

Collagen dressings

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Introduction

Collagen is a key component of the extracellular matrix (ECM) and plays a critical role in all phases of wound healing. There are a number of advanced wound care dressings available that incorporate collagen to enhance wound bed preparation. Some comprise type I collagen and may be combined with other ingredients such as alginates or oxidised regenerated cellulose (ORC). This article focuses on the use of fish-derived type I collagen dressings in the treatment of stalled traumatic and surgical wounds or hard-to-heal chronic ulcers.

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ADVANCES IN WOUND DRESSINGS

Over the last 30 years there has been a shift from traditional wound dressings towards those advanced therapies that aim to optimise the wound healing environment (Enoch and Harding, 2003). In more recent years, wound care products have been developed that aim to replicate or add to the ECM. The ECM is the major component of the dermis and provides a structural support for cells, growth factors and receptors that are essential to wound healing (International Consensus, 2011).

With a wide range of dressings to choose from, dressing selection is a significant challenge for wound care clinicians. Increased costs and the need for evidence-based treatment approaches are creating a demand for well-designed randomised controlled trials to support purchase and use (Rudnick et al, 2006). The ideal dressing should achieve rapid healing at reasonable cost with minimal inconvenience to the patient (Boateng et al, 2007).

WHAT IS COLLAGEN?

Collagen is the most abundant protein in the human body and is a major component of the ECM. It comprises three polypeptide chains that are rich in hydroxyproline amino acids (Mian et al, 1992) and are twisted together into a triple-helical structure.

Over 20 different types of collagen have been identified in humans; the main types are type I, II and III and together they make up 80% of the body's collagen. Type I and III are important for wound healing (Li et al, 2007).

ROLE OF COLLAGEN IN WOUND HEALING

In a healing wound a cascade of events occurs that includes platelet accumulation, inflammation, fibroblast proliferation, cell contraction, angiogenesis and re-epithelialisation (Moore, 2010), ultimately leading to scar formation (Rudnick, 2006) and wound remodelling (Brett, 2008).

Collagen plays an important role in each of these phases of wound healing due to its chemotactic role. It attracts cells such as fibroblasts and keratinocytes to the wound. This encourages debridement, angiogenesis and re-epithelialisation (Weber et al, 1984; Zbigniew, 2003).

A chronic wound is stalled at one of these healing stages (Vowden, 2011). This usually occurs during the inflammatory phase and is linked to elevated levels of matrix metalloproteinases (MMPs) in the wound (Singh et al, 2011; Gibson et al, 2009). In normal wound healing, proteases such as MMPs are attracted to the wound during the inflammatory phase and have an important role in breaking down unhealthy ECM so that new tissue forms (Parks, 1995; Jeffrey, 1995). However, when MMPs are present in a wound at elevated levels for a prolonged period of time, this results in the destruction of healthy ECM, which is associated with delayed wound healing and an increase in wound size (Vowden, 2011).

When the excess of MMPs is not balanced by normal physiological processes, alternative methods are required to reduce protease levels in the wound. This suggests a role for dressings containing collagen in the management of wounds where healing is stalled (Rangaraj et al, 2011).

WHAT ARE COLLAGEN DRESSINGS?

Native intact collagen provides a natural scaffold or substrate for new tissue growth (Ruszczak, 2003). Dressings containing collagen are thought to provide the wound with an alternate collagen source that can be degraded by the high levels of MMPs as a sacrificial substrate, leaving the endogenous native collagen to continue normal wound healing (Brett, 2008).

There are a number of different collagen dressings available that use a variety of carriers and combining agents such as gels, pastes, polymers and oxidised regenerated cellulose (Brett, 2008). The collagen contained in these products also varies in type and source. Certain dressings contain native (type I) collagen in which the triple helix formation is intact; others contain denatured or reconstituted collagen, which is referred to as gelatin.

Most collagen dressings contain collagen derived from bovine and porcine sources (Vivas et al, 2011). Although these collagens are purified, there remains a theoretical concern regarding the potential for prion diseases such as bovine spongiform encephalopathy (BSE) (Liu et al, 2006; Jabar, 2011). There have also been concerns regarding the integration of porcine collagens into scar tissue (Burns et al, 2010), while cultural/religious issues may prevent their use on some patients (Jabar, 2011). Human-derived collagens are linked with fewer immunological concerns, however they tend to be more expensive than animal-derived collagens (Vivas et al, 2011). More recently collagen derived from fish has been proposed as a cost-effective source of collagen for use in dressings.

