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Commentary

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Topical odour management in burn patients

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Abstract

Preventing microbial colonization or infections that cause offensive smells may lead to odor reduction. As both anaerobic and aerobic bacteria cause the release of malodor from wounds, the most direct way of avoiding or eliminating wound odor is to prevent or eradicate the responsible infection through the debridement of necrotic tissues. However, some burn patients with malodorous wounds are unable to undergo debridement due to systemic conditions, especially in the acute stage. Moreover, the optimal drug doses and dressings to ensure the efficacy and cost-effectiveness of odorous burn wound management is unclear. The purpose of this commentary is to outline the odor management options available for burn patients, focusing on topical strategies. Numerous potential therapies for treating odorous wounds after burn injuries are suggested.

Key words: Odour, Wounds, Topical management, Burns, Natural substance

In chronic wounds, unpleasant odours are caused by tissue degradation and bacterial colonisation. These conditions result in the emission of odorous compounds, such as dimethyl trisulfide, cadaverine, sulfur, putrescine, ammonia and short-chain fatty acids [1, 2]. Both aerobic and anaerobic bacteria release malodorous vapours from infected wounds [3]. Consequently, the most direct way to avoid or eliminate wound odour is to prevent or eradicate the infection. Approximately 5–10% of patients with advanced cutaneous cancer, metastases of the breast or internal organ cancers which have penetrated the skin demonstrate malodorous cutaneous ulcers. These disorders markedly reduce the patient's quality of life (QOL) [4]. Malodor in patients with terminal cancer is the most frequently reported physical symptom. However, other symptoms, such as massive exudate,itching, pain, risk of haemorrhage and reduced QOL are typical [5]. In these patients, surgical procedures may lead to symptom relief and a postoperative improvement in QOL [6]. Although, the optimal management of malodorous wounds remains unknown, this is especially true for burn patients (Figure 1).

Preventing microbial colonisation or infections that result in offensive odours may lead to odour reduction. This can be accomplished by using systemic antibiotics and/or topical exudate-control dressings. Some burn patients with malodorous wounds do not receive sufficient odour management because of their systemic conditions. This is often observed in the acute stage of the injury. Debridement of burn eschar causing malodour is extremely painful unless performed under general or local anaesthesia. This further adds to the emotional and physical stress as well as the overall risk of treatment. Therefore, it is essential to be aware of the fundamental mechanisms of malodorous burn wounds and to establish a treatment plan for optimal odour management.

Chemical compounds associated with odour

Burns are prone to infection as the burn wound environment is ideal for the proliferation of infectious organisms [7, 8]. Bacteria proliferate rapidly, and the mean cell generation time under optimum conditions is ~20 min. Therefore, a single bacterial cell can proliferate to over 10 billion cells within a

Table 1. Species and characterization of organisms

Species	Representative organic compounds	Odour characterization
Staphylococcus aureus	Acetic acid, isovaleric acid, isobutyric acid	Sour, cheese and foot, Cheesy, fruity
Staphylococcus epidermidis	Butyric acid	Cheese and vomit-like
Streptococcus pyogenes	–	–
Pseudomonas aeruginosa	Dimethyl trisulfide	Sulfury
Escherichia coli	Indole, dimethyl sulfide	Sulfur-like

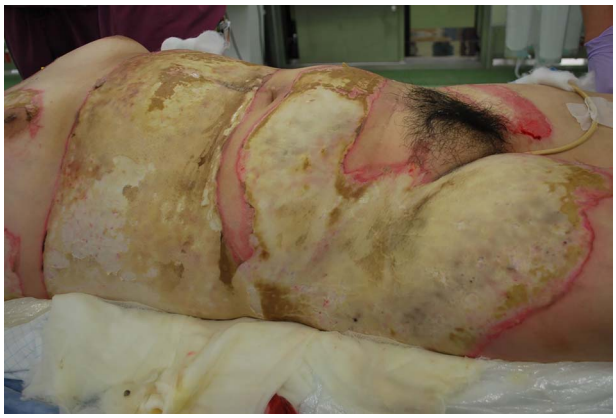

Figure 1. Burn patient with malodorous wounds

24 h period [9]. In burn patients, the most common bacterial species are *Staphylococcus aureus,* followed by *Pseudomonas aeruginosa*, including multi-resistant *Pseudomonas*, *Streptococcus pyogenes* and others [10–13]. The odour of burn wounds can be attributed to a combination of two factors (necrotic tissue and bacteria). Although anaerobic bacteria are considered the major producers of malodour, Bowler *et al*. showed that both aerobic and anaerobic bacteria contribute to unpleasant odours in the wound environment [3]. Bacterially produced malodorous molecules encompass a range of volatile metabolites such as cadaverine, sulfur, putrescine and short-chain fatty acids, including *n*-butyric, *n*-caproic, *n*-haptonic, *n*-valeric and caprylic acids [14, 15].

