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A Comprehensive Review of Topical Odor-Controlling Treatment Options for Chronic Wounds

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ABSTRACT

The process of wound healing is often accompanied by bacterial infection or critical colonization, resulting in protracted inflammation, delayed reepithelization, and production of pungent odors. The malodor produced by these wounds may lower health-related quality of life and produce psychological discomfort and social isolation. Current management focuses on reducing bacterial activity within the wound site and absorbing malodorous gases. For example, charcoal-based materials have been incorporated into dressing for direct adsorption of the responsible gases. In addition, multiple topical agents, including silver, iodine, honey, sugar, and essential oils, have been suggested for incorporation into dressings in an attempt to control the underlying bacterial infection. This review describes options for controlling malodor in chronic wounds, the benefits and drawbacks of each topical agent, and their mode of action. We also discuss the use of subjective odor evaluation techniques to assess the efficacy of odor-controlling therapies. The perspectives of employing novel biomaterials and technologies for wound odor management are also presented.

KEY WORDS: Chronic wound, Control, Dressing, Infection, Malodor, Odor, Therapy.

INTRODUCTION

Common clinical manifestations associated with wounds include pain, itch, odor, bleeding, and production of exudate; however, malodor is recognized as one of most distressful aspects of some wounds.¹ Malodor from a wound has been shown to produce psychological discomfort and embarrassment among patients and clinicians caring for these patients.² It has also been shown to increase social isolation.³⁻⁵ While some researchers have addressed this bothersome symptom,

evidence concerning the efficacy of various interventions designed to reduce malodor produced by some chronic wounds remains sparse.⁵

Unpleasant odor is often found in chronic wounds, and especially those that have not closed following 3 months of treatment.^{6,7} However, our knowledge regarding the epidemiology and pathogenesis of malodorous wounds remains limited. Several reports have examined the associations between wound type, duration of treatment, degree of inflammation, level of bacterial contamination, and development of malodor.^{8,9} Howell-Jones and colleagues¹⁰ evaluated findings from 95 microbiology laboratories; they found that 41% of swabs from venous leg ulcers were associated with an unpleasant odor. Foot ulcers occur in approximately 15% of persons with diabetes mellitus.¹¹ Diabetes mellitus, symptomatic bacterial wound infection, vascular diseases, and necrosis of tissues may trigger and prolong inflammation,⁸⁻¹¹ thus impeding the healing process; these sequelae increases the risk for development of wound malodor.¹¹⁻¹⁵

The fetid odor associated with some wounds is attributable to a combination of factors such as necrotic tissues and bacteria.^{8,16} It has been shown that both anaerobic and aerobic bacteria contribute to the release of unpleasant odors from wounds; although anaerobic bacteria are considered the major producer of malodor.¹⁷ Bacteria responsible for odor include the anaerobes: *Bacteroides*, *Clostridium* sp,¹⁷ *Prevotella* sp, *Porphyromonas* sp, *Fusobacterium nucleatum*,¹⁷ beta-hemolytic *Streptococci*,¹⁸ and aerobes: *Proteus* sp,¹⁹ *Klebsiella* sp, *Pseudomonas* sp, methicillin-resistant *Staphylococci*.¹⁹ Bacterially produced malodorous molecules encompass a range of volatile metabolites such as cadaverine, putrescine, sulfur,⁸ and short-chain fatty acids including *n*-butyric, *n*-valeric, *n*-caproic, *n*-haptonic, and caprylic acids.²⁰ Putrescine and cadaverine have an intense acrid smell²¹; they tend to linger and can cause vomiting.²²

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No widely used classification system for characterizing odors produced by wounds exists; patients and clinicians often described these unpleasant smells as foul, putrid, sweet, acrid, pungent, and offensive.^{1,14} Nevertheless, it has been observed that specific species of bacteria produce specific types of odor. For example, Shirasu and colleagues²³ used gas chromatography–mass spectrometry to evaluate wound odor and demonstrated that dimethyl trisulfide from exudate was a common source of “sulfury” odor emitted from wounds. Dimethyl trisulfide is a known end product of *Pseudomonas aeruginosa*. Refer to Table 1 for a summary of the range of malodors associated with chemical compounds frequently found in the beds of chronic wounds with bacterial colonization or infection.¹⁹

Odor is frequently used as an indicator of bacterial colonization in the wound bed.²⁴ Colonization is typically accompanied by formation of a biofilm.²⁵ Bacterial biofilms are more prevalent in chronic wounds than in acute wounds. For example, James and associates²⁶ demonstrated that 60% of chronic wounds contained biofilms as compared to 6% of acute wounds. Biofilms are communities of bacterial species living within a exopolysaccharide shield (EPS).²⁵ The EPS acts as a barrier for both antibiotics and innate cells of the host’s immune system, thus preventing effective wound healing and odor management.

The purpose of this article is to summarize studies focusing on odor control in the management of chronic wounds therapies. In comparison with other systematic reviews on malodorous wounds such as the work conducted by da Costa Santos and colleagues,²⁸ this article synthesizes findings from all available studies that included odor reduction in different types of chronic wounds and it summarizes potential therapies for preventing or controlling wound-associated odors.

