The use of MelMax® in the healing of chronic wounds

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Abstract

Chronic wounds can have detrimental consequences for the quality of life of patients as well as presenting a huge financial burden to the NHS. An imbalance in the level of matrix metalloproteinases (MMPs) and the tissue inhibitors of MMPs (TIMPs) in chronic wounds impedes the healing process. In addition, high levels of bacteria in the wound bed are a common feature of chronic wounds and also cited as a major cause of delayed healing. The aim of this article is to look in more detail at the role of MMPs in wound healing as well as the antimicrobial properties of honey when combined with a dressing to combat wound infection. The article also introduces a new dressing, MelMax® (CliniMed), which utilizes protease regulation and the antimicrobial properties of honey when addressing chronic wound infection. Short-term case studies are used to demonstrate how the dressing was successfully incorporated into the author's practice.

Key words: Chronic wounds ■ Honey ■ Proteinase regulator ■ MelMax

Wound healing is a complex and dynamic process that results in the restoration of damaged tissue. The healing process is triggered by tissue injury and can be described in four overlapping stages (Enoch et al, 2006):

- Haemostasis
- Inflammatory
- Proliferative
- Maturation.

With the advances in wound care over the past 20 years, and the application of evidence-based care, it is realistic to expect the majority of wounds to heal within a reasonable timeframe (Moffatt and Vowden, 2008). However, in some patients, healing is compromized in one or more of the above stages, resulting in delayed healing and the formation of a chronic wound (Cole-King and Harding, 2001). Ayello and Cuddigan (2004) describe chronic wounds as those that fail to proceed through an orderly and timely process to produce an anatomical and functional result.

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Chronic wounds can have a direct effect on patients' quality of life and incur a huge financial burden for the NHS. Posnett and Franks (2007) state that the cost of treating chronic wounds for the NHS was estimated between £2.3–3.1bn (in 2005–6), which is set to increase over the next 20 years due to the increasing elderly population.

In order to prevent routine and ritualistic care, every patient with a wound should be subjected to an ongoing process of assessment and review – this will allow for the prompt identification of a chronic wound in order that optimal care can be provided. Schultz (2009) lists the different factors involved in healing wounds compared to chronic wounds (*Table 1*), including levels of bacteria and matrix metalloproteinases (MMPs).

The aim of this article is to look in more detail at the role of MMPs in wound healing as well as the antimicrobial properties of honey in combating wound infection. The article also introduces a new dressing, MelMax® (distributed by CliniMed), and demonstrates how it was used on patients with chronic wounds.

Proteases and wound chronicity

As mentioned above, wound healing is a complex process that can be described in four overlapping stages (Enoch et al, 2006). Schultz (2009) explains that the healing process involves an interaction between several different cell types, which include the inflammatory cells, neutrophils, macrophages and lymphocytes – these inflammatory cells destroy micro-organisms and release proteases.

MMPs facilitate the removal of denatured extra-cellular matrix (ECM) components present in the wound, which need to be removed in order to allow healing to progress. Providing there is no bacterial colonisation, after 7–10 days of healing the inflammatory response begins to resolve and by the 14th day, the inflammatory cells and mediators return back to baseline levels allowing the repair process to begin (Schultz, 2009).

MMPs are zinc-dependent endopeptidases and are part of a larger family of proteases known as the metzincin superfamily. Schultz (2009) explains that MMPs are continually active throughout the healing process, for example, degrading the capillary basement membrane allowing angiogenesis to occur. They also have a role to play in the contraction of the ECM and in the migration of epithelial cells across the extracellular membrane. During the final stage of healing, MMPs help with the degradation of the disorganized matrix, allowing a more organized structure to be laid down.

Tissue inhibitors of MMPs (TIMPs) are responsible for inhibiting the activity of MMPs and in normal wound healing the levels of both TIMPs and MMPs are balanced. This allows the new wound structure to be laid down in an orderly and controlled manner (Schultz, 2009).

In the past, the same wound healing theory was applied to both acute and chronic wound healing (Dowsett and Newton, 2005). However, it is now recognized that chronic wounds become 'stuck' in the inflammatory stage of healing (Ayello and Cuddigan, 2004; Dowsett and Newton, 2005; Schultz, 2009), resulting in a tendency for the inflammatory response to become exaggerated. This results in increased MMP levels and a reduction in TIMPs (Vowden et al, 2008), whereas successful healing is dependent on the correct balance between the two (Greener et al, 2005). This is supported by Enoch et al (2006), who states that raised MMP levels can be detrimental to wound healing. Ayello and Cuddigan (2004) state that the higher levels of MMPs present in chronic wounds compared with acute wounds, along with neutrophil elastase activity, results in the degradation of proteins and the inactivation of growth factors – this eventually causes a delay in wound healing (Vowden et al, 2008).

A review of the literature demonstrates that although MMPs are essential for wound healing, the balance between MMPs and TIMPs must be appropriate, otherwise raised MMP levels will be detrimental to wound healing. Greener et al (2005) state that regulating protease activity aids wound healing and therefore the development of dressings to counteract the detrimental effect of MMPs in chronic wounds is beneficial.

