The properties of an activated carbon-containing agarose film for the amelioration of 2-amino acetophenone malodour as produced in chronic wounds infected with *Pseudomonas aeruginosa*

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Abstract (250 words)

Malodorous chronic wounds are associated with significant patient morbidity and can be responsible for patient social isolation and depression. A new material with favourable physical properties for easy application to difficult-to-dress bodily surfaces was tested for its ability to reduce the human detection of malodorous 2-aminoacetophenone, the dominant odour associated with chronic ulcers infected with *Pseudomonas aeruginosa*. The material consisted of activated carbon (AC) particles held within a plasticised agarose (PA) film. This material, PA-AC, was relatively thin and could be folded and cut to shape without appreciable loss of the AC particulates. In a study using human volunteers, the intensity of 2-AAP odour was (strongly) significantly lower for the PA-AC material when compared with controls. Additionally, mechanical studies indicated that the presence of AC did not alter the maximum load, extension at maximum load, or percentage elongation of the PA films, with no statistically significant difference between PA-AC and PA. Supplementation of the agarose films (with or without AC) with carboxymethylcellulose (CMC) enabled fluid handling to be increased by 176% and 163%, respectively.

PA-AC, PA and PA-AC-CMC, PA-CMC allowed water vapour transmission at a rate previously reported to promote wound healing, while preventing tissue maceration caused by excessive sweat retention. A range of agarose films with variable odour and fluid handling properties are envisaged for further development towards wound management applications.

Graphical Abstract

Key words (5)

Activated-carbon, dressing, malodour, wound, ulcer

Introduction

Chronic wounds are breaks to the epidermis that fail to heal in a timely manner or reoccur frequently. There are numerous medical conditions that are associated with chronic wound occurrence, these can include diabetes, peripheral arterial disease, venous insufficiency and long-term immobilisation [1-3]. A study investigating the costs associated with chronic ulceration in Wales [4] reported that chronic wounds were found to affect 6% of the population, representing 5.5% of the total expenditure of the Welsh health service budget. Kerr et al [1] estimated the costs of diabetes-related ulceration and amputation in 2014 – 2015 to be between £837 - £962M; with 90% of this expenditure being linked to ulceration costs. Thus, the true overall financial burden of ulceration expenditure is vast. A typical Clinical Commissioning Group (CCG)/health board was predicted to manage approximately 23,200 wounds per annum by 2019/2020 [5]. Guest et al [6] reported that 2.2 million adults in the UK had a wound during 2012 / 2013, a situation which was expected to increase with the current aging population. Venous leg ulcerations are the most common type of leg ulceration, affecting 1% of the UK population and 3% over the age of 80. Healing times of such chronic wounds are notably variable with 97% reported to be healed within 12 months, and 7% of the remainder still ulcerated after 5 years [2]. When considering diabetic foot ulceration, many ulcers persist for months; some never heal, and some lead to amputation [1]. It has been well documented that the presence of a chronic wound can have significant impacts on the health of a patient. These can range from wound infection [7], cellulitis and sepsis [8], amputation and loss of life due to spreading infections [1, 8].

Chronic wounds are composed of tissue at various stages of devitalisation/regeneration and contaminating bacteria may be present [9]. The potential of these bacteria to cause infection and further deterioration of the wound depends on bacterial virulence and the immune status of the patient.Current research is focused on developing materials for clearing wound infections [10, 11, 12], and for modulation of the excessive immune response present in chronic wounds {13, 14] to allow complete resolution of the wound. However, due to the current unavailability of such products in clinic, there is a need for the development of materials to manage the unpleasant odours produced by such wounds. Such malodours can have significant negative impacts on patient wellbeing 9-15], such as depression, social isolation and reduced quality of life [16].

Pseudomonas aeruginosa is well known to cause wound infections [9]. This bacterium produces volatile organic compounds (VOCs), such as dimethyl sulphide (DMS), dimethyl disulphide (DMDS), 2.5-dimethylpyrazine (2,5-DMP) 1-undecene, 2-nonanone and 2'– aminoacetophenone (2-AAP) [17]. 2'-AAP is responsible for the characteristic grape-like odour produced by *P. aeruginosa*. Anecdotal reports suggest this odour can readily be detected in wards where patients with chronic leg ulcers infected with *P. aeruginosa* are present.