There is no widely used classification system for characterising odours from wounds. Caregivers or patients often describe these unpleasant odours as sour, cheesy, vomit-like, sulfur-like and foul. Interestingly, some studies have shown that specific species of bacteria produce a specific type of odour. For example, whereas foul odour is typically under the influence of the presence of gram-negative bacteria, fruity odour may indicate the presence of *Staphylococcus aureus* [16]. Shirasu *et al*. used gas chromatography/mass spectrometry to assess wound odour and demonstrated that dimethyl trisulfide (an end-product of *Pseudomonas aeruginosa*) from exudate was a common source of the 'sulfury' odour produced by wounds. [2]. Surgeons have specifically used their sense of smell to predict the infection of surgical wounds. In general, it was accepted that foul-smelling watery and bloody pus from wounds indicated the presence of pus-forming bacteria or their toxins in the tissues or blood [17]. Recognising various types of odours to identify specific pathogens is important for both chronic and acute wounds. A summary of the range of odours associated with chemical compounds frequently found in the beds of burn wounds with bacterial colonisation is shown in Table 1 [1, 18, 19].

However, as bacteria have various bacterial enzymes, their decomposition capacities vary. Thus, various metabolites are produced. Moreover, bacterial growth has four phases: lag phase, log phase, stationary phase and death phase. The volatile compound concentration of a bacterium differs at its various growth phases. This is especially seen in burn patients who experience various phases of wound healing. Therefore, it is difficult to detect pathogens that cause malodour in wounds.

Scales or tools for assessing wound odour

Most of the scales used to distinguish odour intensity use low, medium and strong as the classification categories. Tools for the subjective assessment of wound odour are the visual analogue scale, support team assessment schedule, verbal rating scale and overall valuation scale [6, 20–24]. The overall evaluation scale is generally used to evaluate the effectiveness of drugs or dressings to control odours. According to statistical analyses, the scale scores before and after treatment show improvement. This supports the responsiveness to the specific intervention. However, statistical analyses are not always possible because of differences in the responses reported by healthcare givers vs. patients [23]. Odour perception is affected by various factors, including reduced olfactory sensitivity. Therefore, some articles have described more objective instruments for measuring wound odour. However, none have gained widespread acceptance in clinical settings [16, 18, 25, 26].

Volatile organic compounds (VOCs) are a diverse group of carbon-based molecules, including sulfides, alcohols, ketones, isocyanates, aldehydes and hydrocarbons [18, 27]. VOC sampling has some advantages, such as being painless, reproducible and non-invasive. Also, some bacterial culture studies using gas chromatography/mass spectrometry have identified a lot of volatile metabolic compounds [27–29]. The electronic nose (e-nose can imitate the olfactory system of humans and recognise odourant gases [30]. Compared to traditional evaluating methods, the e-nose is potentially superior at detecting wound infections. It is noninvasive, convenient, highly efficient and it functions in real-time [31]. Tian *et al*. reported that the identification of single and mixed

components using the e-nose reached 100 and 94.4%, respectively [30]. However, the e-nose cannot provide details regarding the individual VOCs from bacteria. Further studies are expected to develop the e-nose as a clinical diagnostic tool for detecting burn wound infections to expedite appropriate management.

Non-invasive approaches to wound odour management

Metronidazole

Currently, the recommended topical therapy for wound odour control is metronidazole [32–34]. It is a topical agent that can be used for infected wound management and impair the DNA activity of radical species [21, 35]. Bower *et al*. reported a pilot study of 11 patients with malignant fungating wounds randomly distributed to receive either metronidazole gel or placebo gel [36]. Unfortunately, the study lacked sufficient power to achieve a statistically significant difference in the evaluation of odour. Watanabe *et al*. reported findings from a multi-center clinical trial of 21 breast cancer patients treated with metronidazole gel [37]. The metronidazole gel treatment successfully achieved deodorization of wounds in 20 of the 21 participants (95.25%) within 14 days. George *et al*. reported a 10-year retrospective study of topical, oral and maintenance metronidazole for the management of malignant wound odour [33]. In that study, the proportion of patients with odour problems decreased from 12.5 to 1.5% as determined by healthcare visits per patient. Although this topical antimicrobial agent has been recommended as a first-line intervention to relieve malodour [34], it has not been approved by the US Food and Drug Administration or other countries' pharmaceutical and medical device agencies for the management of burn wound odours.

