

# Hyaluronic acid and metallic silver treatment of chronic wounds: healing rate and bacterial load control

**Objective:** To confirm the safety and wound healing activity of a topical spray powder containing hyaluronic acid (HA) and metallic silver (Hyalosilver, Fidia Farmaceutici S.p.A., Italy), and investigate its effect on the control of bacterial load in vascular ulcers or category I-II pressure ulcers (PU).

**Methods:** This is a single site, prospective, open label study involving patients with a vascular ulcer or category I-II PUs, presenting signs of critical bacterial colonisation. Patients with a wound size of  $\leq 15\text{cm}^2$  were enrolled. At baseline, a swab was taken of each wound for a semi-quantitative analysis of bacterial load and the first treatment of topical spray powder was applied. The patient was then requested to self-apply the medication once a day for 28 consecutive days and to return on days one, seven and 28 for clinical and microbiological assessments.

**Results:** A total of 25 patients were enrolled in the study. Treatment with the topical spray powder enhanced the healing rate of chronic wounds in terms of a reduction of wound area as well as bacterial load ( $p < 0.025$ ) and the overall clinical status of wound (odour, exudate, erythema of periwound skin;  $p < 0.017$ ). Moreover, the spray powder increased overall patient perception of improvement in the wound ( $p < 0.05$ ).

**Conclusion:** The data demonstrated good safety and tolerability of the topical spray powder suggesting that the product is effective not only in reducing wound area, due to the presence of HA, but in keeping the bacterial colonisation under control.

**Declaration of interest:** There is no conflict of interest to declare. The study materials used in the trial were supplied free of charge by Fidia Farmaceutici S.p.A.

hyaluronic acid • infection • pressure ulcer • silver • vascular ulcer • wound healing

**S**kin wounds are common complications of primary vascular diseases such as peripheral artery disease (PAD), diabetes, chronic venous insufficiency (CVI) or due to prolonged immobility.<sup>1</sup> Cost-effectiveness studies show that treatment of such wounds is expensive, and that due to population ageing and high rates of chronic conditions, including diabetes and obesity, these costs are unavoidable and place a significant burden on patients and the health service.<sup>1</sup>

Wound healing involves different physiological and biological phases, including inflammation, neo-angiogenesis, development of granulation tissue and cellular remodelling, culminating in wound re-epithelialisation.<sup>2</sup> However, the progression of a wound to healing can be impaired by many factors, in particular wound bed colonisation by pathogenic microorganisms, chronic inflammation, elevated levels of matrix metalloproteinases (MMPs) and proinflammatory cytokines, and lower levels of growth hormone (GH).<sup>3</sup> It is therefore important to use a reliable wound dressing that promotes the healing process and demonstrates activity against pathogenic microorganisms.

Despite the broad use of silver in wound care, the reasons for its effectiveness remain unclear. Some authors refer to its widely broad-spectrum antimicrobial activity.<sup>4,5</sup> Systematic reviews have stated its role in reducing the rate of bacterial load in wounds and burns of various aetiology is unclear.<sup>3,4</sup>

Interest in the use of silver in wound treatment has increased due to its antimicrobial properties, with many applications including pharmacology and human medicine.<sup>8</sup> The interaction of metal nanoparticles with microorganisms (from fungi to viruses such as human immunodeficiency virus) is an expanding field of research. The basis of this is the mechanism of the antibacterial effect of silver ions ( $\text{Ag}^+$ ). This involves their absorption and accumulation by bacterial cells and shrinkage of the cytoplasm membrane or its detachment from the cell wall. As a result, bacterial DNA condenses and loses the ability to replicate.<sup>9</sup>

This action is effective against Gram-positive and Gram-negative cocci.<sup>10</sup> A good 'zero' effect was proved after 7–14 days of exposure to test fungi with no appearance of mould in the area treated with silver. The results are promising for the use of silver in antimicrobial applications.<sup>10</sup> Moreover, a secondary effect of reduction in bacterial load may be a reduction in smell; this is particularly evident in fungating wounds.<sup>11</sup>