Current established clinical approaches for the management of infected chronic wounds consist of direct antimicrobial therapy to tackle the infection, including the use of antimicrobial-infused wound dressings and the application of odour adsorbent wound dressings to contain the liberated odours [18]. The Wound Care Handbook [19] produced by the Journal of Wound Care documents the dressings currently available for use on wounds and has a section designated to odour control. There are six products described for use on wounds that have the specific aim of helping to manage wound odour. Five of these dressings contain activated charcoal/carbon (AC). The odour adsorbing capacity of AC is well documented and is due to its porous structure which gives it an exceptionally high surface area to volume ratio thus enabling the capture of small molecules [20].

It is clinically useful to have dressings that are easy to apply and that can be cut to shape without loss of structural integrity and functional quality, especially when dressing difficult areas. Of the five AC-containing dressings listed in the Wound Care Handbook [19], three need to be used as manufactured and cannot be cut to conform to difficult anatomical positions, potentially influencing the frequency of their use and causing discomfort to the patient and increasing costs - leaving only two listed products that can be cut to the required size. All the dressings listed can be used as primary dressings with some being reported to require an additional secondary dressing..

A study by Gethin et al [21] highlighted the need for improved odour adsorbing products to be available on the market. It was reported that only 48.4% of clinicians from a multinational study considered currently available charcoal dressings as being effective at managing wound odours.

A candidate dressing material intended to manage wound malodour was developed for this study. This consisted of a base film of plasticised agarose that was formulated using the method developed by Shamsuri and Daik [22], supplemented with activated carbon and, in some iterations, carboxymethylcellulose (CMC). The aim of this study was therefore to evaluate anAC-containing film composite for its ability to capture malodorous 2-AAP, characteristic of *P. aeruginosa* wound infections. In addition, the fluid handling capacity and the mechanical properties of this material, and additional CMC-containing forms, were investigated to ascertain the potential of these materials for clinical application.

Materials and methods

PA-AC film and control material

To manufacture the PA-AC film, 5 g agarose, 5 g ionic liquid (2:1 molar ratio of choline chloride and urea) and 0.5 g activated carbon particles (Norit A SUPRA EUR) were each added to a 200 ml volume of deionised water. The mixture was boiled to dissolve the agarose, cooled to 60ºC, then cast into a 28 cm^2 polystyrene dish and allowed to set at room temperature. A polytetrafluoroethylene (PTFE) cork-borer of 48 mm diameter was used to excise discs which were then dried on a PTFE-coated tray at 37ºC for 24 h to produce the PA-AC films. A PA control film was produced using the same method, but without the AC particles. Similarly, films intended for moisture handling were supplemented with CMC (Sigma, UK), with 5 g incorporated into the formulation mix above, with or without AC (PA-AC-CMC and PA-CMC).

Fluid handling tests on PA-AC and PA (+/- CMC)

To evaluate the fluid handling capacity of the materials constructed, the guidelines set out in 'BS EN 13726-1, Test methods for Primary Wound Dressings: Aspects of Absorbency' [23] were followed to measure the removal of artificial exudate through absorbency and permeability (also known as moisture vapour transmission). The PA-AC and control materials were sectioned and applied to a standard Paddington cup with an opening of 10 cm^2 which was covered by the material. The cup was pre-weighed with the sample material (W1). Artificial exudate (30 ml NaCl solution) was introduced into the cup and a lid applied to form a closed system and weighed (W2). Following 24-hour incubation at 37ºC, the cup was removed and allowed to cool to ambient temperature for 30 minutes. The cup

and contents were then weighed (W3) to calculate exudate handled via moisture vapour transmission. The lid of the cup was removed, and remnant exudate drained. The cup was then re-weighed (W4) to calculate the mass of exudate absorbed by the wound dressing. This procedure was repeated for a total of six times per sample type.

Mechanical tests on PA-AC and PA

To establish the mechanical properties of the films, each formulation was prepared in a sheet form, measuring 25 mm by 100 mm, to ensure a 50 mm test strip with 25 mm either side for attaching the clamps.

The materials were then tested using an Instron tensile machine 1 kN load cell. Initial test samples were found to tear at the edge when clamped into the standard sample grips, therefore new grips were manufactured with a 4 mm radius using 3D printing. Each sample type was tested with six replicates, with results recorded for extension at maximum load, and percentage elongation.