Polyhexamethyl biguanide

Polyhexamethyl biguanide (PHMB) is a common antiseptic agent used in mouthwash and skin disinfectant solutions. It has broad antimicrobial activity against gram-positive/negative bacteria, fungi and viruses [38]. Since the risk of cytotoxicity and bacterial resistance to PHMB exists, it has not been widely used in wounds including burns [39]. However, in clinical settings, PHMB has been shown to be effective in the treatment of local burn infections [40]. A prospective randomized clinical study found that there was significantly faster pain reduction observed in patients treated with PHMB both before and during dressing changes, compared to silver-sulfadiazine cream. Villela-Castro *et al*. found that the topical antiseptic capacity of PHMB was as effective as metronidazole in managing malodour [32]. This double-blinded randomized study revealed that topical application of 0.8% metronidazole and 0.2% PHMB significantly reduced odour over a period of 4 days. In addition, neither topical therapy was superior in terms of odour reduction. These findings have implications for clinical practice, particularly for caregivers who cannot order metronidazole directly. Since caregivers cannot prescribe antibiotics in general, PHMB may provide an excellent alternative in these cases. It can be less costly than metronidazole for burn patients. However, we need to keep an eye on bacterial resistance to PHMB.

Sugar

Sugar has been used to reduce wound odours by preventing bacterial growth via osmosis. The benefits of sugar dressings are likely related to its high osmolality, as decreased amino acid breakdown reduces wound odour [41]. The use of granulated sugar for burn patients was first described by Knutson *et al*. in 1981. It was used to treat wounds, reduce bacterial contamination and allow for rapid debridement of eschar [42]. Murandu *et al*. reported an *in vitro* study that evaluated the antimicrobial effects of granulated sugar [43]. They demonstrated that sugar inhibits bacterial growth at high concentrations *in vitro*. Moreover, a pilot clinical study showed that pain and malodor were markedly reduced in all participating patients by using granulated sugar for 21 days.

Sugar-based wound dressings have the advantage of easy application. However, cost-effectiveness is the greatest advantage. Chiwenga *et al*. reported a simple sugar dressing cost of US $0.04 per dressing [44]. The dressing was easy to apply and did not require frequent changes, as its odour-reducing capability was maintained over several days. However, this study did not measure bactericidal activity.

Honey

Honey has been used for a variety of wounds over the years because of its broad-spectrum antimicrobial and wound-healing activities [45]. Nair reported a prospective case series of patients with diabetic foot ulcers treated with medical-grade honey [46]. This case series demonstrated that honey helped to draw out lymph fluid, clean the infected wounds and stimulate autolytic debridement of slough and necrotic tissue. In addition, there was the remarkable fact that the high sugar content of honey did not affect blood glucose levels in diabetic patients. Bayron *et al*. reported medical-grade honey as an alternative to surgical debridement [47]. In this study, patients requiring operative debridement of necrotic tissue had a high risk of surgical complications. However, the use of honey facilitated autolytic debridement and the wounds healed without surgery.

The benefits of honey for burn wounds have been well described from the perspective of efficiency [48, 49]. Despite these effects, the application of honey is reserved and often limited to later lines of therapy. This is because caregivers or medical staff tend to adhere to conventional treatments including metronidazole or antibiotics. Therefore, more clinical trials using honey are required for it to become a mainstay for odour-control treatment.

Iodine

Iodine has an indirect effect on wound odour by reducing the bacterial bioburden in colonized wounds. In the situation of treating a biofilm infection (e.g. pressure ulcer or diabetic

foot ulcer), it is necessary to apply an appropriate topical care capable of preventing the formation of bacterial biofilms. It is well known that iodine can penetrate biofilms and destroy nuclear structures in bacteria [50, 51]. However, iodine itself has a uniquely unpleasant odour. In addition, iodine can be cytotoxic to the wound environment. Therefore, iodine is not recommended as an option for odour control, especially in patients with burns.