Hyaluronic acid (HA) is a biological polysaccharide (glycosaminoglycan) distributed in the extracellular matrix (ECM) of most tissues, where it binds a large

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amount of water and forms a viscous hydrated gel, even at low concentrations. It has been shown that HA activity is associated with multiple biological events in wound healing promoting tissue repair and angiogenesis in experimental models.<sup>12</sup> Observations from preclinical studies have shown that HA induces angiogenesis, fibroblast migration and collagen deposition, keratinocyte proliferation, migration and cell detachment, and mitosis in general.<sup>13</sup>

HA has demonstrated anti-inflammatory and anti-oedema effects.<sup>14</sup> The anti-inflammatory effects may be due to the action of exogenous HA as a scavenger by draining prostaglandins, MMPs and other bioactive molecules. The anti-oedema effect may be related to its osmotic activity.<sup>14</sup> During the wound repair process, HA allows the rapid diffusion of water-soluble molecules, enhances cell migration and promotes a balanced wound environment.<sup>15,16</sup>

### Aim

The main objective of this study was to evaluate the efficacy and safety of a topical spray powder containing HA and metallic silver (Hyalosilver, Fidia Farmaceutici S.p.A, Italy) in terms of wound size reduction, bacterial load control and number of adverse events. A secondary objective is the evaluation of the efficacy in bacterial load reduction of chronic wounds of various aetiology showing a critical bacterial colonisation.

### Method

This investigation was a monocentric, prospective, open label study. Before starting the clinical phase of the study, ethical approval was obtained from the Competent Ethics Committee (Internal Review Board) of the clinic.

The topical spray powder used is an EC-certified class III medical device. The powder dressing contains HA sodium salt 0.2% and metallic silver 2.0%.

Patients able to comply with the study protocol for its duration and who had not used a topical antiseptic therapy within a week or antibiotics within 48 hours before inclusion in the study, were enrolled. All participants gave written informed consent including for the use of photographs.

Patients also had vascular chronic wound ulcers of arterial, venous or mixed (arterial-vascular) aetiology or pressure ulcers (PU) at category I or II (according to the National Pressure Ulcer Advisory Panel/European Pressure Ulcer Advisory Panel and Pan-Pacific Pressure Injury Alliance (NPUAP/EPUAP/PPPIA),<sup>17</sup> with a diameter of  $\leq 15\text{cm}^2$ . Patients also presented with either partial or total loss of dermis with at least one of the following clinical signs of bacterial colonisation: cellulitis (pain, heat, and swelling in the surrounding area); suppuration (purulence); lymphangitis; bacteraemia; change in appearance of tissue of granulation; smelly exudate; reduced or delayed wound healing.<sup>18–20</sup>

Exclusion criteria were signs of malignancy related to the wound; patients receiving palliative cares or who

were immunocompromised; patients who had certain or suspected contraindications related to the investigated product; patients whose wound showed necrotic tissue, black eschar, exposed bone, tendon or muscular fascia.

### Treatment

An evaluation of vascular (arterial/venous) diseases and comorbidities affecting all patients was performed and adequate stabilisation of the patient's clinical condition was obtained before enrolment.

A complete medical history was collected. All patients underwent a Duplex ultrasound scan. In addition, for patients with venous ulcers, a photo-plethysmography was performed, while for the patients with PAD, the ankle-brachial index (ABI) was calculated. For some patients with a pathological ABI of  $<0.5$  (indicating severe arterial disease), a more in-depth evaluation was performed using an angio computerised axial tomography (CAT) scan.

Wounds were initially cleansed with saline solution, after which the medication was administered then covered with non-adherent gauzes and secondary sterile dressings were applied. In all cases, a multilayer, multicomponent short-stretch bandage or stocking was also applied, suitable for each specific clinical case.

A swab sample was collected at baseline, after 24 hours and at seven days. A semi-quantitative analysis of the bacterial load of the wound was performed in order to evaluate any reduction in bacterial load after one day, and any variation after seven days. Patients were requested to self-apply the medication once a day for 28 consecutive days and to return to the clinic on days one, seven and 28 for clinical assessments.