Table 1. Biochemical differences between acute and chronic wounds

Healing wounds	Chronic wounds
Low level of bacteria	High level of bacteria (frequently present as biofilms or resistant organisms, such as MRSA)
Low level of inflammatory cytokines	High level of inflammatory cytokines
Low levels of MMPs and reactive oxygen and nitrogen species	High levels of MMPs and reactive oxygen and nitrogen species
Functional, intact matrix	Degraded non-functional matrix
High mitogenic activity	Low mitogenic activity
Mitotically competent cells	Senescent cells

(Schultz, 2009)

Honey

Honey is a natural substance produced by bees to preserve nectar – it is made up of a combination of enzymes contained in secretions from the hypopharangeal gland (Molan, 2005; Molan, 2008).

The use of honey in wound care dates back as far as 2000 BC, where there is evidence that it was used by the ancient Egyptians (Dunford et al, 2000). More recently, the use of honey has increased, due to factors such as bacterial resistance to antibiotics and the difficulty of promoting healing in chronic wounds (Bardy et al, 2008).

The antibacterial activity of honey is due to its high sugar content and low pH. The majority of microbes thrive in a pH environment of between 7.2 and 7.4, while the pH of honey is more acidic (between 3.2 and 4.5), which impedes microbial growth. The high sugar content causes moisture to be drawn from the wound bed, denying bacteria sufficient water to support their growth (Blair, 2008; Bardy et al, 2008).

Honey is also effective in wound debridement – Morris (2008) explains that the debriding action of honey is due to the fact that it promotes the conversion of inactive plasminogen, which is found in the wound matrix, into its active form, plasmin. Plasmin is an enzyme that is responsible for the breakdown of fibrin clots, which attach slough and eschar to the wound bed (Morris, 2008). The increase in lymphocytes and phagocytes facilitated by honey also means that monocytes release cytokines and interleukins, which then stimulate the healing process (Bardy et al, 2008).

Honey also has a role in the management of malodour as it both inhibits bacterial growth and provides glucose as an alternative form of fuel, resulting in the production of lactic acid as opposed to malodorous compounds (Molan, 1999).

Honey can be used in the treatment of several different wound types, including pressure ulcers, necrotizing fasciitis, leg ulcers and diabetic foot ulcers. Honey has also been shown to be as effective as silver sulphadiazine in the management of burns (Molan, 1999). Although adverse effects from the application of honey are rare, an assessment to eliminate any possibility of reaction to bee products should be made prior to application (Cutting, 2008).

MelMax

Alongside the issues of delayed healing, chronic wounds regularly contain a high level of bacteria, which often develops into a biofilm (Schultz, 2009) (*Table 1*). Although, dressings containing protease modulators and protease regulators are becoming commonplace, MelMax is unique in that it combines the antimicrobial properties of honey with the MMP regulatory property of ionogens formulation. MelMax has been scientifically designed to cleanse and aid healing in colonised and infected wounds. It is made up of a sterile acetate mesh fabric dressing, which is impregnated with a blend of buckwheat honey (75%) and ionogens formulation (25%).

Buckwheat honey is a rich source of phenolic compounds, which have antibacterial properties (Van Den Berg et al, 2008). In addition, buckwheat honey has a low pH of 3.3 and a high free acid content, which contribute to the regulation of bacterial colonisation.

MelMax is intended for use with infected and/or critically infected wounds, which have diminished healing properties, for example, acute wounds including:

- Leg ulcers
- Pressure ulcers
- Surgical wounds
- Trauma wounds
- Burns.

It can also be used in chronic wounds, including:

- Diabetic foot ulcers.

Figure 1. Skin tear on first assessment.

Figure 2. Skin tear four days after first application of Melmax.

The application of MelMax is simple as it can be cut to fit the wound or folded. Overlapping the wound is not contraindicated, however, it is important to ensure that the dressing is in contact with the wound bed. To achieve best results, the manufacturers recommend daily dressing changes at the start of treatment. Once the wound starts to heal, dressing changes can be reduced – in studies the average dressing change was 2–3 times per week.

MelMax is not recommended for dry necrotic wounds, clean granulating wounds or where the patient has a known sensitivity to buckwheat honey, acetate or ionogens formulation, or where there are no signs of infection or critical colonisation.

The dressings are available in three sizes:

- 5 x 6 cm (£4.75)
- 8 x 10cm (£9.75)
- 8 x 20 cm (£19.50).

Case Studies

Case Study 1

Mrs M is a 72-year-old lady who had paper thin ecchymotic skin. She was admitted to hospital with an exacerbation of her chronic obstructive pulmonary disease (COPD), however, she also had a history of skin tears and in January 2009 she developed a small category 2a skin tear (Payne and Martin, 1993). This was initially treated as per trust protocol (cleansed with warm normal saline and the flap replaced and held in place with a soft silicone dressing) then with various dressings as the tear was slow to heal, taking nearly 10 weeks to resolve. In April 2009, Mrs M developed a second category 2a skin tear on the same leg. Again, following local protocols the skin flap was replaced and held in place with a soft silicone dressing. One week later, the nurses became concerned as there was an increase in the level of exudate and slight malodour. As there were no signs of healing, the tissue viability nurse was asked to assess the tear but found no signs of infection, apart from a slight malodour and an increase in the level of exudate (*Figure 1*). However, because of the possibility of colonisation, it was decided to apply MelMax to the wound.