Silver

Silver is commonly used as an adjunct in burn wound care due to its strong antimicrobial activity. While silver metal (Ag) has no medicinal activity, silver ions (Ag^+) have a broad antimicrobial spectrum and are cytotoxic to bacteria via nucleic acid denaturation [52]. Isolated antibiotic-resistant bacteria have rarely been reported in burn patients [53]. Silver directly reduces odour via its antimicrobial properties. However, silver itself has the potential of impairing wound healing by exerting toxic effects on fibroblasts and keratinocytes in the wound environment [54]. Therefore, the proper use of silver-containing dressings is essential for optimizing burn wound healing. In extensive burns, silver dressings are beneficial for reducing bacteria. However, they lead to slower epithelialization, higher costs and increased pain. We believe that silver is not suitable for odour control in burn wounds.

Green tea

Green tea for the treatment of wounds has been evaluated in clinical studies over the past few decades. Since a lot of studies have shown that the polyphenolic compounds in green tea have antibacterial properties, a systematic review of the effectiveness of green tea for odour production has been conducted [55]. Green tea was shown to be as effective as metronidazole in reducing the odour of fungating malignant wounds. In addition, we can see no risk of drug resistance due to the prolonged use of green tea as there is with metronidazole powder. QOL for cancer patients and their caregivers is enhanced through the effectiveness of odour control. Additionally, green tea bags are more affordable than other commercial dressing materials. However, the effectiveness of using green tea to eliminate odour from burn wounds must be assessed because there is no evidence in both acute and non-acute burns. A clinical trial using green tea for odour control must be conducted in patients with burns to confirm its effectiveness.

Charcoal (direct and indirect applications)

Wound malodour may be addressed using a direct or indirect approach. The direct approach focuses on absorbing or trapping the VOCs that can create malodour. In distinction to the direct approach, the indirect approach seeks to reduce odours by lowering the bacterial bioburden in the wounds. Charcoal can be used for either direct or indirect malodorous management. Activated carbon is a charcoal derivative that is typically made from natural substances such as wood. It can provide a large area for the adsorption of various types of gases [1]. Although activated charcoal dressings have been proven to be comfortable and effective for managing wound odours with level of evidence 4 [56], there is no specific evidence of this in burn wounds.

Rice bran (direct and indirect applications)

Rice bran is the most abundant and valuable byproduct produced during the rice milling process [57, 58]. Taniguchi and co-workers identified multifunctional cationic peptides from the enzymatic hydrolysates of rice bran proteins with antimicrobial activities [59, 60]. They found that these peptides were non-toxic agents with multiple functions for wound healing *in vitro*.

In addition, rice bran contains microorganisms that have been shown to effectively reduce bacteria that have deodorant effects *in vitro* [61]. One pilot case study evaluated the anti-odour effects of a dressing containing rice bran in the management of malodorous acute or chronic wounds, including burns [20]. Patients were assessed at two time points upon entry into the study: just before the application of rice bran sheets and 7 days after the application. These preliminary data suggested that the rice bran sheets were effective with no side effects in burn patients. However, as the number of patients in this pilot study was only 15, specific conclusions from the data regarding wounds of varying aetiologies should be drawn with caution.

Invasive approach (debridement) to wound odour management

Surgery

Simple debridement of necrotic tissues is the most effective procedure for eliminating odours. However, one potential drawback of debridement surgery is that surgical stress may induce the production of various cytokines and growth factors [62]. This can worsen the general condition of burn patients. Therefore, physicians must carefully consider all options prior to debridement. Several criteria are indispensable for debridement [6]. First, surgery must effectively reduce the patient or caregiver's distress and improve their circumstances. Second, the patient or patient's family should understand their condition and voluntarily desire to receive invasive treatment (debridement). Third, surgeons should perform a simple and easy debridement over a short period with as little blood loss as possible. This is in consideration of the poor general condition of burn patients.

Laser treatment may reduce the burden of burn malodour. The Er,Cr:YSGG solid-state laser has been shown to be effective in reducing oral biofilms [63–65]. Krepsi *et al*. performed laser tongue debridement in a prospective randomized controlled study in burn patients with halitosis, which is caused by a variety of systemic and local factors [66]. This study investigated the potential function of the Er,Cr:YSGG laser in

the treatment of halitosis by targeting the tongue. However, so far, other invasive treatments for odorous burn wounds have not advanced.