### Outcome parameters

Data were collected in order to evaluate the efficacy and safety of the medical device, at baseline (V0) and all subsequent visits in the facility (day one (V1), day seven (V2) and day 28 (V3)) on the following parameters:

- Skin wound area: using ImageJ, opensource image processing and analysis software in Java, developed by National Institute of Health of the United States<sup>21</sup>
- Bacterial load: evaluating the microbiological count of the wound swab, bacterial load was expressed in colony forming units (CFU)/ml
- Status of wound bed: assessing wounds in terms of odour, exudate and erythema; the investigator was requested to score the odour as 'absent', 'minimal', 'tolerable', 'intense' or 'repulsive'; the exudate and the erythema/redness as 'absent', 'minimal', 'moderate' or 'abundant'<sup>19,20</sup>
- Patient's global assessment (PtGA): patient was requested to indicate on a visual analogue scale (VAS, of 0–10 where 0=no pain and 10=unbearable pain) his/her assessment of the wound in answer to the question 'How do you feel about your wound today?'<sup>22</sup>
- Clinical observer's global assessment (COGA): as requested for evaluating PTGA. Also, the COGA of the

wound was recorded at each post-baseline assessment visit; the clinician was requested to score the wound on a five grade Likert's scale: 1=worsening, 2=no change, 3=minimal improvement, 4=moderate improvement, 5=good improvement.

### Statistical analysis and data management

The full analysis set included all patients receiving at least one dressing with the topical spray powder. Statistical analysis was performed on absolute values or on changes from baseline, as applicable, and at a level of significance of 0.05, or adjusted for the number of comparisons. All comparisons were performed using V0 data as baseline.

Wilcoxon non-parametric test was used to assess the changes from baseline data on wound area size, bacterial load, the status of the wound bed and the COGA of the wound. The analysis of variance for repeated measures was used to analyse the PTGA of the wound and a contrast against baseline was performed.

Given the number of patients visiting the clinic and the potential rate of drop out, a sample size of 30 patients was established to evaluate the efficacy and the safety of the topical spray powder.

### Results

Of the 25 enrolled patients, 24 (96%) completed the study as planned and were fully adherent with the study treatment scheme.

Wounds included 22 (88%) vascular ulcers and (12%) PUs. Both male and female patients were represented, all patients were Caucasian, with a mean age of 74 years (standard deviation (SD) 16.4; range: 38–89). The majority of patients were overweight (median body mass index [BMI]: 27kg/m<sup>2</sup>, SD 4.19) and had various comorbidities including hypertension, CVI and PAD (Table 1).

At the start of the study, patients presented with wounds with moderate exudate (76%), odour (72%), while erythema was present in the periwound skin in 48% of patients. All patients presented with at least one sign of bacterial colonisation at baseline, the most relevant of which was reduced or delayed wound healing (92%), changes in granulation tissue (72%) and smelly exudate (56%) (Table 2).

At baseline, median wound area was 7cm<sup>2</sup> (mean: 8.5cm<sup>2</sup>; SD: 4.71; range: 1.5–18.3cm<sup>2</sup>) and a median bacterial load of 5.1log<sup>10</sup> CFU/ml (mean: 4.9log<sup>10</sup> CFU/ml; SD: 1.30; range: 2.08–6.78log<sup>10</sup> CFU/ml).

### Wound area

The reduction in wound area was evident from one day after the first application with the topical spray powder (at V1, 56% of patients presented with a reduction of the wound area). These results were more evident at V2 and V3, with 96% of patients showing a reduction in wound area, including complete healing (range: 44%–100% (p<0.017) (Table 3 and 4).

