

Evidence Summary:

Biological dressings: Collagen-based dressings

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QUESTION

What is the best available evidence on collagen-based dressings for improving wound healing outcomes in adults?

SUMMARY

Collagen-based dressings are advanced wound dressings that provide an extracellular matrix to support tissue and microcirculation growth. Collagen dressings are able to change the wound biochemistry through modulation of protease activity, creating an environment more favourable for healing¹ (Level 1). Oxidised regenerated cellulose (ORC) is commonly combined with collagen to create a collagen-based composite dressing with enhanced ability to reduce protease activity (Level 4).² Collagen dressings are designed for wounds with stalled healing^{2, 3} (Levels 4 and 5).

There is limited evidence on efficacy and no recent cost effectiveness studies for collagen-based dressings. Available evidence, mostly conducted on venous leg ulcers (VLUs), indicates that collagen-based dressings are at least as effective in improving healing as other contemporary wound dressings⁴⁻⁷ (Level 1).

BEST PRACTICE RECOMMENDATIONS

Use collagen-based dressings when a wound (particularly a venous leg ulcer) displays stalled/delayed healing (Grade B).

The following considerations are recommended for using collagen-based dressings:

- Wound dressings should be reviewed third daily (or more frequently for moderate-heavy wound exudate). If there is gel residue from the collagen dressing remaining on the wound bed/secondary dressing the collagen dressing should remain untouched until the next review.^{2, 10} (Level 4 and 5).
- Collagen-based dressings are recommended for four weeks' treatment. If inadequate healing has occurred, a review of the individual's full management plan should be conducted. If the wound is healing after four weeks, a contemporary dressing can be used² (Level 4).

- Collagen-based dressings can be used to prepare a wound bed prior to skin grafting¹⁰ and for wounds showing clinical signs of infection¹⁰ (Level 5).
- Optimising the individual's condition (e.g. nutrition) and the wound bed (e.g. with cleansing, debridement and/or infection management) is essential to promoting healing with any wound dressing^{2, 10} (Level 4 and 5).
- Collagen-based dressings are **not** recommended for wounds with dry eschar, or active vasculitis¹⁰ (Level 5).

BACKGROUND

Collagen dressings are biological dressings developed from animal collagen. Collagen is a protein produced by fibroblasts that has a role in all stages of wound healing. Collagen is a major component of the extra-cellular matrix, providing strength. Both collagen and ORC, with which collagen is frequently combined, also reduce protease activity.² Proteases have numerous roles in wound healing, but usually decrease as the wound heals. In chronic and/or infected wounds, inflammation can lead to continuously high protease levels. This can damage new tissues, contributing to delayed healing.^{1, 2} Collagen-based dressings are designed to modulate protease activity^{8, 9} and to balance wound moisture,¹⁰ while providing a mechanical scaffold for tissue growth and angiogenesis.^{8, 9} This promotes cell proliferation and stimulates microcirculation, providing a favourable healing environment.^{8, 9} Oxidised regenerated cellulose (ORC) is considered to have haemostatic properties, which may decrease wound bleeding.¹⁰

EVIDENCE

Collagen dressings

There is some evidence that collagen dressings are at least equivalent to other contemporary wound dressings for treating **venous leg ulcers**.⁴⁻⁷ A systematic review⁴ reported from one small trial (n=22)⁵ that when compared to daily application of a topical antiseptic, a collagen dressing was associated with greater likelihood of reduction in VLU area after 26

SOURCES OF EVIDENCE				
Level 1	Level 2	Level 3	Level 4	Level 5
Experimental designs	Quasi-experimental designs	Observational – Analytic designs	Observational - descriptive studies	Expert opinion Bench research
2 systematic reviews ^{1, 4} 6 RCTs 5, 6, 7, 9, 14, 16	Prospectively controlled study ¹¹	Cohort study with control group ¹³	Case series ¹² Case study ²	Expert consensus 3, 8, 10