METHODS

We completed a comprehensive review, using some techniques characteristic of systematic analysis of available literature and data sources. We searched the following electronic databases for research related to wound odor, PubMed, MEDLINE, Web of Sciences, Google Scholar, LISTA (EBSCO), Wiley Online Library, Cochran Library, and the Library of Nazarbayev University databases. We also searched hard copies of peer-reviewed publications (available in English). The literature search was conducted without any restrictions on language and date of publication. The key words used were: odor, malodor, wound, chronic wound, infection, antimicrobial therapy, septic wound, trophic ulcer, bed sores, diabetic foot, leg ulcer, wound dressing, topical treatment, and odor absorption.

Study Quality

The quality of each study covered in this review was evaluated independently by the authors with the use of online version of

Study Quality Assessment Tools (National Heart, Lung, and Blood Institute, Bethesda, Maryland, <https://www.nhlbi.nih.gov/health-pro/guidelines/in-develop/cardiovascular-risk-reduction/tools>), which was adapted for purposes of this review.

Techniques for Assessing Wound Odor

A recent online survey found low overall satisfaction of odor management and the need to develop more effective strategies and guidelines in this field.¹ The majority of the conducted studies included in this review used subjective analysis to determine presence of wound odor. In most cases, only the presence and intensity of odor were recorded; few studies evaluated the efficacy of its control. Table 2 summarizes the scaling systems used in questionnaire studies for identification of intensity of wound odor.^{2,13,21,29,32,33,87,98,127} Most of the scales distinguished odor intensity as low, medium, or strong. An “Overall Evaluation Scale” was usually used to measure the effectiveness of a dressing to control odor rather than odor intensity.²⁹ The scales changed statistically before and following treatment using either paired *t* test,³⁰ the Friedman test,³¹ the Spearman test,³² or Mann-Whitney *U* test,³³ supporting their responsiveness to intervention. Nevertheless, statistical analysis was not always possible due to differences in responses reported by health care providers versus patients.²¹ We hypothesize that odor perception may be affected by various factors, including reduced sensitivity, and recommend additional research on this topic.

Some researchers have attempted to develop more objective instruments techniques for objectively measuring wound odor, but none has gained widespread acceptance in clinical practice.^{34,35} Thomas and colleagues¹⁹ proposed a novel method for identification of volatile organic compounds (VOCs) as a proxy for odor intensity, which could be used for characterization of the metabolism and bacterial colonization of chronic wounds. The VOC samples were analyzed by a gas chromatography–ion trap mass spectrometry.

Application of “electronic nose” (e-nose) has also been used to quantify wound odor.³⁶ The e-nose measures changes in electrical resistance using special sensors usually made of polymers. The signal is processed and analyzed via software providing an opportunity to recognize the odor.

Some researchers have been exploring array-based gas sensors as a potential “fast method” for detecting bacterial colonization or infection within a wound. For example, Byun and associates³⁷ developed an e-nose that incorporated an automated solid-phase microextraction desorption system. This method allowed recognition of 3 bacteria species at the early stage of wound infection. Bailey and coworkers³⁸ developed a portable e-nose based on an array of conducting polymer gas sensors used to analyze VOC’s from wounds along with identification of bacterial species. Tian and colleagues³⁹ used a gas sensor array with 6 metal oxide gas sensors and one electrochemical gas sensor to determine 7 species of wound pathogens (*Pseudomonas aeruginosa*, *Escherichia coli*, *Acinetobacter baumannii*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Klebsiella pneumoniae*, and *Streptococcus pyogenes*). This system was able to detect both single and mixed pathogens among the 7 species.

There are other reports on instruments capable of detecting various compounds, including those from venous leg ulcers, and some of them correlate data to the presence of certain bacterial species.^{18,40,41} However, current odor-sensing devices

TABLE 1.
Compounds Associated With Specific Odor Description

Compounds	Odor Characterization
Dimethyl trisulfide	Sulfur-like
Acetic acid	Sour
Isobutyric acid	Cheesy
Butyric acid	Cheese and vomit
Isovaleric acid	Cheese and foot

TABLE 2.**Tools for the Subjective Assessment of Wound Odor**

Odor Assessment	Scale System	References
Visual Analogue Scale	Scale from 1 to 10, where 1 is no odor and 10 is extremely strong odor	13, 87, 88
Verbal Rating Scale	Scale from 1 to 4, where 1 is no odor and 4 is strong odor	33
Verbal Rating Scale	Strong (intolerable), moderate (noticeable), minimal (barely noticeable), absent (no odor)	21
Baker and Haig method	Scale from 1 to 4, where 1 is strong odor and 4 is no odor	127
Not indicated	Scale from 0 to 4, where 4 is strong odor and 0 is no odor	32
Overall Evaluation scale	Scaled from 1 to 10, where 10 is excellent odor control	29
Teller Odor Indicator	Scaled from 0 to 5, where 0 is no odor, 4–0 is when odor is sensed during dressing changes and at certain distances from the patient.	2