Due to the variability in the percentage of wound area reduction observed at each study timepoint, the median

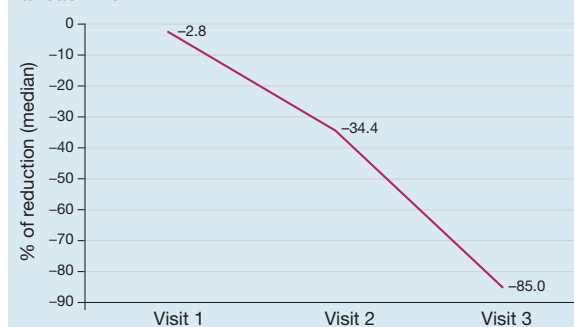
**Table 1. Demographic data of patients and comorbidities at baseline**

Patients (n=25)	Median	SD	Range
Age, years	74	16.40	38–89
Height, cm	168.20	8.52	150–186
Weight, kg	78.12	15.51	52–100
Body mass index, kg/m <sup>2</sup>	27.39	4.19	17.90–35.80
<b>Sex</b>	<b>n</b>	<b>%</b>	
Female	14	56	
Male	11	44	
<b>Comorbidity</b>	<b>n</b>	<b>%</b>	
Hypertension	17	68	
Venous insufficiency	8	32	
Peripheral arterial occlusive disease	6	24	
Deep vein thrombosis	2	8	
Diabetes	3	12	
Hypothyroidism	2	8	
Cardiac failure	2	8	
Others	19	76	
SD—standard deviation			

**Table 2. Macroscopic signs in wounds, regarding bacterial colonisation at baseline (none had bacteraemia)**

Signs of bacterial colonisation	Number of patients (n=26)	% of total number of patients
Reduced or delayed wound healing	23	92
Tissue granulation changes	18	72
Smelly exudate (or increase in it)	14	56
Lymphangitis	9	36
Increased pain	9	36
Cellulitis	6	24
Pus	1	4

**Fig 1. Percentage of reduction of lesion area (median) at each visit**



**Table 3. Clinical results of treatment of wounds, classified by changes in lesion area from baseline (p<0.017)**

n=25		n	%
Visit 1 (day one)	Decreased	14	56.0
	No change	10	40.0
	Increased	1	4.0
Visit 2 (day seven)	Decreased	24	96.0
	No change	0	0.0
	Increased	1	4.0
Visit 3 (day 28)	Decreased	24	96.0
	No change	0	0.0
	Increased	0	0.0
	Missing	1	4.0

**Fig 2.** Case 2, 83-year old male patient with hypertension, diffuse arthrosis, peripheral arterial disease stage IIb Leriche-Fontaine with a history of recurrent leg ulcers, presenting with vascular arteriopathic lesion (size: 18.3cm<sup>2</sup>) at baseline (a). At day 28 (visit 3), a pronounced reduction of 78% in wound area is observed (size: 4.02cm) (b)



value is more informative than the mean value. At V1, a median wound area reduction of 2.8% is observed. This increases to a median value of 34.4% at V2 and

**Table 4. Details of percentage of wound area reduction (per patient/visit) from baseline. Patient 25 discontinued the study due to lack of compliance with self-administration of medication (p=0.017)**

Patient ID	V1 (Day 1)	V2 (Day 7)	V3 (Day 28)
1	0	-22.58	-67,74
2	-4.37	-34.43	-78,14
3	0	-33.33	-100.00
4	0	-33.33	-44.44
5	0.95	-54.29	-100.00
6	400.00	-26.00	-88.00
7	0	-33.33	-81.48
8	-15.15	-27.27	-100.00
9	0	-60.00	-86.67
10	0	-24.43	-100.00
11	0	-37.50	-100.00
12	0	-82.50	-100.00
13	0	-46.67	-100.00
14	-16.67	-50.00	-100.00
15	-5.00	-35.00	-70.00
16	-16.67	-33.33	-79.17
17	-45.45	-72.73	-100.00
18	-14.29	-42.86	-74.29
19	-16.00	-34.40	-64.00
20	-8.33	-33.33	-76.67
21	-14.63	-45.12	-87.80
22	-1.41	-35.21	-72.54
23	0	-40.00	-83.33
24	-4.26	-4.26	-46.81
25	-13.51	21.62	—

