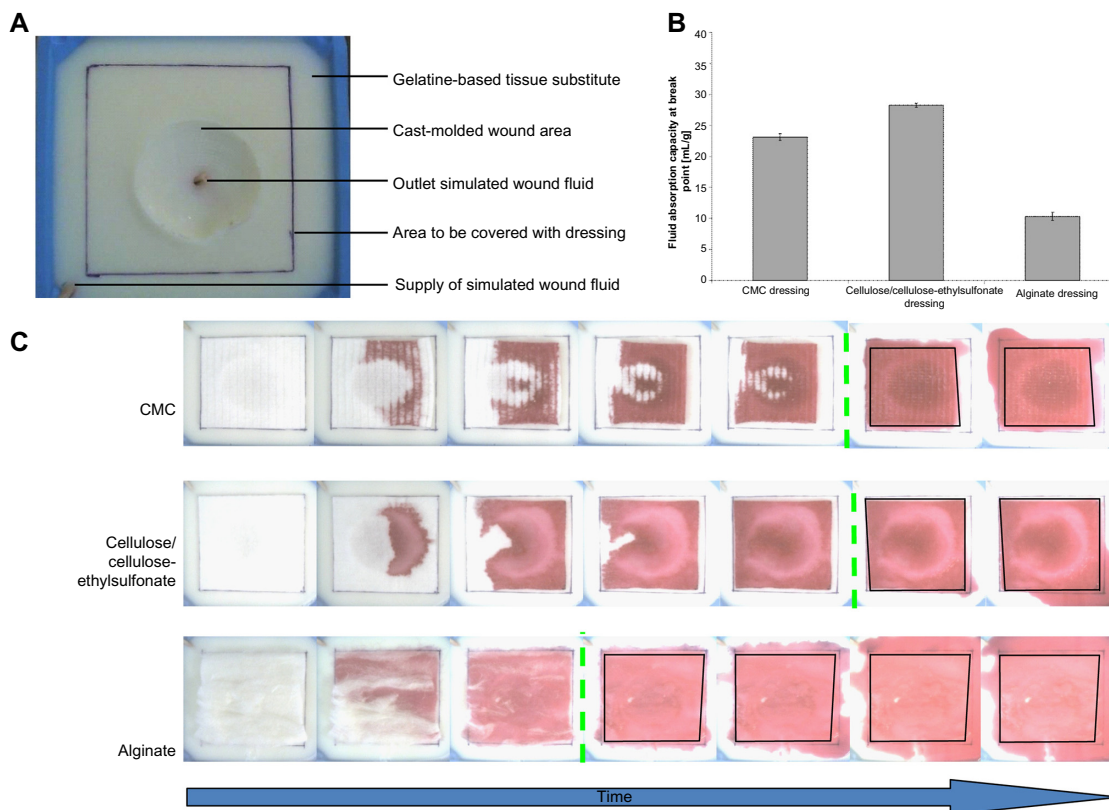
**Notes:** <sup>#</sup>Note that the description given here is based on experience, make sure to check the manufacturers' description for complete information; <sup>#</sup>dressings mainly used in the wound clinic at the Department of Dermatology, University Hospital Center Jena, Jena, Germany.

**Abbreviation:** CMC, carboxymethylcellulose.

most readily feature a bioburden consisting of polymicrobial populations of bacteria and fungi, require vigilant monitoring for any signs of microbial progression and infection. If any of those signs are present, timely use of dressings with antimicrobial properties may be required, as well as effective exudate management. Dressings that contain and release antimicrobial agents at the wound surface have now entered the marketplace.<sup>7</sup> These dressings usually provide continuous or sustained release of an antiseptic agent (silver, polyhexanide, iodine) at the wound surface to provide long-lasting antimicrobial action in combination with maintenance of a physiologically moist environment for healing. Superabsorbent dressings containing polyacrylates have been found to be beneficial in lowering the bacterial burden by efficiently trapping bacteria in their core structure and reducing the number of viable organisms with each dressing change.<sup>39,48–50</sup> Hydrofiber or alginate dressings may allow similar (but probably considerably weaker) entrapment of bacteria and subsequent reduction of microbial progeny.<sup>51,52</sup> These dressings are most commonly equipped with ionic or nanocrystalline silver as an antimicrobial agent, which considerably increases the antimicrobial activity of alginate dressings.<sup>51</sup> Moreover, increased clinical efficacy was demonstrated for silver-containing alginate<sup>7,53,54</sup> and silver-supplemented hydrofiber dressings.<sup>55,56</sup> Similarly, foam dressings have been successfully fitted with silver.<sup>57</sup>

## Correction of biochemical imbalance

Newer and more advanced dressings focus on more than just managing moisture levels in the wound environment; they aim to address specific biochemical imbalances commonly found in chronic, non-healing wounds. It is now widely acknowledged that chronic wounds contain high amounts of MMPs<sup>14,58</sup> and elevated levels of PMN elastase.<sup>13,15,59</sup> Unchecked activity of these proteases leads to substantially decreased amounts of growth factors<sup>60</sup> and proteinase inhibitors, like tissue inhibitors of MMPs,<sup>61</sup> shifting the balance of matrix degradation and synthesis toward tissue destruction. Hence, current concepts of wound management focus on reduction of these proteolytic enzymes. Active, protease-modulating wound dressings designed to address the biochemical imbalance of the chronic wound are commonly composed of collagen, collagen with oxidized regenerated cellulose, or, recently, a nano-oligosaccharide factor. Studies demonstrated that bovine collagen type I is able to bind considerable amounts of proteases in vitro and ex vivo.<sup>62</sup> Further, it aids in establishing a more physiologic