Odour adsorption testing of PA-AC and PA using human nose assessment

Ethical approval was obtained via the University of Brighton Cross School Research Ethics Committee (CREC). All participants were required to be over the age of 18. Those presenting with symptoms of a respiratory tract infection or with diagnosis of a condition affecting the olfactory senses were excluded from this repeated measures, quantitative study of 53 volunteers.

85 mm diameter polystyrene petri dishes containing an odourless gel of 1% agarose (Molecular Biology Grade, Fisher Scientific, UK) had a 25 mm diameter central portion of the gel removed and replaced with a 1% agarose plug, either unsupplemented (A, B & C, Table 1), or supplemented with 2-AA (D, E & F Table 1). The supplemented gel was made by dissolving three tablets of 2-AAP (Aroxa, Cara Technology Ltd, UK) in 500ml of a molten 1% agarose solution. The resultant 25 mm diameter gel inserts had a 2-AAP content of 0.013 mg. Samples were either uncovered (A&D), or covered with PA (B&D), or PA-AC (C&F), see Table 1.

Table I. Set up of human nose assessment of 2-AA odour breakthrough

	No material	**PA film**	**PA-AC film**
No odour	**A**	**B**	**C**
Odour	**D**	**E**	**F**

Participants were presented with the six different containers labelled A-F, in a random order. The contents were hidden from the participants by either eye closure or by the wearing of a blindfold. A member of the research team presented the containers, and the participants were asked to make an olfactory assessment of the contents. Each participant was permitted to sniff the contents of each container up to three times with new samples being used for each participant.

Samples were then ranked by the participants as having: no odour, slight odour, or strong odour. These responses were assigned numerical values of 0, 1 or 2, respectively.

Statistical analyses

For fluid handling and mechanical properties testing, differences between PA-AC and PA in terms of moisture vapour loss (M), fluid absorption (A), maximum load (N) and percentage elongation (%) were statistically tested using a series of Wilcoxon rank sum tests, as data deviated from a Gaussian distribution and variances were unequal.

For the odour adsorption tests, statistical analysis was performed using R version 3.61 (The R Foundation for Statistical Computing 2019, Vienna, Austria). A statistical comparison of human nose assessment of 2-AAP odour breakthrough from composite films of different formulation was conducted using logistic regression within a generalised linear model (GLM) framework where the response variable was measured as no odour/odour (0,1) and the explanatory variable was categorical (treatment) with three levels (no dressing, control PA, PA-AC).

Results

Plasticised agarose films with or without activated carbon (PA-AC and PA, respectively), were produced. The PA control film was transparent, and the PA-AC material opaque (black in colour). Both films were thin and flexible after drying, with both being amenable to being cut to a required shape, and, in the case of PA-AC, without appreciable loss of AC.

Figure 1. Fluid handling tests of the film formulations PA-AC and PA (+/- CMC)

Bars with the same letters denote no significant differences (Wilcoxon rank sum test; W = always 25, p always >> 0.05); bars with different letters denote a statistically significant difference at the 99% level (Wilcoxon rank sum test; W = always 0.34, p always <0.01).

The results of the fluid handling tests indicated that there was no statistical difference in moisture vapour loss (M) between all dressing formulations tested (Figure 1). Further analysis of the fluid handling rates indicated that fluid absorption (A) was significantly lower for PA-AC relative to PA (Figure 1), with 0.48 g and 0.63 g fluid absorbed, respectively. The fluid absorbed by the materials containing the CMC addition was significantly greater when compared with the materials without CMC. No statistically significant difference was observed between the CMC-containing films (Figure 1). The combined fluid handling capacity (M+A) of PA-AC and PA was similar, being 2.30 g and 2.38 g, respectively. The films containing CMC (PA-AC-CMC and PA–CMC) absorbed significantly more fluid than their non-CMC-containing counterparts, with values of 4.05 g and 3.88 g, respectively, but there was no statistically significant difference between the combined fluid handling capacities of the two CMC-containing products (Figure 1).