V1—visit 1; V2—visit 2; V3—visit 3

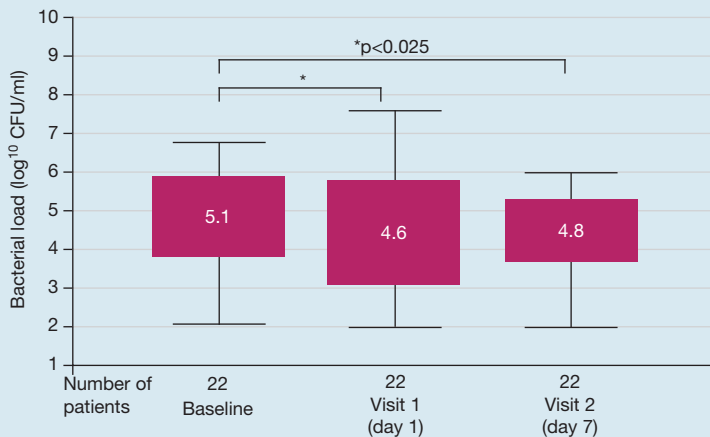
reaches a median value of 85% at V3 (Fig 1). Fig 2 shows clear reduction in the wound area of a male patient with a vascular arteriopathic lesion after 28 days treatment.

**Bacterial load**

A base-10 log transformation of data was used to analyse data from swabs from 22 of the 25 participants. Of the remaining patients, two did not demonstrate bacterial colonisation at the baseline swab, while one patient did not provide a usable measurement at baseline.

The percentage of patients showing a reduction in bacterial load, with respect to the baseline, moved from 77% at V1 to 64% at V2. The Wilcoxon test was used to

**Fig 3.** Bacterial load at each visit ( $\log^{10}$  colony forming units (CFU)/ml) For each box plot, the median values are represented by the line within the box. The box represents 50% of the values (the 25th and 75th centiles), with the bars presenting the highest and lowest values excluding outliers. Statistical analysis was performed against baseline using the Wilcoxon test correcting the alfa level as per Bonferroni method ( $\alpha=0.05/2=0.025$ )



**Fig 4.** Case 7, a 85 year-old female patient with hypertension, arthritis, chronic venous leg ulcer (size: 13.5cm<sup>2</sup> at baseline). Macroscopic aspect of lesion at baseline with cellulitis, lymphangitis, pain, delayed wound healing, changes in granulation tissue, fibrin in wound bed, moderate exudation, perilesional erythema and bacterial load at baseline (a). At day 28 (Visit 3), wound almost completely re-epithelialised (b)



compare changes from the baseline and demonstrates a significant decrease in bacterial load both at V1 and V2 ( $p<0.025$ ).

The median bacterial load reduces from  $5.1\log^{10}$  CFU/ml at baseline (mean:  $4.9\log^{10}$  CFU/ml; SD: 1.30; range:  $2.08\text{--}6.78\log^{10}$  CFU/ml) to a median value of  $4.6\log^{10}$  CFU/ml at V1 (mean:  $4.5\log^{10}$  CFU/ml; SD: 1.5; range:  $2.00\text{--}7.60\log^{10}$  CFU/ml) and  $4.8\log^{10}$  CFU/ml at V2 (mean:  $4.4\log^{10}$  CFU/ml; SD: 1.2; range:  $2.00\text{--}6.00\log^{10}$  CFU/ml) ( $p<0.025$ ) (Fig 3).

#### Wound bed status

At baseline, clinical signs such as odour ('minimal' or 'tolerable', in 21 (84%) patients) disappeared completely at V3 ( $p<0.017$ ). Level of exudate ('minimal' or 'moderate' in all wounds) throughout the treatment improved significantly ( $p<0.017$ ). Specifically, at V1 exudate reduced in 12 (48%) wounds, in 17 (68%) wounds at V2 and in 22 (92%) wounds at V3.

Moreover, all wounds presented with erythema of the periwound skin that completely disappeared in 87% of patients at V3 (with a residual, but ameliorated, presence in the remaining 13% of patients;  $p<0.017$ ) (Fig 4).