**Figure 2** Maceration model for determination of fluid management by hydroactive dressings (carboxymethyl cellulose [Aquacel Extra], cellulose/cellulose-ethylsulfonate [Suprasorb Liquacel], alginate [Suprasorb A tamponade] over time employing a tissue substitute model (A) and video documentation (VF0700, Creative Labs, Milpitas, CA, USA). Different fluid absorption capacities at the maceration breakpoint were observed for the dressings investigated (B). The spread of the colored, simulated wound fluid solution allows measurement of the breakpoint of maceration (green dotted line) at which the dressings stop taking up fluid and start to leak (C). Image courtesy of Cornelia Wiegand.<sup>46</sup>  
**Abbreviation:** CMC, carboxy methylcellulose.

wound milieu, supporting leg ulcer healing in a clinical situation.<sup>16</sup>

Many studies have been published on other protease-modulating dressings consisting of collagen and oxidized regenerated cellulose, and lately also containing silver. Smeets et al demonstrated a significant reduction in protease activity after only 5 days of treatment with a collagen/oxidized regenerated cellulose matrix compared with a control group that received a hydrocolloid dressing.<sup>63</sup> In addition, Gottrup et al observed a significantly increased healing rate using collagen/oxidized regenerated cellulose/silver dressings versus a standard of care control group, which they attributed to the ability of the dressing to rebalance the inflammatory milieu by reducing the elevated protease activity detrimental to wound healing.<sup>64</sup> Others have used lipocolloid dressings incorporating nano-oligosaccharide factor, an oligosaccharide that decreases the activity of MMPs,<sup>65</sup> and reported outcomes that were clinically superior to alternative treatments.<sup>65,66</sup> It has been suggested that these active dressings (directly interacting with wound binding to and inactivating proteases) be reserved for individual cases due

to their high costs,<sup>1</sup> but other dressings that target exudates and remove proteases through sequestration might also effectively reduce the concentration and activity of proteolytic enzymes and aid healing. Polyacrylate-containing dressings were also shown to sequester and remove MMP and elastase activity in vitro.<sup>37,41,49,67,68</sup> Eming et al further reported an indirect effect of SAP particles on MMP activity by binding of essential  $\text{Ca}^{2+}$  and  $\text{Zn}^{2+}$  ions.<sup>37</sup> Protease sequestration capabilities could also be shown for alginates.<sup>51</sup> Moreover, alginates and hydrofibers exhibit significant antioxidative capacities.<sup>51,69</sup> Such a property is of significance to the wound healing process, because despite the beneficial role that reactive oxygen species play in killing invading microbial pathogens, excessive production of reactive oxygen species can be detrimental to host tissues.<sup>69</sup>

## Negative pressure wound therapy

NPWT, also called controlled negative pressure, topical negative pressure, or vacuum-assisted closure therapy, has been advocated for virtually all acute and chronic wounds. The treatment is based on evenly distributed local negative



pressure applied to the wound surface,<sup>70</sup> which effectively removes excess exudate. Besides providing a moist wound environment, NPWT may also promote healing by increasing blood flow,<sup>71</sup> reducing edema<sup>72</sup> and wound area,<sup>73</sup> as well as stimulation of formation of granulation tissue,<sup>74,75</sup> cell proliferation,<sup>76</sup> and angiogenesis.<sup>74-76</sup> In addition, it was been proposed that NPWT influences the microenvironment of the wound by eradication of inflammatory proteases<sup>77</sup> and decreasing bacterial burden.<sup>74</sup> For application of NPWT, a wound dressing, mostly foam but also gauze, which could more correctly be designated as “wound filler”, is placed on the wound. In most systems, the wound filler is “black” foam (large-pored polyurethane foam), although polyvinyl alcohol (“white”) foam, saline-soaked gauze, or antimicrobial-impregnated gauze is also used. Several studies showed that differences in the quality of granulation tissue formed by gauze or foam exist, eg, wound bed tissue grows into the foam during NPWT and often more force is required to remove the foam from the wound when compared with gauze.<sup>78-80</sup> In contrast, tissue damage caused by removal of gauze-based NPWT was reported to be less than 2% in a non-comparative series of 152 patients.<sup>81</sup> On the other hand, gauze dressings produce lower levels of tissue microdeformation and an uneven distribution of pressure in the wound bed compared with open-cell polyurethane foams.<sup>82</sup> Hence, they would lead to a smaller amount of granulation tissue due to smaller micromechanical forces.<sup>78</sup> However, it is thought that these physical effects initiate signaling cascades that encourage cell proliferation.<sup>83</sup>

## Conclusion

The customary practice of using the same wound dressing during the entire healing period is no longer reasonable. Instead, multiple types of dressing may be needed for a single wound over its healing trajectory.<sup>5</sup> This concept requires selection of the most appropriate dressing with regard to patient needs, wound etiology and localization, economic considerations, and last but not least, wound status.<sup>1,5</sup> The latter in particular should drive the choice of local wound product considering wound phase, depth, signs of infection, and the level of exudate. For example, a venous stasis ulcer producing a high amount of exudate will require a highly absorptive dressing. Patient preference will also actively influence the choice of dressing. It is the caregiver’s task to listen to a patient’s opinion and concerns as well as provide the patient with information on the best treatment to ensure compliance.

Several main types of dressings, including hydrogels, hydrocolloids, alginates, hydrofibers, foams, and

superabsorbent dressings, have been summarized here and evaluated with regard to their efficacy for highly exuding wounds. Their ability to manage exudate increases from hydrogels to hydrocolloids, alginates, hydrofibers, and foams, to superabsorbent dressings containing polyacrylates (Figure 1). Hence, the latter seems most favorable for highly exuding wounds. While large randomized trials confirming the superiority of one dressing over another are still lacking, management of exudate remains a key point in chronic wound therapy, and one that has to be addressed daily by caregivers.

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## Disclosure

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