TABLE 3.**Products Used to Manage Wound Odor**

Main Component	Products	Description	Application	References
Activated Charcoal	CarboFlex (Convatec)	Five-layered alginate, hydrofiber, nonwoven dressing, impregnated with charcoal	Malodorous fungating wounds	45
	Carbonet (Smith & Nephew)	Charcoal cloth sandwiched between polyethylene layers, which is attached to fibrous cellulose that is covered with knitted viscose	Malodorous wounds, including fungating lesions, fecal fistulae, necrotic pressure sores, and leg ulcers	43
	Clinisorb (CliniMed Ltd)	Charcoal impregnated into viscose rayon, covered with polyamide	Malodorous fungating wounds	46, 47
	Actisorb Plus (Systagenix)	Charcoal impregnated into viscose rayon, covered with nonwoven nylon	Malodorous wounds	54, 55, 126
Silver	Actisorb Silver 220 (Systagenix)	Carbon fibers bound to silver particles, covered with nylon layer	Chronic, malodorous, infected wounds: venous and pressure leg ulcers	54, 55
	UrgoCell Silver (Urgo Medical)	Lipido-colloid layer with incorporated silver salts and attached to polyurethane foam covered with polyurethane	Venous leg ulcers	53
	Allevyn Ag (Smith & Nephew)	Hydrocellular foam with silver sulfadiazine covered with film	Malodorous chronic wounds	a, b
	Acticoat (Smith & Nephew)	Nonwoven material sandwiched between polyethylene coated with nanocrystalline silver	Malodorous malignant wounds	a, c
Iodine	Iodosorb (Smith & Nephew)	0.9% w/v cadexomer iodine	Leg ulcers, pressure injuries, and diabetic ulcers	122
Honey	Activon Tulle (Advancis Medical)	Medical grade Manuka honey	Malodorous fungating wounds	a, d
	Algivon (Advancis Medical)	Honey-impregnated alginate	Chronic malodorous wounds	33
Sodium chloride	Mesalt (Molnlycke HealthCare)	Gauze impregnated with crystalline sodium chloride	Cancerous skin lesions	29
Metronidazole	Metrotop (Molnlycke HealthCare)	0.8% metronidazole gel	Malodorous leg ulcers	13
	Metrogel (Galderma)	0.75% Metronidazole gel	Malodorous fungating wounds	127
Sugar	Sugar	Paste like consistency due to using glycerine or petroleum jelly	Malodorous wounds	87
	Caster sugar	Paste achieved by mixing sugar with polyethylene glycol 400 and hydrogen peroxide.	Malodorous bed sores	87
Honey	Wound Care 18+ (Comvita)	Manuka honey can be used in combination with primary nonadhesive dressing Tricotex	Malodorous leg ulcers	80
Oils	Megabac (Nicrosol Laboratories)	Spray mixture of eucalyptus oil, tea tree oil, grapefruit oil	Malodorous ulcers in oral cavities	128
	KM-PT 70 (Klonemax)	Eucalyptus oil, melaleuca oil, lemongrass oil, lemon oil, clove leaf oil, thyme oil	Malodorous malignant wounds	98

^aManufacturer/product webpage.

^b<http://www.smith-nephew.com/professional/products/advanced-wound-management/acticoat/acticoat-absorbent/>.

^c<http://www.smith-nephew.com/professional/products/advanced-wound-management/allevyn/more-allevyn-options/allevyn-ag-adhesive/>.

^d<http://www.advancis.co.uk/products/activonmanukahoney/activon-tulle>.

require further improvement for clinical use in terms of price, portability, and analysis rate.^{19,35}

Compounds Used to Control or Eradicate Wound Odor

Wound malodor may be addressed using a direct or indirect approach (Table 3). The direct approach focuses on trapping or absorbing the VOCs that create wound malodor. In contrast, the indirect approach seeks to reduce fetid odors by lowering bacterial bioburden in the wound. Aromatherapy can be also categorized as a form of indirect malodor management; it is designed to distract the individual or care provider from the fetid wound odor.

Charcoal

Substances that possess a large active surface area and are biocompatible may be used to absorb or trap the VOCs that produce fetid wound odors. Examples include charcoal and its derivative “activated carbon.” Activated carbon is typically made of natural sources such as rice, coconut shells, or other woods; these highly porous materials provide a large area for adsorption of various types of gases, bacteria, and liquids. Activated carbon has been used in various biomedical applications.^{43,44} It is obtained by combustion or decomposition of carbonaceous materials.⁴³ They are incorporated into multiple commercially available dressings such as Carboflex (ConvaTec Inc, Uxbridge, UK), Carbonet (Smith-Nephew plc, UK), Clinisorb (CliniMed Ltd, High Wycombe, UK), and Actisorb Plus (Systagenix, San Antonio, Texas). These dressings contain charcoal cloth that are 85% to 98% active carbon.⁴³ The main difference between these products is the materials used to cover the charcoal cloth; examples include viscose rayon, alginate,⁴⁵ polyethylene, polyamide,^{46,47} and nylon.⁴⁸ Several products may be used in combination with antibiotics or primary dressings to neutralize bacteria caught within the charcoal^{45,46} (Table 3).

