Introduction

Honey is an ancient remedy for the treatment of infected wounds and was first recognised as a topical antibacterial agent in 1892 (Molan, 2001). There are now many published reports describing the effectiveness of honey products in all phases of wound healing, with no adverse effects on the healing process. This article describes the role of Medihoney™ dressings in the management of hard-to-heal wounds.

WHY DOES HEALING STALL IN SOME WOUNDS?
Normal wound healing is a staged process that comprises inflammation, cell proliferation and tissue remodelling. The inflammatory phase has an essential role in cleaning the wound of bacteria and debris and in initiating the later stages of wound healing. Most wounds heal uneventfully and in a timely manner, requiring minimal input from clinicians. However some wounds have the potential to become chronic, where healing is stuck in the inflammatory stage (Boyd et al, 2004). This may be due to the patient’s age and the presence of co-morbidities, as well as factors related the wound itself (EWMA, 2008).

For wounds that are not progressing, wound bed preparation is essential for effective management. It enables clinicians to remove the barriers that may lead to delayed wound healing, by identifying the presence of infection, devitalised tissue or moisture imbalance (Falanga, 2004).

WHAT ARE MEDIHONEY™ DRESSINGS?
The Medihoney™ antibacterial range of dressings include: Medihoney™ Medical Honey; Medihoney™ Wound Gel; Medihoney™ Gel Sheet; Medihoney™ Apinate Dressing; Medihoney™ Tulle Dressing and Medihoney™ Barrier Cream.

These products can be considered for use as part of a wound bed preparation protocol to:
- Promote a moist wound environment
- Debride sloughy wounds
- Reduce inflammation
- Stimulate the immune system.

All products contain medical honey of standardised antibacterial activity, which is derived predominantly from Leptospermum sp (including manuka). Additionally, Medihoney™ Wound Gel contains natural waxes and oils and Medihoney™ Barrier Cream contains natural oils, aloe vera and vitamin E. Medihoney™ Apinate Dressing is a calcium alginate dressing and Medihoney™ Tulle Dressing is a non-adherent wound contact dressing. Medihoney™ Gel Sheet comprises manuka honey and sodium alginate. All products are sterilised by gamma irradiation, which does not affect the antibacterial properties of honey.

HOW DOES HONEY WORK?
The role of honey in the management of wounds is based on its antimicrobial properties and its ability to influence wound healing (Molan, 1999). This is achieved in a number of ways:

Antibacterial action
In laboratory studies, manuka honey has been shown to have an antibacterial action against a broad spectrum of bacteria and fungi, including:
- Staphylococcus aureus (Cooper et al, 2002; Blair et al, 2009)
- Pseudomonas aeruginosa (Cooper and Molan 1999)
- MRSA, vancomycin-sensitive and vancomycin-resistant enterococci (Cooper et al, 2002; George and Cutting, 2007).

Although undiluted honeys are active against a broad spectrum of pathogens, not all exhibit similar activity on dilution (Cooper and Jenkins, 2009). Manuka honey has a distinctive, heat stable antibacterial component, known has as methylglyoxal (MGO) (Mavric et al, 2008). It is formed from dihydroxyacetone, which is typically found in the nectar of manuka flowers (Adams et al, 2008). This allows it to maintain its antibacterial activity even when diluted, such as when it comes into contact with wound fluid.

Removal of biofilms and MRSA
Biofilms are now recognised to impede wound healing and there is a need to inhibit their development (Phillips et al, 2011). Honey supplemented with MGO (ie equal to manuka honey) has been shown to inhibit S. aureus biofilms (Jervis-Bardy et al, 2011). Inhibition of P. aeruginosa biofilms was dependent on contact time and concentration of manuka honey (Okhiria et al, 2009).