Mechanical testing of PA and PA-AC

Table 2. Mechanical properties of PA and PA-AC films

	Extension at maximum load (mm)	**Maximum load (M)**	**Elongation (%)**
PA	21.67 (SD +/- 1.41)	28.68 (SD +/- 1.97)	43.33 (SD +/- 2.85)
PA-AC	21.17 (SD +/- 1.66)	30.69 (SD +/- 2.42)	42.34 (SD +/- 3.32)

SD = standard deviation

The PA-AC material had an extension under load of 21.17 mm while the PA control material had a value of 21.67 mm (Table 2). The maximum load of the PA-AC material was 30.69 N, compared with 28.68 N for the PA control film. The percentage elongation observed in the material samples was 42.34% for the PA-AC material and 43.34% for PA alone.

None of the above comparisons revealed any statistically significant difference between PA-AC and PA for all mechanical measures (extension at maximum load, maximum load and percentage elongation) [Wilcoxon rank sum test, W always < 24.5, p always » 0.05].

Human nose assessment of 2-AAP breakthrough from agarose films

The probability of 2-AAP odour detection by the human nose was significantly lower for the PA-AC material when compared with all other test parameters (Figure 2). Samples covered with films containing activated carbon had the lowest reported odour intensity including those spiked with 2-AAP, as well as those without. No statistical difference in the reported odour intensity of 2-AAP-spiked samples was apparent between uncovered samples and those covered with the control plasticised agarose, with the highest recorded odour values occurring in these variables (Figure 2). A strongly significant reduction in odour intensity was reported when 2-AAP-spiked samples were covered with PA-AC. compared with spiked samples, uncovered or covered with control PA (Figure 2).

Figure 2. The efficacy of PA-AC material in masking 2-amino acetophenone odour as assessed by human volunteers.

Bars with same letters denote no significant difference; bars with different letters denote a statistically significant difference at the 95% level. Comparisons between bars with different numbers additionally denote statistical significance at the P<0.001 level i.e., strongly significant (logistic regression, deviance = 103.71, df = 5, p <<0.001).

Discussion

A thin and flexible material containing activated carbon was produced, these favourable physical properties being suggestive of potential for the material to be applied to chronic wounds situated on difficult to dress contoured areas such as ears, joints, hands, feet, heels and peri-stomal areas [24]. The PA-AC and the PA films could also be augmented with CMC to increase the fluid handling capacities of these materials.

The AC particles were retained within the material with no appreciable release of the AC upon cutting the material. The Wound Care Handbook states that there are currently six other odour control dressings available on the wound care market [19]. The formulation of one of these products is a gel (Anabact) and thus is not comparable to the materials developed here. Of the other AC dressings on the market, two of the products can be cut to size (Askina Carbosorb & Clinisorb), and three products are unable to be cut (Actisorb Silver 220, Carboflex and Odolock- Activated Carbon). There is a note on the 'indications of use' leaflets for the latter three products to not cut the material, as this permits the carbon or charcoal particles to enter the wound which may cause wound bed discolouration [19]. Additional clinical complications that can occur when dressings are not able to be 'cut to size' is increased dressing bulk and the formation of creases over already vulnerable ulceration sites. This lack of versatility would likely mean that a clinician will prioritise

materials which can be adjusted and altered to fit the ulceration site. The future clinical introduction of the described PA-AC material would increase the number of available materials which are able to be cut to the desired shape to dress malodourous wounds.

Dressings providing a moist wound healing environment are typically defined in the literature as having a moisture vapour transpiration rate (MVTR)(also called water vapor transpiration rate (WVTR)), of less than 840 g/m^2/24 h, with some wound dressings having a MVTR significantly higher than this recommended limit [25]. There are reports that intact skin has a transpiration rate of 9.0 ± 4.50 g/m²/h [26], which would indicate the range of MVTR of normal skin to be in the range of 108 – 324 g/m²/24 h. Using the figures shown in figure 1 in this format, the PA and PA-AC samples developed in this study had MTVR values of 1750 g/m²/24 h and 1820 g/m²/24 h, respectively. The results demonstrated that these samples were able to allow the passage of moisture vapour at a greater rate than skin, indicating that they should not contribute to skin maceration. Moreover, the MVTR values obtained here were close to the reported optimum rate of 2028.3 g/m²/24 h in a study investigating the effect on healing of the MVTR of a range of polyurethane membranes covering both cultured cells and wounds [27. Dressings can be described according to absorption capabilities and as such are categorisedas low, moderate, high and super absorbent dressing, however, at present, there is no separate MVTR component that is listed as contributing to these dressing classifications. It must be noted that the MVTR of all dressings is altered when the environmental humidity is increased, which may be a reason why the MVTR of commercially available dressings is not easily sourced. This lack of published information disadvantages clinicians and product users as it does not allow comparison of product characteristics.