Silver

Silver products indirectly reduce odor via their antimicrobial properties; interest in clinical application of the antimicrobial and anti-inflammatory properties of silver has sharply increased in the last decade.⁴⁹⁻⁵² Silver-based wound care dressings contain nano-sized silver particles that significantly enlarge the surface area of the silver and enhance its antimicrobial actions when compared to bulk silver metal.⁵⁷ Charged nanoparticles adhere to the bacterial cell wall impairing function of key proteins and enzymes.^{57,58} This process increases the permeability of the bacterial cell wall causing its destruction.^{49,58} Silver products also produce reactive oxygen species.^{49,50} Some manufacturers impregnate silver nanoparticles into foam dressings; examples include Allevyn Ag (Smith-Nephew plc, UK),⁷ Urgocell Silver (Urgo Medical, Chenove, France),⁵³ and Acticoat (Smith-Nephew plc, UK).³³ Another dressing (Actisorb Silver 220, Systagenix) contains silver particles attached to carbon particles.^{54,55} This product exerts both direct and indirect odor control properties; the charcoal directly absorbs odorous gases, while the silver indirectly reduces odor by killing any bacteria captured by the charcoal.^{54,56}

Iodine

Iodine may be used to indirectly effect wound odor by reducing bacterial bioburden in the wound bed. Iodine is destructive to a wide range of microorganisms, but its action is not entirely understood.^{59,60} Iodine disrupts bacterial wall membranes by interacting with carbon double bonds of fatty

acids. Once inside, iodine disturbs normal cell functioning by affecting the function of proteins, enzymes, and nucleotides, consequently resulting in cell death.^{60,61} Iodine is an antiseptic rather than an antimicrobial; despite more than 100 years of intensive use of iodine, its effectiveness against a variety of bacterial species has not diminished.⁶²

Despite its actions against a wide variety of pathogenic microorganisms, iodine can be cytotoxic. Since 1950, iodine has been manufactured as an iodophor (combination of iodine and a surfactant) to reduce its toxicity toward human cells.⁶¹ Cadexomer iodine is a well-known iodophor that facilitates the formation of a hydrophilic complex⁶¹ between iodine and a polymer (eg, dextrin, epichlorohydrin) that acts as a carrier and, upon swelling, releases iodine to the wound site.⁶⁰ An *in vitro* study⁶³ showed no toxicity of cadexomer iodine to human cells at concentration of 0.45% (weight per volume, w/v). Nevertheless, this iodophor was found to reduce the numbers of *S aureus*^{64,65} and capture different microorganisms onto cadexomer iodine.⁶³

In a systematic review of 27 clinical trials, Vermeulen and co-workers⁶⁶ compared iodine (in the form of Povidone or cadexomer iodine) versus control (gauze dressing); analysis found significant differences between iodine versus topical therapies based on complete wound healing, reduction in wound surface, and reduction in wound pain. One study reported that Rifamycin SV MMX prevented postoperative infection better than Povidone iodine,⁶⁷ while another found no difference between infection prevention by iodine, paraffin gauze, and a hydrogel dressing.⁶⁸

Honey

Manuka honey may be used to indirectly reduce wound odor by 2 methods. It exerts antimicrobial properties that reduce bacterial bioburden. It also provides an alternative nutrient source for bacteria present within wounds, resulting in a shift to lactic acid production as a bacterial waste product, rather than malodorous sulfur-containing compounds.⁶⁹ Manuka honey is derived from a single flower source; it has a low pH of 3.2 to 4.5,⁶⁹⁻⁷¹ high sugar content (up to 79% w/v), and low water content.⁷⁰ This combination of factors creates an unfavorable environment for bacterial growth and reproduction. While all forms of honey exhibit some antibacterial properties, Manuka also contains methylglyoxal that inhibits the growth of gram-negative bacteria and disrupts the cell wall of gram-positive bacteria.^{72,73,75} Methylglyoxal has also been found to suppress the growth of a methicillin-resistant strain of *P aeruginosa*.⁷⁶ Emerging research suggests that lepsin also may enhance the antibacterial effect of Manuka honey.⁷⁷ Manuka honey can further disrupt bacteria by reducing iron-sequestering siderophore production in *P aeruginosa*⁷⁸ and biofilm formation in *S pyogenes* by preventing it from binding to fibronectin.⁷⁹ However, some patients may be sensitive to honey and its components,⁸⁰ especially those with diabetes mellitus⁸¹ and methylglyoxal may delay wound healing.⁸² *In vitro* studies found that certain strains of bacteria such as *P aeruginosa*, *S aureus*, *E coli*, and *S epidermidis* did not generate resistance to Manuka honey,⁷¹ which may be explained by the different modes of action.