Eradication of MRSA from colonised wounds following topical application of manuka honey has been reported in patients with leg ulcers (Natanaj et al, 2001; Chambers 2006) paediatric oncology patients (Blaser et al 2007) and in patients with maxillofacial wounds (Visavadia et al, 2006). The removal of MRSA from wounds reduces the risk of systemic infection and cross infection to other individuals.
Reduction in malodour
Patients with exuding and/or infected wounds may experience malodour. The ability of honey to eliminate unpleasant odours from wounds may be due to the inhibition of anaerobic bacterial growth. Honey has been shown to have a rapid deodorising effect in patients with malodorous fungating wounds (Segovia 2010) and in leg ulcers (Gethin and Cowman, 2008).

Debriding effect
Wounds that are not progressing require repeated debridement to remove necrotic and sloughy tissue to establish a healthy wound bed (Falanga, 2004). Honey provides an autolytic debriding effect whereby the osmotic action of honey encourages lymph fluid to rehydrate devitalised tissue, helping to remove sloughy and necrotic tissue (Gethin et al, 2008). Hydrogen peroxide produced in honey by the enzyme glucose oxidase is thought to contribute to the debridement process (Pieper, 2009).

Anti-inflammatory effect
Chronic wounds have increased inflammation, giving rise to elevated levels of proteases that delay healing. Manuka honey has a low pH, which may help to control protease activity in the wound (Gethin, 2007) and may be associated with a reduction in wound size (Gethin et al, 2008). It is likely that the antioxidants in honey also confer anti-inflammatory influences by scavenging free radicals that arise in both acute and chronic wounds (Henriques et al, 2006).

Immune-modifying effect
Manuka honey stimulates the immune system to produce inflammatory cytokines, which are important for wound healing. It is likely this stimulation of the immune system helps to promote progression towards healing (Tonks et al, 2007).

WHEN IS MEDIHONEY™ INDICATED?
The antibacterial properties of manuka honey indicate a role in the management of locally infected wounds, wounds colonised by antibiotic-resistant bacteria, malodorous wounds and chronic wounds such as venous leg, diabetic foot and pressure ulcers. In addition it may be used in patients with fungating lesions, radiotherapy-impaired wounds, burns and surgical incisions, including donor and recipient graft sites.

Patients with leg ulceration and diabetic foot ulcers are at high risk of developing multiple episodes of infection. Identification of local symptoms can promote timely intervention to reduce bacterial bioburden and help to avoid the need for systemic antibiotics.

HOW TO APPLY MEDIHONEY™ DRESSINGS
Patients may present with a variety of challenging wounds so it is essential that the product chosen is able to meet the needs of individual patients (Table 1). When honey is applied to the wound bed, it becomes less viscous and is diluted through exudation. High levels of exudate require more frequent dressing changes to maintain a good therapeutic effect. For deep wounds or cavities the wound bed can be filled with medical honey before applying the honey-impregnated dressing.

HOW FREQUENTLY SHOULD THE DRESSINGS BE CHANGED?
All of the Medihoney™ products are licensed to remain on the wound for a 7-day period. The frequency of dressing changes, however, will depend on how rapidly the honey is diluted by the wound fluid and may require daily changes in the initial stages of wound healing. As exudate levels decrease, fewer dressing changes are required and they can be left in situ for up to 3-7 days. If strike-through occurs on the secondary dressing, it may need to be changed more often to prevent maceration.

Tip: Medihoney™ Antibacterial Medical Honey and Medihoney™ Wound Gel can be removed by rinsing with saline or tap water at dressing change. Sometimes the plant waxes leave a residue on the wound surface and can be irrigated away.