Fluid absorption is a measure of the capacity of a dressing to absorb fluids when in contact with the wound surface (but does not consider the MVTR). The medium to high absorbent properties of dressings can be achieved through possession of a variety of characteristics. Some foams rely on porosity and capillary action for absorption, whereas others form gelson contact with aqueous fluids (e.g., alginates). Some materials utilise superabsorbent polymers to bind fluid and prevent reflux of harmful proteinases onto the wound surface [19].

The measured fluid handling capacity of all the samples in this study had good consistency, indicating homogeneity between samples following the formulation process. The fluid absorption of the PA-AC material was observed to be statistically significantly lower than that of the PA control material ($P<0.01$). The PA film has an overall higher fluid handling capacity than PA – AC, probably due to the AC particulates occupying areas within the agarose matrix to the exclusion of water.

It was observed that when the agarose film formulations were augmented with CMC, the resultant PA-AC-CMC and the PA-CMC films both demonstrated significantly greater fluid absorption capabilities than the original formulations, with values of 2430 g/m²/24 h and 2280 g/m²/24 h (Wilcoxon rank some test; $W = 0.34$, $p < 0.01$), respectively, being a 5-fold increase in the case of PA-AC-CMC and 3.5-fold with PA-CMC.

The overall fluid handling capacity of a dressing is the combination of its fluid absorption capacity, and the MVTR. The samples produced here have an overall fluid handling capacity of 2300 g/m²/24 h and 2380 g/m²/24 h for the PA – AC and the PA materials, respectively (using the data presented in figure 1). With the addition of CMC, the fluid handling capacities of the resultant PA-AC- CMC and the PA-CMC materials were 4050 g/m²/24 h and 3880 g/m²/24 h, respectively. It is speculated that further quantities of CMC could be added to increase the fluid and overall moisture handling capacities further, provided that the spatial limitation of the agarose matrix in holding additional water is not exceeded. Such tunable fluid handling through incremental formulation changes to CMC content could enable the management of wounds of differing exudate volumes.

The materials produced in this study have versatility in terms of their potential clinical application. The PA-AC formulation could be used as an odour adsorbing backing film, or as a low moisture absorbent film dressing. With the addition of CMC, PA and PA-AC would be expected to absorb more wound fluid *in situ*. The various materials produced here can be laminated together by application of heat to form composites with differing characteristics. In one possible formulation, PA-CMC could be the wound contact layer to promote wound exudate management functionality. A secondary PA-AC laminate would allow for wound odour control with the overall composite maintaining an acceptable wound moisture environment due to the inherent MTVR properties of the individual layers. Moreover, the AC particles in the composite interior would be protected from fouling with wound detritus by a barrier effect of the underlying PA-CMC (or PA) layer, thus maximising the odour adsorbing functionality.

Wound dressings are required to have reasonable tensile strength to ensure easy application and removal without rupture. When these materials are to be used on wounds located on high pressure or shear areas, such as the sacrum and the plantar surface of the foot, they need to have sufficient tensile strength to prevent disintegration of the material while being exposed to the normal forces placed on these areas during routine daily activities. Mechanical testing was performed to obtain values relating to the elasticity (elongation value) and tensile strength of the PA-AC test material and the PA control material. The tensile data for PA and PA-AC did not yield any discernible differences (table 2), the maximum load for PA-AC being 30.7N compared with 28.7N for the PA control

material. The percentage elongation for these materials was approximately 43%. When comparing these results with the tensile strength of other dressings currently available for wound dressing use, the results displayed here are favourable. In a study by Uzun et al [28] into the performance characteristics of sliver-treated absorbent wound dressings, it was found that the tensile strength of CMC, CMC Ag, Alginate and Alginate Ag was 51.7N, 22.8N, 5.4N and 4.1N, respectively. This indicates that both the materials produced and tested here have tensile strengths within the range of comparable relevant dressings currently on the market. Alginate Ag and CMC Ag are routinely used for the management of foot ulceration - the 30.7N and the 28.7N values obtained for PA and PA-AC suggests that, in terms of mechanical strength, they would be suitable for such application.