Maggot therapy

Acute and non-acute burns have occasionally been debrided with maggots. Laboratory data have demonstrated that maggot digestive extracts dissolve eschar effectively in a rat burn model [67–69]. Maggot debridement therapy (MDT) involves the use of medical-grade maggots of the fly *Lucilia sericata* for wound debridement. MDT is useful only for wounds on the body's surface. The fact that maggots can separate the necrotic tissue from the wound bed (living tissue) is the biggest advantage of MDT. This results in less bleeding during surgical debridement. Mumcuoglu reported that with the clinical application of maggots for wound care [70], significant or complete debridement of the necrotic tissue was achieved in 80–95% of cases. Moreover, the offensive odour emanating from the necrotic tissue decreased significantly. A randomized controlled trial was conducted to compare MDT to topical application of silver sulfadiazine and surgical debridement and topical application of silver sulfadiazine in 19 patients [71]. MDT was as effective as surgical debridement associated with topical silver sulfadiazine during wound debridement and size reduction. However, the number of odours increased in the MDT group. More controlled clinical studies of MDT for burn treatment, including odour management, are required to determine the efficacy and safety of this controversial method.

In burn patients with malodorous wounds, treating the infection ultimately eliminates odour. However, some burn patients with odorous wounds cannot undergo invasive management because of their systemic condition. The optimal drug doses and dressings used to ensure the cost-effectiveness and efficacy are poorly understood. Moreover, such treatments have provided less than satisfactory results. In many cases, burn patients have no choice but to endure undesirable symptoms. More research is required regarding the causes of odorous burn wounds and how to treat them effectively.

In addition, although wound management has recently improved, evidence and knowledge related to natural substances for controlling wound odour are limited. Further research, including basic studies on these cost-effective natural substances for treating odorous burn wounds, are required.

Authors' contributions

K.H. and S.Y. wrote the manuscript. All authors have read and approved the final manuscript.

Ethics approval and consent to participate

Patient consent for inclusion in the Shimane University Hospital Registry includes the potential use of patient information for research purposes and publications.

Competing interests

None declared.

References

1. Akhmetova A, Saliev T, Allan IU, Illsley MJ, Nurgozhin T, Mikhalovsky S. A comprehensive review of topical odor-controlling treatment options for chronic wounds. *J Wound Ostomy Continence Nurs*. 2016;43:598–609.
2. Shirasu M, Nagai S, Hayashi R, Ochiai A, Touhara K. Dimethyl trisulfide as a characteristic odor associated with fungating cancer wounds. *Biosci Biotechnol Biochem*. 2009;73:2117–20.
3. Bowler PG, Davies BJ, Jones SA. Microbial involvement in chronic wound malodour. *J Wound Care*. 1999;8:216–8.
4. Dowsett C. Malignant fungating wounds: assessment and management. *Br J Community Nurs*. 2002;7:394–400.
5. Alexander S. Malignant fungating wounds: managing malodour and exudate. *J Wound Care*. 2009;18:374–82.
6. Hayashida K, Murakami C, Fujioka M. Palliative surgery for cutaneous ulcers improves the symptoms of patients with terminal cancer. *J Palliat Med*. 2013;16:831–2.
7. D'Abbondanza JA, Shahrokhi S. Burn infection and burn sepsis. *Surg Infect (Larchmt)*. 2021;22:58–64.
8. Dokter J, Brusselaers N, Hendriks WDH, Boxma H. Bacteriological cultures on admission of the burn patient: to do or not to do, that's the question. *Burns*. 2016;42:421–7.
9. Edwards-Jones V, Greenwood JE. What's new in burn microbiology? *Burns*. 2003;29:15–24.
10. Li L, Dai JX, Xu L, Chen ZH, Li XY, Liu M, *et al.* Antimicrobial resistance and pathogen distribution in hospitalized burn patients: a multicenter study in Southeast China. *Medicine*. 2018;97:e11977.
11. Wang LF, Li JL, Ma WH, Li JY. Drug resistance analysis of bacterial strains isolated from burn patients. *Genet Mol Res*. 2014;13:9727–34.
12. Fransén J, Huss FR, Nilsson LE, Rydell U, Sjöberg F, Hanberger H. Surveillance of antibiotic susceptibility in a Swedish burn Center 1994-2012. *Burns*. 2016;42:1295–303.
13. Yeong EK, Sheng WH, Hsueh PR, Hsieh SM, Huang HF, Ko AT, *et al.* The wound microbiology and the outcomes of the systemic antibiotic prophylaxis in a mass burn casualty incident. *J Burn Care Res*. 2020;41:95–103.
14. Dankert J, Holloway Y, Bouma J, van der Werf J, Wolthers BG. Metronidazole in smelly gynaecological tumours. *Lancet*. 1981;2:1295.
15. Holloway S. Recognising and treating the causes of chronic malodorous wounds. *Prof Nurse*. 2004;19:380–4.
16. Ousey K, Roberts D, Gefen A. Early identification of wound infection: understanding wound odour. *J Wound Care*. 2017;26:577–82.
17. Manring MM, Hawk A, Calhoun JH, Andersen RC. Treatment of war wounds: a historical review. *Clin Orthop Relat Res*. 2009;467:2168–91.
18. Ashrafi M, Bates M, Baguneid M, Alonso-Rasgado T, Rautemaa-Richardson R, Bayat A. Volatile organic compound detection as a potential means of diagnosing cutaneous wound infections. *Wound Repair Regen*. 2017;25:574–90.
19. Fromantin I, Seyer D, Watson S, Rollot F, Elard J, Escande MC, *et al.* Bacterial floras and biofilms of malignant wounds associated with breast cancers. *J Clin Microbiol*. 2013;51:3368–73.