### Table 1 Application guide to Medihoney™ dressings

<table>
<thead>
<tr>
<th>Product name</th>
<th>Indications/application</th>
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<tbody>
<tr>
<td>Medihoney™ Antibacterial Medical Honey</td>
<td>For all types of wounds with low to moderate exudate as well as deep cavity wounds</td>
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<tr>
<td></td>
<td>Apply 3mm layer to the wound directly and cover with an absorbent secondary dressing</td>
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<tr>
<td></td>
<td>It can be applied in and around the mouth and is safe if ingested</td>
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<tr>
<td>Medihoney™ Antibacterial Wound Gel</td>
<td>For surface wounds with low to moderate exudate and partial and full thickness wounds</td>
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<tr>
<td></td>
<td>Designed to be static at the wound site even in the presence of wound fluid and body heat</td>
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<tr>
<td></td>
<td>Apply 3mm layer and cover using a secondary absorbent dressing</td>
</tr>
<tr>
<td>Medihoney™ Barrier cream</td>
<td>Use to protect the skin from breakdown (eg skin damaged by irrigation treatment or in wet areas due to incontinence)</td>
</tr>
<tr>
<td></td>
<td>Use to maintain the pH of the skin and prevent damage caused by shear and friction</td>
</tr>
<tr>
<td></td>
<td>Apply three times daily or as required and repeated after bathing, at each dressing change or after each episode of incontinence</td>
</tr>
<tr>
<td>Medihoney™ Gel Sheet</td>
<td>Suitable for use in wounds requiring autolytic debridement of slough and necrotic tissue</td>
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<tr>
<td></td>
<td>For mild to moderately exuding wounds and in patients with pressure ulcers presenting with leathery eschar</td>
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<tr>
<td></td>
<td>To apply, remove the liners and place in direct contact with the wound bed. Cover with an absorbent secondary dressing</td>
</tr>
<tr>
<td>Medihoney™ Tulle Dressing</td>
<td>For use on lightly exuding wounds with a suspected biofilm and on first and second degree burns, donor sites and superficial wounds</td>
</tr>
<tr>
<td></td>
<td>Cut dressing to size and place in direct contact with the wound bed. Cover with an absorbent secondary dressing</td>
</tr>
<tr>
<td>Medihoney™ Apinate Dressing</td>
<td>Suitable for use in wounds requiring autolytic debridement</td>
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<tr>
<td></td>
<td>Can be used under compression in patients with leg ulcers due to low profile of the dressing</td>
</tr>
<tr>
<td></td>
<td>Also available as a rope for use in cavity wounds such as pressure ulcers and dehisced surgical wounds</td>
</tr>
<tr>
<td></td>
<td>Cut dressing to size and place in direct contact with the wound bed. Use with a secondary absorbent dressing</td>
</tr>
</tbody>
</table>
Gel Sheet or Medihoney™ Apinate Dressing. It is contraindicated to use alternative product where gravity may affect it staying in place (eg leg ulcers) and particularly suited for use in cavity or deep wounds. However, due to the viscosity (thickness) of Medihoney™ Wound Gel it is important to monitor all patients regularly and check for signs of improvement or deterioration of the wound. If there is no response to treatment after 14 days an alternative approach should be considered (Stephen-Haynes, 2011). Medihoney™ Gel Sheet was applied to the skin and ulcers on his lower legs to reduce bioburden and malodour while promoting autolytic debridement. After 22 days of treatment the patient reported a reduction in odour and improved comfort levels. It was felt that the product was a safe choice for this particular patient.

### WHEN SHOULD MEDIHONEY™ BE DISCONTINUED?

It is important to monitor all patients regularly and check for signs of improvement or deterioration of the wound. If there is no response to treatment after 14 days an alternative approach should be considered (Stephen-Haynes, 2011). Medihoney™ dressings should be discontinued when the primary objective is achieved, ie a healthy wound bed, reduction in bioburden and odour, with evidence of granulation and epithelisation. In the case of the barrier cream, this should be discontinued when the skin is no longer at risk of breakdown.

### WHEN ARE MEDIHONEY™ DRESSINGS CONTRAINDICATED?

Medical honey should not be used in patients with a known sensitivity to honey, calcium alginate or sodium alginate. Due to the viscosity (thickness) of Medihoney™ Wound Gel it is particularly suited for use in cavity or deep wounds. However, where gravity may affect it staying in place (eg leg ulcers) an alternative product may need to be selected such as Medihoney™ Gel Sheet or Medihoney™ Apinate Dressing. It is contraindicated in very deep wounds or where there is undermining/tracking with sinuses. This is due to the fact that the plant waxes can potentially block sinuses.