Malodour is a known component of many chronic wounds and is the cause of considerable distress for the person affected [15]. There appears to be a variety of methods used to evaluate the odour management capabilities of wound dressings. Many use subjective methods to evaluate odour breakthrough, including using human evaluators applying verbal rating scales e.g., strong, moderate, minimal and absent odour [29], patient and practitioner verbal rating [30], TELER odour scale, [31], as well as visual analogue scales [32]. Of the clinical studies identified, some are case reports [33-35], or have low participant numbers [29, 30]. There are also laboratory-based methods to evaluate odour absorption such as assessing small molecule capture, e.g., crystal violet [36], 2% diethylamine [20,37-38] and thiol adsorption [39]. Test standard organisations have standardised the methods for evaluating wound dressings, e.g. BS EN 13726-6:2003 [37], where the dry test sample is evaluated for diethylamine breakthrough. However, this test molecule is not typically found in wound exudate, and the use of a dry dressing, not in contact with the odour source, is arguably not clinically reflective. In the case of activated carbon-based products, odour adsorbing capabilities are reported to be reduced as the product becomes moistened with wound fluid [40]. This highlights the difficulty and subjectivity when assessing wound odour and, as such, is a difficulty which translates to clinical practice. Gethin et al [21] found that only 12% of health professionals assess wound odour and, of those, only 4.5% used a rating scale. This may be attributable to there being no internationally agreed standard for assessing wound odour.

In this study, a clinically reflective approach that incorporated a three-point verbal rating scale of no odour, mild odour and strong odour, using healthy individuals representative of the population of people who may encounter an individual with a chronic wound, was used. The odour molecule evaluated, 2-AAP, is known to be the principal one responsible for the characteristic malodour associated with *P. aeruginosa* infections of chronic wounds [9, 33]. The dressing material was in direct contact with the odour source, such as would occur *in vivo*. When assessed by human

volunteers, the PA-AC material was found to be able to adsorb 2-AAP odours in a laboratory setting. Odour detection was significantly lower for the PA-AC material compared with the PA control material ($P<0.05$). It was noted that as well as the PA-AC being able to significantly reduce the 2-AAP odour, it also removed the background odours present in the non-spiked control vessels, of which the dominant one was adjudged to be from the polystyrene sample housing (Figure 5). The odour removal capability when in contact with the moist odour source indicated promising clinical functionality. It is expected that the AC present in the formulation described will be able to adsorb other malodours present in infected wounds. Infection with common wound pathogens such as *Staphylococcus aureus*, *S. epidermidis* and *Escherichia coli* will generate necrotic tissue in wounds which will produce malodour.Further testing of the formulations described here against a range of relevant malodours will be required to further demonstrate the utility of these materials

Conclusions

In this study a breathable and robust, agarose-based film material supplemented with activated carbon particles was demonstrated to reduce human detection of 2-AAP, a malodorous molecule that is commonly associated with *P. aeruginosa* infected chronic ulcers. No significant difference in the mechanical properties of the PA-AC and PA materials was observed and the values obtained were found to be comparable with those of current commercially available wound dressings. It was found that the PA–AC and PA formulations could be augmented with CMC to facilitate a significant increase in fluid absorption and thus improve the fluid handling capacity of these films. It is envisaged that a range of agarose films supplemented (as appropriate) with AC and/or CMC could be constructed into laminated composites. These could be cut and shaped to enable clinical use in hard-to-treat areas. Such films would have mechanical properties appropriate for use on load-bearing areas, such as the foot and heel, with a tuneable capacity for wound exudate handling and wound odour management.

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Compliance with Ethical Standards

Ethical approval for odour sampling with human volunteers was obtained via the University of Brighton Cross School Research Ethics Committee (CREC).