days (odds ratio [OR] 26.6, 95% confidence interval [CI] 2.3 to 308)^{4, 5} (Level 1). A small trial (n=40) showed statistically significant greater reduction in VLU area after 12 weeks treatment with a collagen dressing 45% compared with an alginate dressing 20% (p<0.001).⁶ There was no difference in the per cent of VLUs fully healed at 12 weeks (approximately 25% in each group)⁶ (Level 1). In another small trial with non-healing VLUs (4 participants per group), the percent reduction after four weeks of treatment was similar for a collagen plus foam dressing (mean reduction 31.8%, range 28% to 34%) compared to a regular foam dressing (mean reduction 26.4%, range 17.3% to 32%)⁹ (Level 1). Another study that included VLUs (n=12) found a collagen dressing was associated with significantly shorter time to complete healing compared with polysaccharide beads (36 days versus 60 days, p<0.005) for VLUs⁷ (Level 1).

There is limited evidence that collagen dressings are at least equivalent to conventional wound dressings for treating **diabetic foot ulcers** (DFUs). When a collagen dressing was compared to moistened gauze, healing time was significantly faster with collagen (4.63±1.18 weeks versus 7.79±1.61 weeks, p=0.001) (Level 2).¹¹

Limited evidence is available on efficacy for collagen for treating **pressure injuries** (PIs). In a small trial (n=12 PIs), a collagen dressing was associated with significantly shorter time to healing (20 days versus 47 days, p<0.001) than the comparison polysaccharide bead treatment.⁷ (Level 1).

Evidence on efficacy of collagen dressing for treating **burns** is also available. Partial thickness burns (n=42) took an average of 18.5 days to reach complete re-epithelisation (average 40.5 days for four full thickness burns in the study) when managed with a collagen dressing. The authors reported none, or only mild to moderate scarring after six months for most participants.¹² (Level 4).

Another study (n=120) included **wounds of various aetiology** (chronic and acute) in a retrospective comparison of collagen dressing versus conventional dressings designed to manage infection (e.g. iodine, honey, topical antibiotics). There was no significant difference in the percent of wounds in each group that completely healed after six weeks (collagen 70% versus conventional 63%, p=0.22). There was also no difference in percent of wounds reaching at least 75% closure by eight weeks (p=0.21). Wounds treated with a conventional dressing were more likely to require a split skin graft (25% versus 13%, p=0.04). Swab cultures were more favourable in the wounds treated with collagen dressings; however, none of the wounds were reported to have clinical signs of infection at trial commencement or thereafter¹³ (Level 3).

Oxidised regenerated cellulose (ORC)/collagen dressings

There is some evidence that ORC/collagen dressings are at least equivalent to other contemporary wound dressings for treating **VLUs**.¹⁴⁻¹⁶ In the largest trial (n=73), an ORC/collagen dressing used for non-healing VLUs was associated with a non-significant 20% better improvement in wound condition (p=0.079) than a non-adherent dressing. The greater reduction in ulcer surface area that the ORC/collagen dressing group showed at 12 weeks compared to the control group was significant (average decrease 54.4%±10.9 versus 36.5%±11.4, p<0.0001) (Level 1).¹⁴ A small trial (n=27)

showed that an ORC/collagen dressing was not significantly different from hydrocolloid dressing for decreasing wound size over 12 weeks. There was a favourable association between the collagen-based dressing and reductions in protease activity¹⁶ (Level 1). An ORC/collagen dressing was shown to be associated with significantly greater reduction in VLU area over 12 weeks compared with another protease modulating matrix dressing with nano-oligosaccharide factor (NOSF) as the active ingredient (mean area reduction 54.4% versus 12.9%, p=0.0029)¹⁵ (Level 1).

METHODOLOGY

The development of this evidence summary is based on the Joanna Briggs Institute methodology.¹⁷

A structured database search using variations of the search terms collagen, protease-modulating and wound dressings was employed. Searches were conducted in EMBASE, Medline, Google Scholar and the Cochrane Library for evidence from 2000 to February 2018 in English. Two systematic reviews^{1, 4} that conducted searches covering pre-2000 identified few additional studies to the current search – these pre-2000 studies were included in this summary. The evidence review did not include biological dressings in which collagen was combined with other active ingredient besides ORC (e.g. silver

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