#### Patient's global assessment (PTGA)

The parametric test analysis of the variance (ANOVA) for repeated measures was used to analyse the changes from baseline. A statistically significant difference resulted at each study timepoint against baseline ( $p<0.05$ ). Furthermore, the multiple comparisons analysis shows that an increasing overall improvement of the wound was perceived by the patient at each study point ( $p<0.05$ ) (Table 5).

#### Clinical observer's global assessment (COGA)

Analysis of data from the clinical observer's global assessment shows results consistent with those obtained on other study variables, including wound bed status and area reduction. With regard to wound appearance at V1, the investigator observed significant improvement at V2, which was confirmed at V3 where 83% of patients reported improvement in wound appearance when compared with V1 ( $p<0.025$ ).

A single adverse event was reported during the study. In one patient, a moderate erythema appeared locally at the site of wound, but it was considered by the investigator to be unrelated to the application of the topical spray powder. The patient completely recovered after four days and did not require any additional treatment.

#### Discussion

Wound bed colonisation by pathogenic microorganisms represents one of the most important adverse factors responsible for delaying the wound healing process.<sup>18</sup> Furthermore, chronic inflammation and increasing exudate promotes progression to a chronic, non-healing wound.<sup>23</sup>

An ideal treatment in wound management should combine the beneficial effect of a moist environment

to support the wound repair process with an antimicrobial effect able to prevent and control wound bed colonisation.<sup>5</sup> The topical spray powder used in this study is intended for the management of non-infected cutaneous wounds. The main role is played by HA, which promotes the healing process, whereas the antimicrobial component MS plays an ancillary role, creating a barrier against external microbial contamination, preventing microbial contamination of the dressing and keeping the wound environment free from additional exogenous bacterial sources.<sup>5</sup> The particular spray formulation used in this study (which contained kaolin and silicon dioxide, with absorbent properties) allows easy control of exudate, creating an environment that facilitates the natural healing process and provides an effective barrier to microbial penetration.

Data from this study suggest that the topical spray powder is effective not only in reducing the wound area since the first application (Fig 1), but it may also be effective in reducing bacterial load (Fig 2). Measurements of bacterial load confirm a significant reduction at one and seven days post-treatment, although there was no case where it was completely eradicated.

Data from the literature suggests that silver probably has a positive effect on the proportion of burns completely healed,<sup>24</sup> on the average healing time of treated burns,<sup>25</sup> on the bacterial load<sup>26</sup> and bacteriological status<sup>27</sup> of chronic wounds when used in addition to 'dry' dressings versus standard care (vaseline gauze or advanced dressing without antiseptics). However, because these studies are affected by methodological imprecision, the results deriving from them are uncertain.

The results of our study seem to be in line with those of some *in vitro* and *in vivo* studies conducted with HA, which would seem to show improved neo-angiogenesis (and consequently blood flow which is useful in controlling bacterial load).<sup>28</sup> Other authors have found that the combined use of silver and HA has an *in vivo* combined antioxidant action. Finally, it seems that HA plays a role in immune-modulation (required for tissue repair) and stimulation of growth factor release, a major hormone involved in the healing of wounds.<sup>29</sup>

In this study, signs of bacterial colonisation (smell, exudate and erythema of the periwound skin) improved at the end of the 28 days of treatment (with the exception of two cases where exudate did not modify against baseline). At the end of the 28 days of treatment, all wounds were odourless.

## References

- 1 Nunan R, Harding KG, Martin P. Clinical challenges of chronic wounds: searching for an optimal animal model to recapitulate their complexity. *Dis Model Mech* 2014; 7(11):1205–13. <https://doi.org/10.1242/dmm.016782>
- 2 Reinke JM, Sorg H. Wound repair and regeneration. *Eur Surg Res* 2012; 49(1):35–43. <https://doi.org/10.1159/000339613>
- 3 European Wound Management Association. Position document. Hard-to-heal wounds: a holistic approach. MEP, 2008. <https://tinyurl.com/yyyycv5m> (accessed 20 June 2019)

**Table 5. Patient's Global Assessment score of the wound at each visit (p<0.05)**

	V1 (day 1)	V2 (day 7)	V3 (day 28)
Mean	75.24	83.08	94.17
Median	84.00	90.00	95.50
SD	23.324	19.700	6.850
Minimum	17.00	27.00	75.00
Maximum	100.00	100.00	100.00
Patients, n	25	25	24
V1—visit 1; V2—visit 2; V3—visit 3; SD—standard deviation			

Using a spray application avoids direct physical contact with the wound, eliminating potential contamination and pain associated with dressing changes. The safety of the product was confirmed by study results.