Conflicts of Interests of Authors

The authors have no relevant financial or non-financial interests to disclose.
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All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest or non-financial interest in the subject matter or materials discussed in this manuscript.
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References

1. Kerr M, Barron E, Chadwick P, Evans T, Kong WM, Rayman G, et al. The cost of diabetic foot ulcers and amputations to the National Health Service in England. Diabet Med. 2019;36(8):995-1002.
2. Harrison MB, Graham ID, Friedberg E, Lorimer K, Vandevelde-Coke S. Regional planning study. Assessing the population with leg and foot ulcers. Can Nurse. 2001;97(2):18-23.
3. Elstone. Does venous intervention combined with compression therapy improve outcomes for patients with venous ulceration? Wounds UK. 2020;16(1):20-5.
4. Phillips CJ, Humphreys I, Fletcher J, Harding K, Chamberlain G, Macey S. Estimating the costs associated with the management of patients with chronic wounds using linked routine data. Int Wound J. 2016;13(6):1193-7.
5. Guest JF, Vowden K, Vowden P. The health economic burden that acute and chronic wounds impose on an average clinical commissioning group/health board in the UK. J Wound Care. 2017;26(6):292-303.
6. Guest JF, Ayoub N, McIlwraith T, Uchegbu I, Gerrish A, Weidlich D, et al. Health economic burden that wounds impose on the National Health Service in the UK. BMJ Open. 2015;5(12):e009283.
7. Zarghooni K, Bredow J, Siewe J, Deutloff N, Meyer HS, Lohmann C. Is the use of modern versus conventional wound dressings warranted after primary knee and hip arthroplasty? Results of a Prospective Comparative Study. Acta Orthop Belg. 2015;81(4):768-75.
8. Guttormsen K. This is your early warning wake-up call. The Diabetic Foot Journal. 2018; 21(3):172-9.

9. Edwards Jones V. Microbiology and malodorous wounds. Wounds UK. 2018;14(4):72-5
10. He, X., Dai, L., Ye, L., Sun, X., Enoch, O., Hu, R., Zan, X., Lin, F., Shen, J., A Vehicle-Free Antimicrobial Polymer Hybrid Gold Nanoparticle as Synergistically Therapeutic Platforms for Staphylococcus aureus Infected Wound Healing. Adv. Sci. 2022, 9, 2105223. https://doi.org/10.1002/advs.202105223
11. Rodriguez-Arguello J, Lienhard K, Patel P, Geransar R, Somayaji R, Parsons L, Conly J, Ho C. A Scoping Review of the Use of Silver-impregnated Dressings for the Treatment of Chronic Wounds. Ostomy Wound Manage. 2018 Mar;64(3):14-31. PMID: 29584609.
12. Dumville JC, Lipsky BA, Hoey C, Cruciani M, Fiscon M, Xia J. Topical antimicrobial agents for treating foot ulcers in people with diabetes. Cochrane Database Syst Rev. 2017 Jun 14;6(6):CD011038. doi: 10.1002/14651858.CD011038.pub2. PMID: 28613416; PMCID: PMC6481886.
13. Qian, Y., Zheng, Y., Jin, J., Wu, X., Xu, K., Dai, M., Niu, Q., Zheng, H., He, X., Shen, J., Immunoregulation in Diabetic Wound Repair with a Photoenhanced Glycyrrhizic Acid Hydrogel Scaffold. Adv. Mater. 2022, 2200521. https://doi.org/10.1002/adma.202200521
14. Kharaziha M, Baidya A, Annabi N. Rational Design of Immunomodulatory Hydrogels for Chronic Wound Healing. Adv Mater. 2021 Oct;33(39):e2100176. doi: 10.1002/adma.202100176. Epub 2021 Jul 12. PMID: 34251690; PMCID: PMC8489436.
15. Probst S. Wounds with exudate and odour. British Journal of Nursing. 2015;24(Sup6):S22-S.
16. Lindsay E. Celebrating a collaborative-care approach within the Leg Club network. Wounds UK. 2020;16(1):116 -7
17. Briard B, Heddergott C, Latgé JP. Volatile Compounds Emitted by Pseudomonas aeruginosa Stimulate Growth of the Fungal Pathogen Aspergillus fumigatus. mBio. 2016;7(2):e00219.
18. Fletcher J, Edwards-Jones V, Fumarola S, Milne J, Ousey K, Tickle J, Gray J, Weston V. Best Practice Statement: Antimicrobial Stewardship Strategies For Wound Management. Wounds UK. 2020 https://www.wounds-uk.com/resources/details/best-practice-statement-antimicrobial-stewardship-strategies-wound-management
19. Cowen T (2021) The Wound Care Handbook. 2021-2022. Editor Cowen T, MA Healthcare, p 246 – 248 https://www.woundcarehandbook.com/categories
20. Thomas S, Fisher B, Fram PJ, Waring MJ. Odour-absorbing dressings. J Wound Care. 1998;7(5):246-50.
21. Gethin G, Grocott P, Probst S, Clarke E. Current practice in the management of wound odour: an international survey. Int J Nurs Stud. 2014;51(6):865-74.