The tissue viability nurse felt that the skin flap was still viable and it was left in place. As per the manufacturers' recommendations, a MelMax dressing was applied daily. By the fourth dressing change, the wound was progressing well, the level of exudate had reduced and there was no malodour (*Figure 2)*. Mrs M had been told of the possibility of a drawing pain due to the osmotic effect of the honey and she did experience some discomfort in the first three days, however, this did not require any extra pain relief and the discomfort resolved by the fourth day.

After one week, Mrs M was reassessed and the wound was progressing well – it had reduced in size, there was evidence of epithelialization. As the wound was healing, the MelMax dressing was discontinued and the tear was again covered with a soft silicone dressing. Six days later, Mrs M was discharged home with a healed skin tear.

Age and COPD are both factors associated with a delay in wound healing and despite appropriate care Mrs M's first skin tear was slow to heal. However, at the first signs of delayed healing and the possibility of critical colonisation in the second tear, MelMax was applied and the wound healed within 14 days.

Case Study 2

Mrs P was a 82-year-old woman who had sustained a deep dermal burn to both breasts and upper abdomen in early December 2008. There was slow progress and the tissue viability nurse was asked to assess her in May 2009. The wound on the right breast had healed, however, the wound on the left breast measured approximately 3.75 x 3cm and was completely covered with friable overgranulation tissue. There was a moderate to high level of exudate, no apparent malodour and Mrs P reported a moderate amount of discomfort rather than pain (*Figure 3*). MelMax was first applied on 6 May.

At reassessment on 13 May, Mrs P's wound measured approximately 3.5 x 3.0cm. There was little change in the level of exudate, but the overgranulation was beginning to resolve (*Figure 4*). Mrs P stated that she found the dressing comfortable and did not complain of any discomfort.

Secondary dressings

Mrs M had a surgipad applied as a secondary dressing, which

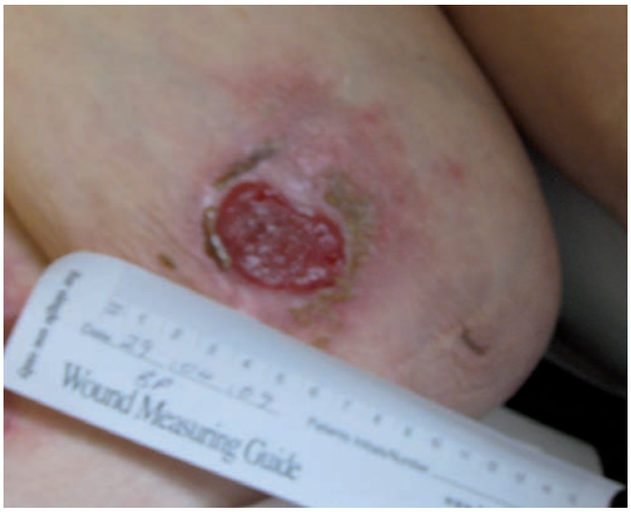

Figure 3. Burn injury prior to application of MelMax.

Figure 4. Burn injury one week after application of MelMax.

was held in place with a tubular dressing, whereas Mrs P was using a silicone dressing before the application of MelMax and this was continued.

These case studies have examined the use of Melmax over five dressing changes – in the case of Mrs M, the dressing was discontinued after one week as the wound was progressing well; in the case of Mrs P, there were changes noted after one week with a reduction in the level of overgranulation.

Conclusion

Chronic wounds represent a huge burden on NHS resources as well as impacting negatively on the quality of life of patients. A review of the literature has demonstrated that an inbalance in proteases, alongside infection, was a common factor in chronic wounds and this is seen as a contributory factor in delayed healing.

MMP regulator dressings, alongside antimicrobials, have an important part to play modern wound care, however, MelMax is unique in that it combines an MMP regulator with honey, which is recognized as having both antimicrobial and debriding properties.. BJN

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KEY POINTS

- Chronic wounds can have a direct effect on the quality of life of the patient.
- Wound healing is a complex and dynamic process that results in the restoration of damaged tissue.
- MMPs facilitate the removal of denatured extracellular matrix (ECM) components present in the wound, allowing healing to progress.
- The antibacterial activity of honey is due to its high sugar content and low pH.
- MelMax® is a unique dressing in that it combines the antimicrobial properties of honey with the MMP regulatory property of ionogens formulation.
- MelMax has been designed to cleanse and aid healing in colonised and infected wounds.
- It is made up of a sterile acetate mesh fabric dressing, which is impregnated with a blend of buckwheat honey (75%) and ionogens formulation (25%).
- Application is simple as MelMax can be cut to fit the wound or folded.
- Overlapping is not contraindicated, however, it is important to ensure that the dressing is in contact with the wound bed.