Sugar

Sugar may be used to reduce wound odor by inhibiting bacterial growth via an osmotic effect.⁸³⁻⁸⁵ However, sugar is rapidly diluted following application and frequent reapplication may be needed to prevent bacterial adaptation.⁸⁶ In order to hold diluted sugars in place, petroleum jelly with glycerin may be

combined to create a paste-like consistency that prevents elution of sugar from the wound bed.⁸⁷

Metronidazole

Metronidazole is a nitroimidazole antibiotic available as a 0.75% or 0.8% w/v concentrated gel that can be used as a topical agent for wound management.⁸⁸ It is not approved by the US Food and Drug Administration for management of wound odor; instead, it is used because of its ability to reduce odor-producing anaerobic pathogens in selected wounds and its use is classified as “off-label” when prescribed for control of wound odor.^{88,89} Metronidazole is activated through reduction of its nitro group (NO₂), resulting in the formation of radical species that impair DNA activity and prevents its replication.^{90,91} The oxygen used by aerobic bacteria suppresses the uptake of metronidazole but the oxidoreductase complexes present in anaerobic bacteria are susceptible to metronidazole therapy.⁹⁰

Other Topical Therapies

Natural compounds of natural origin also may be used to control wound malodor; these compounds act indirectly via their antibacterial properties. One example is application of essential oils such as eucalyptus, lavender, fennel, geranium, pine, peppermint, rosemary, tea tree, thyme, and other oils. Schelz and colleagues⁹³ investigated the antimicrobial and antiplasmid activities of 10 essential oils and menthol on various gram-positive and gram-negative bacteria 2 yeast strains. They found that each of the 10 oils exhibited antimicrobial activity and 3 exhibited antiplasmid activities. They also reported that peppermint oil and menthol demonstrated a synergistic effect when combined with the antibiotic oxytetracycline. The essential oils are multicomponent compounds, and some have been identified as exerting antimicrobial activity, with minimal cytotoxicity activity.^{94,95} Terpenes and phenolic compounds presented in essential oils have been found capable of increasing membrane permeability leading to the leakage of potassium and phosphate ions.^{96,97} Interestingly, gram-negative bacteria such as *E coli* were shown to be more resistant than gram-positive species due to the presence of a lipopolysaccharide layer in their outer membrane.⁹⁸

Sodium chloride has been employed in wound care for a long time at concentration of 0.9% w/v. Isotonic saline is usually applied with gauze and often used for cleaning the wound bed.⁹⁹ Its indirect effect on wound odor may be attributable to mechanically removing bacteria from the wound bed during wound cleansing.^{29,100}

Cyclodextrins (sugar molecules bound together in a ring) have been incorporated into various materials used for wound healing such as hydrogel products.^{101-103,108} They have also been used in applications outside of wound care for control of foul odors.¹⁰⁴⁻¹⁰⁷ Additional research is needed to elucidate the potential role of these substances in the management of wound malodor.

EFFICACY OF VARIOUS TREATMENTS ON WOUND ODOR

Multiple approaches have been used in an attempt to prevent, suppress, or control disagreeable odors associated with chronic wounds. Selecting the best treatment depends on multiple factors such as wound type, presence of comorbid conditions, availability, and systemic factors such as hypersensitivity to ingredients.

Since most fetid wound odors are associated with bacterial colonization or infection, a variety of antimicrobial agents

may be used to reduce bacterial bioburden in the wound bed and control wound odor. Metronidazole has been the most extensively studied for its influence on wound malodor. Paul and Pieper⁸⁹ reviewed 15 articles in which topical metronidazole was specifically used to decrease wound odor; 7 were case reports or multiple cases series; 6 were descriptive longitudinal studies; and 2 were randomized controlled trials. Most reported reduction or eradication of wound odor along with reducing wound drainage and pain. Bale and colleagues¹³ reported results of a randomized, placebo-controlled, double-blind trial that studied the effect of metronidazole gel on wound malodor. They reported a 100% success rate on wound odor after 3 days of treatment. Odor ratings provided by patients and nurses were significantly correlated ($P < .001$). Poteete¹²⁷ reported findings from a case series involving 13 patients whose wound odor had not responded to prior odor control interventions. Patients were treated with topical metronidazole gel to eliminate would malodor, and the author reported that all experienced a decrease in wound odor using this single intervention.

The application of natural substances or compounds for wound odor management has been advocated as a possible alternative to topical antimicrobial or antiseptic agents.⁹³ Sugar is a readily available, cheap, and biocompatible substance that has been used to treat multiple wound types.¹⁰⁹⁻¹¹⁴ Chiwenga and colleagues⁸⁷ treated 71 patients with malodorous, painful wounds by using sugar dressings. They reported a reduction in mean patient odor scores from 5.45 out of 10 at baseline to a mean of 2.94 at 10 days' treatment. Murandu and colleagues¹¹⁵ reported findings from an in vitro study that evaluated the antimicrobial effect of 3 types of granulated sugar (Demerara, granulated beet sugar, and granulated cane sugar). They found that all 3 sugars inhibited bacterial growth in high concentrations, but the magnitude of the effect was influenced by the type of sugar. They also reported findings of a pilot clinical study that enrolled 22 patients with chronic wounds with necrotic tissue. They reported successful debridement of necrotic tissue from all the wound (mean treatment duration 11.13 days) along a significant reduction in wound odor. Other authors have applied sugar to infected wounds and reported amelioration of fetid odors within 3 to 4 days.⁸³⁻⁸⁵

Honey has also gained more widespread clinical use in the past decade for management of chronic wounds.¹¹⁶⁻¹²⁰ In a 4-center feasibility study, Dunford and Hanano¹²¹ evaluated a honey-based product and found that it reduced wound odor in patients with leg ulcers. These findings are consistent with 2 other studies that found that patients managed with a honey-based product achieved a significant statistical reduction of odor³³ or complete elimination of odor.⁸⁰

We found only 1 study that specifically examined the impact of iodine on wound odor. Ormiston and associates¹²² evaluated a cadexomer iodine dressing in the treatment of 61 patients with venous leg ulcers. The main outcomes of the study focused on wound closure; odor was reported as a secondary outcome. The authors reported odor reduction among patients managed by the iodine-impregnated dressing, but the method of measurement was not provided.