## Limitations

Due to the difficulty of enrolling patients using the given inclusion and exclusion criteria, an early termination of the study was decided, the evaluation was limited to 25 patients, rather than the 30 patients planned for.

The lack of a control group does not allow for a comparison of the results obtained for the topical spray powder with those of a standard treatment. However, a preliminary evaluation of the efficacy of the product is possible from the results. A measurable effect of this efficacy, however, would require a properly controlled trial with a larger number of patients.

## Conclusions

Data from this study suggest that a combination of HA and metallic silver is effective from the first application on wound area reduction. Swabs at baseline, at 24 hours and at seven days after first treatment showed the efficacy of the product in reducing the bacterial load from the first application. Clinical characteristics of the wound also showed an overall improvement, including a reduction in wound size, the quantity of exudate and odour. Assessment of product efficacy and patient adherence was satisfactory throughout this study.

Based on the findings of this study and our experience, the topical spray powder can be of benefit to patients with chronic wounds, and can be well integrated with other therapies (for example, compression therapy) which is often applied in these clinical cases. **JWC**

- 4 Kostenko V, Lyczak J, Turner K, Martinuzzi RJ. Impact of silver-containing wound dressings on bacterial biofilm viability and susceptibility to antibiotics during prolonged treatment. *Antimicrob Agents Chemother* 2010; 54(12):5120–5131. <https://doi.org/10.1128/AAC.00825-10>
- 5 Leaper D. Appropriate use of silver dressings in wounds: International consensus document. *Int Wound J* 2012; 9(5):461–464. <https://doi.org/10.1111/j.1742-481X.2012.01091.x>
- 6 Storm-Versloot MN, Vos CG, Ubbink DT, Vermeulen H. Topical silver for

preventing wound infection. *Cochrane Database Syst Rev* 2010; (3):CD006478. <https://doi.org/10.1002/14651858.CD006478.pub2>

**7** Vermeulen H, van Hattem JM, Storm-Versloot MN et al. Topical silver for treating infected wounds. *Cochrane Database Syst Rev*. 2007; (1):CD005486. <https://doi.org/10.1002/14651858.CD005486.pub2>

**8** Lansdown ABG. A Pharmacological and Toxicological Profile of Silver as an Antimicrobial Agent in Medical Devices. *Adv Pharmacol Sci* 2010; 910686:16 pages. <http://dx.doi.org/10.1155/2010/910686>

**9** Russell AD, Hugo WB. Antimicrobial activity and action of silver. *Prog Med Chem* 1994; 31:351–370

**10** Petica A, Gavrilu S, Lungu M et al. Colloidal silver solutions with antimicrobial properties. *Mater Sci Eng B* 2008; 152(1–3):22–27

**11** Adderley UJ, Holt IG. Topical agents and dressings for fungating wounds. *Cochrane Database Syst Rev* 2014; (5):CD003948. <https://doi.org/10.1002/14651858.CD003948.pub3>

**12** Chen WJ, Abatangelo G. Functions of hyaluronan in wound repair. *Wound Repair Regen* 1999; 7(2):79–89. <https://doi.org/10.1046/j.1524-475X.1999.00079.x>

**13** Mekkes JR, Nahuys M. Induction of granulation tissue formation in chronic wounds by hyaluronan. *Wounds* 2001; 13(4):159–164

**14** Laurent TC, Laurent UB, Fraser JR. Functions of hyaluronan. *Ann Rheum Dis* 1995; 54(5):429–432. <https://doi.org/10.1136/ard.54.5.429>