20. Hayashida K, Ogino R, Yamakawa S, Shirakami E. Antiodor effects of rice bran sheets in patients with malodorous wounds. *J Palliat Med*. 2020;23:750–1.
21. Paul JC, Pieper BA. Topical metronidazole for the treatment of wound odor: a review of the literature. *Ostomy Wound Manage*. 2008;54:18–27 quiz 8-9.
22. Lund-Nielsen B, Adamsen L, Kolmos HJ, Rørth M, Tolver A, Gottrup F. The effect of honey-coated bandages compared with silver-coated bandages on treatment of malignant wounds-a randomized study. *Wound Repair Regen*. 2011;19:664–70.
23. Holloway S, Bale S, Harding K, Robinson B, Ballard K. Evaluating the effectiveness of a dressing for use in malodorous, exuding wounds. *Ostomy Wound Manage*. 2002;48:22–8.
24. Upright CA, Salton C, Roberts F, Murphy J. Evaluation of Mesalt dressings and continuous wet saline dressings in ulcerating metastatic skin lesions. *Cancer Nurs*. 1994;17:149–55.
25. Lucas Y, Niri R, Treuillet S, Douzi H, Castaneda BA. Wound size imaging: ready for smart assessment and monitoring. *Adv Wound Care*. 2020. Epub ahead of print.
26. Godwin ZR, Bockhold JC, Webster L, Falwell S, Bomze L, Tran NK. Development of novel smart device based application for serial wound imaging and management. *Burns*. 2013;39:1395–402.
27. Probert CS, Ahmed I, Khalid T, Johnson E, Smith S, Ratcliffe N. Volatile organic compounds as diagnostic biomarkers in gastrointestinal and liver diseases. *J Gastrointestin Liver Dis*. 2009;18:337–43.
28. Mellors TR, Rees CA, Franchina FA, Burklund A, Patel C, Hathaway LJ, *et al*. The volatile molecular profiles of seven Streptococcus pneumoniae serotypes. *J Chromatogr B Analyt Technol Biomed Life Sci*. 2018;1096:208–13.
29. Storer MK, Hibbard-Melles K, Davis B, Scotter J. Detection of volatile compounds produced by microbial growth in urine by selected ion flow tube mass spectrometry (SIFT-MS). *J Microbiol Methods*. 2011;87:111–3.
30. Tian FC, Xu XT, Shen Y, Yan J, He QH, Ma JW, *et al*. Detection of wound pathogen by an intelligent electronic nose. *Sen s Mater*. 2009;21:155–66.
31. Darwin ES, Thaler ER, Lev-Tov HA. Wound odor: current methods of treatment and need for objective measures. *G Ital Dermatol Venereol*. 2019;154:127–36.
32. Villela-Castro DL, Santos VLCG, Woo K. Polyhexanide versus metronidazole for odor management in malignant (fungating) wounds: a double-blinded, randomized, clinical trial. *J Wound Ostomy Continence Nurs*. 2018;45:413–8.
33. George R, Prasoona TS, Kandasamy R, Cherian R, Celine T, Jeba J, *et al*. Improving malodour management in advanced cancer: a 10-year retrospective study of topical, oral and maintenance metronidazole. *BMJ Support Palliat Care*. 2017;7:286–91.
34. Castro DL, Santos VL. Controlling wound odor with metronidazole: a systematic review. *Rev Esc Enferm USP*. 2015;49:858–63.
35. Trend MA, Jorgensen MA, Hazell SL, Mendz GL. Oxidases and reductases are involved in metronidazole sensitivity in helicobacter pylori. *Int J Biochem Cell Biol*. 2001;33:143–53.
36. Bower M, Stein R, Evans TR, Hedley A, Pert P. Coombes RC. A double-blind study of the efficacy of metronidazole gel in the treatment of malodorous fungating tumours. *Eur J Cancer*. 1992;28A:888–9.