Despite widespread clinical use of charcoal products for management of malodorous wounds,¹ we found only 2 reports that specifically evaluated its effect on wound odor.^{46,47} Unfortunately, there was no indication of the magnitude of odor reduction in either study. However, findings from

TABLE 4.
Description of Studies on Wound Odor Controlling Topical Treatments^a

Description of the Study	Wound Information	Odor Measurement	Outcome	References
Metronidazole gel				
1) Metronidazole gel 2) n = 41 (15 M, 26 F); Placebo (n = 21), Treatment (n = 20) 3) Measured, but NA in the article 4) Randomized, placebo-controlled, double-blind trial 5) 7 days	1) Venous, arterial, and pressure leg ulcers, other (eg, surgical) 2) >4–5 y 3) Malodorous, n = 41	No equipment. Subjective by nurse, patient, and caretaker using VAS.	Odor eliminated within 7 d in 100% in treatment group, 76% in placebo.	13
1) 0.8% metronidazole 2) n = 11 (1 M, 10 F); Placebo (n = 5), treatment (n = 4) 3) Age: 51–85 y (mean: 68) 4) Randomized, placebo-controlled, double-blind trial (the first) 5) 6 d	1) Fungating, metastatic tumors 2) NA 3) Offensive odor, n = 11	No equipment. Subjective by nurse and patient using VAS.	Odor reduction in treatment group within 6 d from 7.8 to 6 (graded by patient), from 5 to 4.3 (by nurses)	30
1) 0.75% metronidazole 2) n = 48 (12 M, 36 F); NA 3) Age: 25–93 (mean: 61) 4) Multicenter, open study 5) 14 d	1) 20 fungating wounds, 27 hypostatic leg ulcers 2) 64% of patients 3) Foul smelling, n = 47	No equipment. Subjective by nurse, patient, and doctor using scale 0–4.	Within 14 d odor reduced to 4% patients	32
1) 0.8% metronidazole gel (handmade) 2) n = 5 (F); Treatment (n = 5) 3) Age: 47–71 (median: 59) 4) Open, uncontrolled study 5) 6–131 d	1) Breast cancer (n = 4), recurrent cancer (n = 1) 2) 10 mo 4 y 3) Malodorous, n = 5	No equipment. Subjective by nurse, patient, and doctor. Only day of odor elimination was recorded.	Odor eliminated in 2–5 d in 4 patients	89
1) Metronidazole gel 2) n = 13; NA 3) Age: 44–105 4) Case study 5) 9 d	1) Malignant fungating wounds, pressure injuries 2) NA 3) Malodorous, n = 13	No equipment. Subjective by one person using Baker and Haig.	No odor in 12 patients by day 6. One patient still had slight odor upon removal of dressing.	127
Charcoal				
1) Nonadhesive carbon-impregnated dressing 2) n = 40 (61% M, 39% F); Treatment (n = 40) 3) Age: 70.7 (mean) 4) Open, prospective, noncomparative, multicenter study 5) NA	1) Leg ulcers (59%) 2) 231.6 wk (mean) 3) Malodorous, n = 40	No equipment. Subjective by patient and nurse using VRS.	Odor decreased in 75% of dressing changes.	21
Silver				
1) Silver-impregnated dressing 2) n = 126 (47% M, 53% F); NA 3) NA 4) Retrospective study 5) NA	1) Hard-to-heal wounds 2) NA 3) Malodorous, n = 10	Not indicated	Odor reduced in 5 out of 10 patients with malodor	129
1) Silver-impregnated dressing 2) n = 45 (NA); Treatment (n = 45) 3) NA 4) Prospective multicenter noncomparative clinical trial 5) 4 wk	1) Venous leg ulcers 2) NA 3) NA	No equipment. Subjective by nurse.	Odor eliminated in 70% of patients at week 4.	53
1) Charcoal cloth + silver 2) n = 8 (5 M, 3 F); Treatment (n = 8) 3) Age: 42–78 4) Case series 5) 4 wk	1) Diabetic and venous leg ulcers, surgical wound 2) 5 wk—48 y 3) Malodorous and foul smelling, n = 8	No equipment. Subjective by nurse or doctor.	Odor eliminated in 3 patients on 2–4 wk (chronic wounds), 1 wk (acute wound). No odor reduction in 1 patient.	http://www.woundsinternational.com/media/issues/620/files/content_10586.pdf
1) Nanocrystalline silver 2) n = 37 (NA); Treatment (n = 35) 3) Age: 47–90, median 65.6 4) Randomized clinical trials 5) 28 d	1) Malignant wounds 2) 7 mo 3) Malodorous, NA	No equipment. Subjective by author using VRS and VAS.	Significant statistical decrease (P = .007).	33