**Safety and tolerability**

Some patients may complain of pain, which may be related to the osmotic effect of honey, which may be felt as a drawing sensation. Analgesia may be indicated and in some patients it may be advisable to change to a honey that is less concentrated in sugar and contains waxes (Peiper, 2009). Medihoney™ is safe to use in patients with diabetes and there is no evidence to show that it significantly raises blood sugar levels (Simon et al, 2005).

Recent laboratory investigations suggest that the development of bacterial resistance to honey is unlikely (Blair et al, 2009; Cooper et al, 2010) and no toxic effects have been reported.

### WHAT IS THE EVIDENCE FOR USE?

There is clinical evidence to support the use of honey in wounds with different aetiologies and at different stages of healing (Table 2).

#### Table 2 Summary of clinical studies using medical grade honey

<table>
<thead>
<tr>
<th>Reference</th>
<th>Title</th>
<th>Type</th>
<th>Main findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Johnson et al (2005) <em>J Am Soc Nephrol</em> 16: 1456-62</td>
<td>Randomized, controlled trial of topical exit-site application of honey (Medihoney) versus mupirocin for the prevention of catheter-associated infections in hemodialysis patients</td>
<td>Open-label RCT Catheter exit sites: honey (n=51) vs mupirocin (n=50)</td>
<td>No significant difference in incidence of bacteraemias</td>
</tr>
<tr>
<td>Gethin G and Cowman S (2008) <em>J Clin Nurs</em> 18: 466-74</td>
<td>Manuka honey versus hydrogel – a prospective, open label, multicentre, randomised controlled trial to compare desloughing efficacy and healing outcomes in venous ulcers</td>
<td>Open label, multicentre RCT Lower leg ulcers: honey (Apinate) dressings (n=20)</td>
<td>Use of honey dressings was associated with significant decrease in wound pH and a reduction in wound size</td>
</tr>
<tr>
<td>Lund-Nielsen et al (2011) <em>Ostomy Wound Manage</em> 57: 28-36</td>
<td>Qualitative bacteriology in malignant wounds— a prospective, randomized, clinical study to compare the effect of honey and silver dressings</td>
<td>Prospective, single-blind RCT Malignant wounds in advanced stage: cancer patients: honey dressings (n=34) vs silver dressings (n=33)</td>
<td>61% of wounds reduced in size. No significant differences in type and variety of pathogens, or wound size were found</td>
</tr>
<tr>
<td>Robson et al (2011) <em>Br J Oral Maxillofac Surg</em> (epub 8 Aug)</td>
<td>Randomised controlled feasibility trial on the use of medical grade honey following microvascular free tissue transfer to reduce the incidence if wound infection</td>
<td>Randomised feasibility study Microvascular free tissue transfer reconstruction for cancer of head and neck: honey wound gel (n=25) vs conventional therapy (n=24)</td>
<td>Patients in the honey group had a significantly shorter hospital stay than those in the standard treatment group (p&lt;0.005)</td>
</tr>
</tbody>
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#### Case report

A 64-year-old male patient presented with a history of lymphoma since 2007. He also suffered from chronic venous hypertension resulting in venous leg ulcers. He was treated with a course of radiotherapy in April 2011, which led to skin damage (Fig 1). The ulcers on his legs were sloughy and malodorous.

**Treatment**

Medihoney™ Gel Sheet was applied to the skin and ulcers on his lower legs to reduce bioburden and malodour while promoting autolytic debridement. After 22 days of treatment the patient reported a reduction in odour and improved comfort levels. It was felt that the product was a safe choice for this particular patient.

**Fig 1: Venous leg ulceration following skin damage due to radiation**
AVAILABILITY OF PRODUCTS
Medihoney™ products are available on Drug Tariff through the NHS supply chain or to buy direct.

Summary

Manuka honey has been proven to support moist wound healing and to be effective in both the management of wound infection and debridement of devitalised tissue. It may have a particular role in the management of hard-to-heal wounds and be used as part of a wound bed preparation protocol to promote healing.

REFERENCES


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