37. Watanabe K, Shimo A, Tsugawa K, Tokuda Y, Yamauchi H, Miyai E, *et al*. Safe and effective deodorization of malodorous fungating tumors using topical metronidazole 0.75% gel (GK567): a multicenter, open-label, phase III study (RDT.07.SRE.27013). *Support Care Cancer*. 2016;24:2583–90.
38. McDonnell G, Russell AD. Antiseptics and disinfectants: activity, action, and resistance. *Clin Microbiol Rev*. 1999;12:147–79.
39. Hübner NO, Kramer A. Review on the efficacy, safety and clinical applications of polihexanide, a modern wound antiseptic. *Skin Pharmacol Physiol*. 2010;23:17–27.
40. Piatkowski A, Drummer N, Andriessen A, Ulrich D, Pallua N. Randomized controlled single center study comparing a polyhexanide containing bio-cellulose dressing with silver sulfadiazine cream in partial-thickness dermal burns. *Burns*. 2011;37:800–4.
41. Wu DJ, Figenshau K, Rajpara A, Aires DJ, Elston D. Sugar-based dressings for chronic wound care. *J Am Acad Dermatol*. 2020;82:e73.
42. Knutson RA, Merbitz LA, Creekmore MA, Snipes HG. Use of sugar and povidone-iodine to enhance wound healing: five year's experience. *South Med J*. 1981;74:1329–35.
43. Murandu M, Webber MA, Simms MH, Dealey C. Use of granulated sugar therapy in the management of sloughy or necrotic wounds: a pilot study. *J Wound Care*. 2011;20:206 208, 210 passim.
44. Chiwenga S, Dowlen H, Mannion S. Audit of the use of sugar dressings for the control of wound odour at Lilongwe central hospital, Malawi. *Trop Doct*. 2009;39:20–2.
45. Lusby PE, Coombes A, Wilkinson JM. Honey: a potent agent for wound healing? *J Wound Ostomy Continence Nurs*. 2002;29:295–300.
46. Nair HKR, Tatavilis N, Pospíšilová I, Kučerová J, Cremers NAJ. Medical-grade honey kills antibiotic-resistant bacteria and prevents amputation in diabetics with infected ulcers: a prospective case series. *Antibiotics (Basel)*. 2020;19:529.
47. Bayron J, Gallagher K, Cardenas L. Medical-grade honey as an alternative to surgery: a case series. *Wounds*. 2019;31:36–40.
48. Vandamme L, Heyneman A, Hoeksema H, Verbelen J, Monstrey S. Honey in modern wound care: a systematic review. *Burns*. 2013;39:1514–25.
49. Zbuchea A. Up-to-date use of honey for burns treatment. *Ann Burns Fire Disasters*. 2014;27:22–30.
50. Bigliardi PL, Alsagoff SAL, El-Kafrawi HY, Pyon JK, Wa CTC, Villa MA. Povidone iodine in wound healing: a review of current concepts and practices. *Int J Surg*. 2017;44:260–8.
51. Jeronimo LP, Choi MR, Yeon SH, Park SK, Yoon YH, Choi SH, *et al*. Effects of povidone-iodine composite on the elimination of bacterial biofilm. *Int Forum Allergy Rhinol*. 2020;10:884–92.
52. Abboud EC, Legare TB, Settle JC, Boubekri AM, Barillo DJ, Marcet JE, *et al*. Do silver-based wound dressings reduce pain? A prospective study and review of the literature. *Burns*. 2014;40:S40–7.
53. Percival SL, Thomas J, Linton S, Okel T, Corum L, Slone W. The antimicrobial efficacy of silver on antibiotic-resistant bacteria isolated from burn wounds. *Int Wound J*. 2012;9:488–93.
54. Khansa I, Schoenbrunner AR, Kraft CT, Janis JE. Silver in wound care-friend or foe?: a comprehensive review. *Plast Reconstr Surg Glob Open*. 2019;7:e2390.
55. Wiese F, Kutschan S, Doerfler J, Mathies V, Buentzel J, Buentzel J, *et al*. Green tea and green tea extract in oncological treatment: a systematic review. *Int J Vitam Nutr Res*. 2021;17:1–13.