**15** Meyer LJ, Stern R. Age-dependent changes of hyaluronan in human skin. *J Invest Dermatol* 1994; 102(3):385–389. <https://doi.org/10.1111/1523-1747.ep12371800>

**16** Meran S, Thomas DW, Stephens P et al. Hyaluronan facilitates transforming growth factor-beta1-mediated fibroblast proliferation. *J Biol Chem* 2008; 283(10):6530–6545. <https://doi.org/10.1074/jbc.M704819200>

**17** National Pressure Ulcer Advisory Panel (NPUAP), European Pressure Ulcer Advisory Panel (EPUAP), Pan Pacific Pressure Injury Alliance (PPPIA). *Prevention and treatment of pressure ulcers: quick reference guide*. Cambridge Media, 2014

**18** European Wound Management Association. (2005). *Position document: identifying criteria for wound infection*. MEP, 2005

**19** Cutting KF, Harding KG. Criteria for identifying wound infection. *J Wound Care* 1994; 3(4):198–201. <https://doi.org/10.12968/jowc.1994.3.4.198>

**20** Gardner SE, Frantz RA, Troia C et al. A tool to assess clinical signs and symptoms of localized infection in chronic wounds: development and reliability. *Ostomy Wound Manage* 2001; 47(1):40–47

**Reflective questions**

- What are the advantages/disadvantages of using a topical spray powder containing hyaluronic acid and metallic silver in treating chronic vascular wounds?
- What effect does the topical spray powder have on bacterial loads in chronic ulcers?
- How might you consider using the topical spray powder in your day-to-day practice?

**21** Cromey DW. Digital images are data: and should be treated as such. *Methods Mol Biol* 2013; 931:1–27

**22** Anderson JK, Zimmerman L, Caplan L, Michaud K. Measures of rheumatoid arthritis disease activity: Patient (PtGA) and Provider (PrGA) Global Assessment of Disease Activity, Disease Activity Score (DAS) and Disease Activity Score With 28-Joint Counts (DAS28), Simplified Disease Activity Index (SDAI), CI. *Arthritis Care Res* 2011; 63(S11 Suppl 11):S14–S36. <https://doi.org/10.1002/acr.20621>

**23** Rippon MG, Ousey K, Rogers AA, Atkin L. Wound hydration versus maceration: understanding the differences. *Wounds UK*. 2016; 12(3):62–68

**24** Healy CM, Boorman JG. Comparison of E-Z Derm and Jelonet dressings for partial skin thickness burns. *Burns* 1989; 15(1):52–54. [https://doi.org/10.1016/0305-4179\(89\)90072-7](https://doi.org/10.1016/0305-4179(89)90072-7)

**25** Chen J, Han CM, Lin XW et al. [Effect of silver nanoparticle dressing on second degree burn wound]. *Zhonghua Wai Ke Za Zhi* 2006; 44(1):50–52

**26** Verd Soriano J, Rueda Lpez J, Martnez Cuervo F, Soldevilla Agreda J. Effects of an activated charcoal silver dressing on chronic wounds with no clinical signs of infection. *J Wound Care* 2004; 13(10):419–423. <https://doi.org/10.12968/jowc.2004.13.10.26685>

**27** Trial C, Darbas H, Lavigne JP et al. Assessment of the antimicrobial effectiveness of a new silver alginate wound dressing: a RCT. *J Wound Care* 2010; 19(1):20–26. <https://doi.org/10.12968/jowc.2010.19.1.46095>

**28** Wang Y, Han G, Guo B, ng J. Hyaluronan oligosaccharides promote diabetic wound healing by increasing angiogenesis. *Pharmacol Rep* 2016; 68(6):1126–1132. <https://doi.org/10.1016/j.pharep.2016.07.001>

**29** Fouda MM, Abdel-Mohsen AM, Ebaid H et al. Wound healing of different molecular weight of hyaluronan; in-vivo study. *Int J Biol Macromol* 2016; 89:582–591. <https://doi.org/10.1016/j.ijbiomac.2016.05.021>

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