WHAT IS PISCEAN COLLAGEN?

Piscean collagen is a protein extracted from fish waste, including the scales, skin or air bladders, which is predominantly sourced from fresh water carp, *Labeo rohita* (Pati et al, 2010). Purifying collagen from fish involves: alkaline hydrolysis, returning the collagen to a neutral pH and subjecting it to acid hydrolysis to stabilise it. The collagen is freeze-dried into particles, sponge and sheets that can be cut into the required shape and size (Basha et al, 2011). The film membrane preparation is cast onto slabs and is not freeze-dried.

The extraction process for piscean collagen preserves its triple-helix structure. Dressings containing piscean collagen have demonstrated a high level of biocompatibility, while animal studies have found that collagen extracted from fish did not produce an immunological response or allergic reactions and was comparable to type I bovine collagens (Pati et al, 2010).

AVAILABILITY OF TYPE I PISCEAN COLLAGEN PRODUCTS

In the UK a number of fish-derived collagen products are available (Table 1). These products are non-toxic, non-allergenic, non-immunogenic and non-pyrogenic.

To choose the most appropriate collagen dressing, selection should be approached with care. All dressings are biodegradable, although there may be some variation in the time they take to degrade in the wound. Variation also applies to the absorption capacity of the dressings and in their ability to mould to the contours of the wound. A particle method of delivery (Helisorb® Particles, Medira Ltd) increases the activity of the collagen by providing an increased surface area and allowing for intimate contact with the contours of the wound bed. The particles may be used in infected wounds in combination with appropriate antimicrobial or systemic treatment. All other available piscean products should be used once infection has resolved.

Tip: The particles may be mixed with saline to form a paste for ease of use and to maintain a moist wound environment

WHEN AND HOW TO USE TYPE I PISCEAN COLLAGEN DRESSINGS

Piscean collagen dressings are currently used as a second-line dressings in non-healing wounds that have failed to respond to other treatment approaches or split skin grafting. They are haemostatic and may provide relief from pain. Other indications are described in Table 1. Collagen products should not be used on patients sensitive to collagen from any source.

Case report: Application of a piscean collagen film membrane (Neuskin-F™) to a donor site wound

A 61-year-old lady developed extensive skin necrosis to the breast and abdomen following breast reconstructive surgery. Split thickness skin grafting was performed to provide soft tissue cover to these areas. Both thighs were used as donor sites for the grafts, resulting in almost circumferential wounds.

Kaltostat® (ConvaTec) and gauze were used as initial dressings. At the first donor site check Mepitel (Mölnlycke) was applied to non-healing areas. The patient was discharged out of region to convalesce with relatives.

At follow-up two months later the donor sites remained unhealed and Neuskin-F™ (Medira Ltd) was applied and covered with a double layer of paraffin gauze (Jelonet™, Smith & Nephew). Dressing changes were performed two to three times per week. The donor sites had healed within two months following application of the Neuskin F™.



Figure 1: Unhealed skin graft donor site on the right thigh after two months



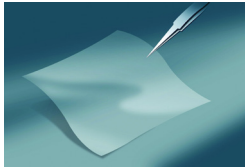



Figure 2: Right thigh of same patient two weeks after first application of Neuskin-F™. Islands of epithelialisation can be seen interspersed throughout the granulation tissue



Figure 3: After two months all donor areas had epithelialised

Table 1 Type 1 fish collagen dressings available in the UK (Medira Ltd)