56. Haynes JS. A clinical evaluation of a charcoal dressing to reduce malodour in wounds. *Br J Nurs*. 2018;27:S36–42.
57. Park HY, Lee KW, Choi HD. Rice bran constituents: immunomodulatory and therapeutic activities. *Food Funct*. 2017;8:935–43.
58. Julião M, Calaveiras P, Costa E, Daniel S, Samorinha C, Faria de Sousa P. Antiodor effect of milled brown rice sheets in a malodorous cancer wound: a case report. *J Palliat Med*. 2021;24:175–6.
59. Taniguchi M, Ochiai A. Characterization and production of multifunctional cationic peptides derived from rice proteins. *Biosci Biotechnol Biochem*. 2017;81:634–50.
60. Taniguchi M, Saito K, Aida R, Ochiai A, Saitoh E, Tanaka T. Wound healing activity and mechanism of action of antimicrobial and lipopolysaccharide-neutralizing peptides from enzymatic hydrolysates of rice bran proteins. *J Biosci Bioeng*. 2019;128:142–8.
61. Fan YV, Lee CT, Klemeš JJ, Chua LS, Sarmidi MR, Leow CW. Evaluation of effective microorganisms on home scale organic waste composting. *J Environ Manage*. 2018;216:41–8.
62. Podnos YD, Wagman LD. The surgeon and palliative care. *Ann Surg Oncol*. 2007;14:1257–63.
63. Rai M, Spratt D, Gomez-Pereira PR, Patel J, Nair SP. Light activated antimicrobial agents can inactivate oral malodour causing bacteria. *J Breath Res*. 2016;10:046009.
64. Kasić S, Knezović M, Beader N, Gabrić D, Malčić AI, Baraba A. Efficacy of three different lasers on eradication of enterococcus faecalis and Candida albicans biofilms in root canal system. *Photomed Laser Surg*. 2017;35:372–7.
65. Bernardi S, Continenza MA, Al-Ahmad A, Karygianni L, Follo M, Filippi A, *et al.* Streptococcus spp. and fusobacterium nucleatum in tongue dorsum biofilm from halitosis patients: a fluorescence in situ hybridization (FISH) and confocal laser scanning microscopy (CLSM) study. *New Microbiol*. 2019;42:108–13.
66. Krespi YP, Kizhner V, Wilson KA, Sivriver A, Low S, Khosravi Y, *et al.* Laser tongue debridement for oral malodor-a novel approach to halitosis. *Am J Otolaryngol*. 2021;42:102458.
67. Namias N, Varela JE, Varas RP, Quintana O, Ward CG. Biodebridement: a case report of maggot therapy for limb salvage after fourth-degree burns. *J Burn Care Rehabil*. 2000;21:254–7.
68. Vistnes LM, Lee R, Ksander GA. Proteolytic activity of blowfly larvae secretions in experimental burns. *Surgery*. 1981;90:835–41.
69. Sherman RA, Shapiro CE, Yang RM. Maggot therapy for problematic wounds: uncommon and off-label applications. *Adv Skin Wound Care*. 2007;20:602–10.
70. Mumcuoglu KY. Clinical applications for maggots in wound care. *Am J Clin Dermatol*. 2001;2:219–27.
71. Contreras-Ruiz J, Fuentes-Suárez A, Arroyo-Escalante S, Moncada-Barron D, Sosa-de-Martínez MC, Maravilla-Franco E, *et al.* Comparative study of the efficacy of larva therapy for debridement and control of bacterial burden compared to surgical debridement and topical application of an antimicrobial. *Gac Med Mex*. 2016;152:78–87.