22. Shamsuri A, Daik R. Plasticizing effect of choline chloride/urea eutectic-based ionic liquid on physicochemical properties of agarose films. BioResources. 2012;7.
23. BS EN 13726-1, (2002) Test methods for primary wound dressings: Aspects of absorbency. British Standards Online. https://shop.bsigroup.com/products/test-methods-for-primary-wound-dressings-odour-control/standard
24. Fletcher J (2007) Dressings: Cutting and application guide. World Wide Wounds. http://www.worldwidewounds.com/2007/may/Fletcher/Fletcher-Dressings-Cutting-Guide.html
25. Wlaschin KF, Ninkovic J, Griesgraber GW, Colak Atan S, Young AJ, Pereira JM, et al. The impact of first-aid dressing design on healing of porcine partial thickness wounds. Wound Repair Regen. 2019;27(6):622-33.
26. Wu P, Nelson EA, Reid WH, Ruckley CV, Gaylor JD. Water vapour transmission rates in burns and chronic leg ulcers: influence of wound dressings and comparison with in vitro evaluation. Biomaterials. 1996;17(14):1373-7.
27. Xu R, Xia H, He W, Li Z, Zhao J, Liu B, et al. Controlled water vapor transmission rate promotes wound-healing via wound re-epithelialization and contraction enhancement. Sci Rep. 2016;6:24596.
28. Uzun M, Anand SC, Shah T. Study of the pH and physical performance characteristics of silver-treated absorbent wound dressings. Journal of Industrial Textiles. 2013;42:231-43.
29. 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(5):22-8.
30. Haynes JS. A clinical evaluation of a charcoal dressing to reduce malodour in wounds. Br J Nurs. 2018;27(6):S36-s42.
31. Browne N, Grocott P, Cowley S, Cameron J, Dealey C, Keogh A, et al. Woundcare Research for Appropriate Products (WRAP): validation of the TELER method involving users. Int J Nurs Stud. 2004;41(5):559-71.
32. 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(1):20-2.
33. White R. Wound malodour and the role of ACTISORB Silver 220. Wounds UK. 2013;9(1):101-104.
34. Sharp A, Brandon T & Thursby L. Treating infection and malodour using a dressing with charcoal and silver: a case study evaluation. Wounds UK. 2014;10(2):110 -114.

35. Murphy N. Reducing infection in chronic leg ulcers with an activated carbon cloth dressing. Br J Nurs. 2016;25(12):S38-44.
36. Minsart M, Mignon A, Arslan A, Allan IU, Van Vlierberghe S, Dubruel P. Activated Carbon Containing PEG-Based Hydrogels as Novel Candidate Dressings for the Treatment of Malodorous Wounds. Macromolecular Materials and Engineering. 2021;306(1):2000529.
37. BS EN13726-6, (2003) Test methods for primary wound dressings: Odour control. British standards online. https://shop.bsigroup.com/products/test-methods-for-primary-wound-dressings-odour-control/standard
38. Lee G, Anand SC, Rajendran S, Walker I. Efficacy of commercial dressings in managing malodorous wounds. Br J Nurs. 2007;16(6):S14, s6, s8-20.
39. Illsley MJ, Akhmetova A, Bowyer C, Nurgozhin T, Mikhalovsky SV, Farrer J, et al. Activated carbon-plasticised agarose composite films for the adsorption of thiol as a model of wound malodour. J Mater Sci Mater Med. 2017;28(10):154.
40. Lipman RD, van Bavel D. Odor Absorbing Hydrocolloid Dressings for Direct Wound Contact. Wounds. 2007;19(5):138-46.