(continues)

TABLE 4.
Description of Studies on Wound Odor Controlling Topical Treatments^a (Continued)

Description of the Study	Wound Information	Odor Measurement	Outcome	References
1) Hydrocolloid dressing + hydroactivated silver 2) n = 43 (NA); 2 treatment groups 3) NA 4) Prospective, open, comparative 5) 10-12 wk	1) Infected wounds, with bioburden or fetid odor 2) NA 3) Malodorous, NA	Not indicated.	Reduction of malodor	130
1) Foam dressing + silver 2) n = 26; Test group (n = 13), control (n = 13) 3) NA 4) NA 5) 4 wk	1) Malignant fungating wounds 2) NA 3) Malodorous, n = 26	N/A	Reduction of malodor in 76.9% in test group, and 30.8% in control group	131 Kalemikerakis J. et al. J BUON. 2012;17(3):560-4.
Salts				
1) Calcium salt of alginic acid (Sorbsan) 2) n = 11 (7 M, 4 F); Treatment (n = 11) 3) Age: 54-67 4) Clinical study 5) 18 d 2 mo	1) Diabetic and trophic ulcers 2) NA 3) NA	Not indicated	Reduction of odor. Statistical data not given	100
1) Saline dressing, sodium chloride 2) n = 11 (10 F, 1 M); NA 3) Age: 45-85 4) Cross-over 5) NA	1) Ulcerating skin metastases 2) 3-35.5 mo 3) Malodorous, n = 6	No equipment. Subjective by nurse and patient using Overall Evaluation Scale and VAS	Ability of the dressing to control odor was evaluated 7/10	29
Sugar				
1) Sugar paste with wool and crepe bandage 2) n = 71 (NA); NA 3) NA 4) Open, uncontrolled study 5) 10 d	1) NA 2) NA 3) Malodorous, n = 71	No equipment. Subjective by nurse and patient using VAS.	Mean odor reduction within 10 d from 5.45 to 2.94. One patient showed no improvement.	87
1) 3 types of sugar tested 2) n = 22 (NA); Treatment (n = 22) 3) NA 4) Open, uncontrolled, comparative study 5) 21 d	1) Acute and chronic wounds, several infected 2) NA 3) Malodorous, NA	No equipment. Subjective by staff and patients using health and satisfactions questionnaire.	Reduction of malodor	115
Honey				
1) Manuka honey 2) n = 38 (NA); Treatment (n = 34) 3) Age: 47-90, median 65.6 4) Randomized clinical trials 5) 28 d	1) Malignant wounds 2) 7 mo 3) Malodorous, N/A	No equipment. Subjective by author using VRS and VAS	Significant statistical decrease ($P = .007$)	33
1) Manuka honey 2) n = 8 (5 F, 3 M); Treatment (n = 8) 3) Age: 22-83 4) Case series 5) 4 wk	1) Leg ulcers and injuries 2) 3 wk-18 mo 3) Malodorous, n = 3	No equipment. Subjective by patient and medical staff	Complete elimination of odor in 1 wk	80
1) Manuka honey 2) n = 1 (F) 3) Age: 80 4) Case study 5) 12 wk	1) Malignant tumor oral cavity 2) NA 3) NA	Subjective by patient and medical staff.	No detectable odor in 1 mo	135
Essential oils				
1) Tea tree, grapefruit, eucalyptus 2) n = 25 (NA); Treatment (n = 25) 3) NA 4) NA 5) NA	1) Head and neck cancer 2) NA 3) Malodorous, n = 25	Not indicated.	Odor eliminated in 2-3 d in all patients	128

(continues)

TABLE 4.
Description of Studies on Wound Odor Controlling Topical Treatments^a (Continued)

Description of the Study	Wound Information	Odor Measurement	Outcome	References
1) Eucalyptus, melaleuca, lemongrass, lemon, clove leaf, thyme 2) n = 30 (NA); Treatment (n = 30) 3) NA 4) NA 5) NA	1) Head and neck cancer 2) NA 3) Foul smelling, n = 30	Not indicated.	Odor eliminated in 3-4 d in all patients	132
Polymer				
1) Ionic sheet (Hydrogel) 2) n = 2 (NA); Treatment (n = 2) 3) NA 4) Case study 5) NA	1) Cancer 2) NA 3) Malodorous, n = 2	Not indicated	Control of odor	133
1) Hydrocolloid dressing + 30% cyclodextrin 2) n = 2 (F); Treatment (n = 2) 3) Age: 81, 74 4) Case study 5) NA	1) Pressure injuries 2) NA 3) Malodorous, n = 2	Subjective by nurse	Elimination of odor	106
1) 0.3% Polyhexamethylene biguanide + Suprasorb X 2) n = 2 (NA); Treatment (n = 2) 3) Age: 38, 79 4) Case study 5) 4 wk	1) Burn and acute wounds 2) NA 3) Malodorous, n = 1	Subjective by nurse and family	Odor eliminated within 4 wk	134
Iodine				
1) Cadexomer iodine 2) n = 61 (21 M, 39 F); Treatment (n = 30), control (n = 30) 3) Mean age: 68 4) Randomized cross-over trial 5) 24 wk	1) Chronic venous ulcers 2) NA 3) NA	Not indicated	Reduction of malodor	122

Abbreviations: NA, not available; VAS, Visual Analogue Scale; VRS, Verbal Rating Scale.