Product	Helisorb® Sheets (backed by a removable nylon mesh)	Helisorb® Particles	Neuskin-F™ (transparent film membrane)	Kolspon® (collagen sponge)
Collagen type	Type I	Type I	Type I	Type I
Wound indications	Low-medium exudate Primary dressing for surgical wounds and wounds up to 0.5cm deep Chronic wounds (eg venous leg ulcers) Partial to full thickness burns	Low-medium-heavy exudate Chronic ulcers (eg diabetic foot, pressure ulcers) Traumatic and surgical wounds Undermined or tunnelling wounds Sloughy wounds	Low exudate Superficial to partial thickness burns/scalds Skin tears, graft donor sites Category II pressure ulcers and non-healing superficial ulcers	Medium-high exudate Traumatic and surgical wounds Chronic ulcers (eg diabetic foot, venous and pressure ulcers) Partial thickness burns Cavity wounds
Clinical contraindications	Hypersensitivity to collagen Do not use on infected wounds	Hypersensitivity to collagen Wounds with dry eschar, dry wounds/arterial ischaemic lesions Venous ulcers under compression	Hypersensitivity to collagen Do not use on infected or heavily exuding wounds	Hypersensitivity to collagen Wounds with dry eschar, dry wounds, arterial ischaemic lesions. Do not use on infected wounds
How to apply	Apply to the wound dry for highly exuding wounds or moisten with saline for dry or lightly exuding wounds to increase conformability Can be cut to size Nylon top layer can be removed	Completely cover wound bed with a layer 2-3mm thick (use thicker layer in moderate to highly exuding wounds) Keep moist and cover with a secondary dressing of choice Do not use with wet to dry gauze dressings, gels or hydrophobic powders Heavily exuding/infected wounds will require frequent re-application (eg daily)	Can be placed either side down Cut to fit or overlap Will adhere immediately to wound bed – can be moistened to assist adherence The dressing is transparent, allowing the wound to be inspected without removal Cover with light non-adherent dressing	May be placed in the wound dry or for conformability as a damp pad (immerse in saline and gently squeeze out excess) Cover wound bed Apply second layer of sponge for heavily exuding wounds Secure with a secondary dressing Do not overfill the wound – the product is highly absorbent and needs room for expansion
Presentation				

How to apply the dressing

First ensure the wound bed is thoroughly prepared according to local protocols. Apply to the wound bed and keep the area moist. A secondary non-adherent dressing (e.g. paraffin gauze, Telfa™, Kendall or Mepitel™, Mölynlycke) should be applied over the collagen dressing. An absorbent layer (e.g. gauze) is then placed on top. Finally the dressing should be secured using an appropriate film or crepe dressing.

Tip: When applying Neuskin-F™, it can curl up at the edges. Simply wet the sheet edges with saline on the fingertips to improve contact area

How frequently should dressings be changed?

Exudate levels may increase due to healing and the inflammatory response. The authors recommend initial dressing changes two to three times per week, depending on the exudate level. Remaining particles in the wound should be rinsed off. Overgranulation may occur with collagen dressings. If this is present, the collagen product can be discontinued and the overgranulation tissue treated for two weeks using a 1% hydrocortisone cream.

EVIDENCE FOR TYPE I PISCAN COLLAGEN DRESSINGS

The use of collagen dressings is supported by relatively sparse data, with much of the evidence derived from non-comparative case reports and clinical experience.

Piscan collagen has been used successfully to treat canine wounds, resulting in normal cell proliferation after treatment (Takai et al, 1997). In a study using a comparable bovine type I collagen matrix dressing faster healing rates were reported in 15 patients with postoperative wounds when compared to conventional treatment (6.1 vs 9.4 weeks for controls) (Kolenik et al 1999).

Anecdotal evidence to date using type 1 piscan collagen products has demonstrated that they are a useful adjunct to facilitate healing in patients with chronic ulcers (including diabetic foot and pressure ulcers), dehisced surgical wounds and donor site wounds (Medira Ltd, data on file). In addition, faster healing rates have been observed in patients with epidermolysis bullosa when using Helisorb® Particles as a primary contact layer. The product was easy to apply and impacted minimally on the patients' normal dressing regimen (De Luca, clinical data).

COST BENEFITS OF USING COLLAGEN DRESSINGS

The potential advantages of advanced wound care products have been summarised by Vowden (2011). These include: the potential to improve healing rate, reduce symptoms, and improve quality of life together with a reduction in healthcare costs. Advanced therapies may add to the initial cost burden of care. It is therefore important that they are used judiciously following accurate assessment in order to avoid inappropriate application or use in inappropriate circumstances.

Summary

This made easy supplement provides a focus on collagen dressings derived from type I piscine collagen. Fish-derived collagen products are able to deliver a wide range of benefits to the wound healing process. When applied topically, the collagen acts as a haemostat and helps to stimulate the growth of new tissue in the wound bed. Piscine collagen appears to have a number of advantages over mammalian derived collagen, including decreased cost and fewer adverse immunological reactions. This advanced wound care intervention has the potential to improve healing rates, reduce symptoms and improve quality of life while reducing long-term healthcare costs.

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