^aDescription of the study: (1) treatment; (2) sample size (M = male, F = female); study groups; (3) age of patients; (4) study design; (5) treatment duration. Wound information: (1) wound type; (2) wound duration; and (3) odor description, the number of patients with odor.

in vitro comparison studies (Carboflex; ConvaTec Inc, Uxbridge, UK) suggest that it may be more effective in odor control than other dressings.¹²³⁻¹²⁵ For example, Thomas and colleagues¹²⁵ tested in laboratory the ability of different commercially available wound dressings to reduce pattern odor (diethylamine), of which concentration in the chamber was constantly monitored by using a Miran 1B2 portable ambient analyzer (Quantitech Ltd, Milton Keynes) and a data-logger. They found that that the first dressing demonstrated more potential for odor reduction than did another dressing (Actisorb Plus, Systagenix).

We found 11 studies using silver-impregnated dressings that evaluated wound odor, in 10 it was a secondary outcome,^{1,7,33,51,53-55,57-59,60} and it was the primary outcome in one clinical case series where silver was used along with activated charcoal.¹²⁶ The authors reported a reduction in wound malodor and an increase of tissue granulation.

Table 4 summarizes research focusing on polymer dressings such as hydrogel and hydrocolloids dressings impregnated with various odor-reducing substances. The most effective seems to be hydrocolloid impregnated with 30% cyclodextrin.¹⁰⁶ Cyclodextrins (cyclic oligosaccharides) have been extensively used for absorption of various odors in industry or households. However, the effective absorption process can be hindered by slow diffusion rate (through adhesive matrix) and water deficiency. The authors found that those obstacles can be overcome by using the combination of cyclodextrins and conventional hydrocolloids, such as sodium carboxymethyl cellulose. Such a combination provides ideal conditions for effective elimination of wound malodor. This technology has been already introduced at the market under brand name “Exuderm Odorshield” (Medline Industries Inc, Mundelein, Illinois).

Limited evidence suggests that each of the products is associated with some reduction in wound odor (Table 3).

TABLE 5.
Number of Studies That Included Odor as an Outcome

RCT	RPCT	Prospective	Open	Multicenter	Uncontrolled	CT	CS	MCS	Others (NA, Retrospective, Cross-over)
2	2	4	4	3	3	2	6	2	3, 1, 2

Abbreviations: CT, clinical trial; CS, case study; MCS, multiple case series; NA, not available; RCT, randomized controlled trial; RPCT, randomized, placebo-controlled trial.

Despite the claimed effectiveness of these agents, they have not been as widely adopted for clinical use as a charcoal. A recent international survey¹ of 1444 clinicians in more than 30 countries found that charcoal was perceived as most effective and was the most often used strategy for reducing fetid wound odors. Nevertheless, respondents indicated that charcoal-based products were deemed effective by fewer than 50% of participants. Silver-containing dressings were ranked second best and rated as very effective by 23% of participants. The authors noted that despite the recent high interest in aromatherapy for odor management, only 8% (n = 115) of study participants have used this method. However, this study did not provide any information on the perceived effectiveness of aromatherapy when compared to other topical agents. Survey findings further indicated that metronidazole use was demonstrated to be the second to last among available agents.¹ In this study, 49.8% (n = 320) of participants described the application of topical metronidazole gel as very effective, 38.1% (n = 250) as somewhat effective, and 12.9% (n = 85) as not effective at all. However, the authors of the survey noted that lack of availability of metronidazole in some countries along with cost issues and special requirements for prescription may influence its use in many areas of the world.

Limitations of Studies Cited

Considered collectively, the studies cited in this comprehensive review had multiple limitations. Many were nonrandomized comparison cohort studies, case studies, or multiple case series (Table 5). We identified only 2 randomized, placebo-controlled, double-blind trials (both evaluated metronidazole)^{13,30} and 2 randomized controlled trials (one evaluated silver and one evaluated medical grade honey).^{33,53} Studies tended to have small sample sizes and short data collection periods. Few employed a validated instrument for grading the magnitude of malodor, the characteristics of wound odor, or an objective for measuring secondary properties of fetid odors such as VOCs.

CONCLUSIONS

Despite recent progress in multiple areas of wound care, knowledge and evidence related to therapies for controlling odor remain limited. We reviewed the literature and found that most studies in this area were observational, and used measured odor as secondary outcome. This review also highlights the need for designing a standardized technique for detecting and monitoring wound odor. Such devices might incorporate biosensors or electronic-nose technologies to optimize and improve odor management in the clinics.

KEY POINTS

- Wound odor is a significant problem for patients and medical staff.
- Current strategies for managing wound odor primarily address reducing bacteria or other pathogens associated with production of gases leading to malodor.
- Limited evidence suggests that there is no effective strategy for odor management.
- There is a need in developing new methods for wound odor control.

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