Are honey and maggots reclaiming their therapeutic positions in the management of chronic wounds?

Ancient remedies are a thing of the past. Or are they? In this second article on wound management Nita Flowers explains how the clinical use of honey and sterile maggots for managing certain types of wounds has experienced a resurgence.

Introduction

In the current climate of increasing rates of Methicillin-resistant staphylococcus aureus (MRSA) and other infections[1,2] both honey and maggots are being rediscovered as wound management preparations. This article looks at the properties of honey and maggots as wound management products and at the evidence for their use in healing wounds.

Honey

The therapeutic use of honey largely went out of fashion when antibiotics were introduced. However, it has several properties that make it attractive as a potential medicament for wounds. For example, it provides a physical barrier to infection, and has antimicrobial, deodorizing, debriding and anti-inflammatory actions as described below.

1. Physical barrier

Honey has high viscosity, which causes it to form a physical barrier to infection.[3] It is also hyperosmolar[3,4] and tends to draw fluid out of the wound area but allows moist healing. This is important because when a wound dries out the epithelial cells have to migrate downwards into the resulting cavity to form the new skin layer, and this results in pitting and scarring. By ensuring a wound area is kept moist — but not wet — scab formation and scarring are minimised. Because excessive inflammation is prevented by honey, fibrotic scarring does not occur and through its antibacterial action[3] it prevents cross-infection. Honey therefore shows some of the properties of an ideal dressing.[5]

2. Antimicrobial actions

The antimicrobial properties of honey are a result of its low water content, hydrogen peroxide formation, flavinoid content and phenolic acid in addition to many other unidentified substances (often collectively referred to as 'inhibines'), which makes honey a poor environment for growth of microorganisms.[3] Bees concentrate the dilute sugar solution (nectar) they collect by evaporating off most of the water, so that mature honey is typically around 17% water and 80% sugar (glucose and fructose). It is characteristically acidic its pH being between 3.2 and 4.5, which is unsuitable for many microorganisms.[3,4] Although acidity of honey promotes its antimicrobial actions bodily fluids from exudates will dilute it and raise its pH, reducing this effect.[4] However, the major antibacterial activity in honey is thought to result from the production of hydrogen peroxide by glucose oxidase, which occurs in more dilute, higher pH honey.[4]

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Investigators have also compared the antibacterial activity of honey derived from different plant sources and found some significant differences in activities.[4,6] For example, a range of honeys produced by bees foraging on different floral sources were tested for antibacterial activity against *S. aureus* in an agar-well diffusion assay with reference to phenol as standard.[6] Antibacterial activity was found to range from the equivalent of less than 2% to 58% of phenol's activity. When antibacterial activity was assayed in the presence of catalase to remove hydrogen peroxide most honeys showed no antibacterial activity.[5] Honeys from some floral sources, however, such as *Leptospermum scoparium* (Myrtle family) and *Echium vulgare* (Borage family) showed additional non-peroxide antibacterial activity in a significant proportion of the samples.[4,5]

Researchers in New Zealand[4] and others have investigated the antibacterial activity of

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honeys derived from *Leptospermum* against several MRSA strains *in vitro* with promising findings.[4] Some preliminary clinical studies have also been conducted, including a case reported of an immunosuppressed patient who developed a hydroxyurea-induced leg ulcer with subclinical MRSA infection, which was subsequently treated with topical application of manuka honey (from *Leptospermum)*, without cessation of hydroxyurea or cyclosporin.[7] In another study of seven cases whose wounds were either infected or colonised with MRSA, honey application was found to produce full healing.[8] If such findings are further substantiated honey may prove useful in the treatment if MRSA.

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3. Deodorising actions

In infected wounds odour is produced when bacteria metabolise amino acids producing amines and sulphur. When honey is applied the odour is not produced. Honey is thought to provide the bacteria with an alternative energy source (sugars) which produce non-odorous metabolites and may therefore play a role in the control of malodorous wounds as suggested by work showing the eradication of odour by honey applied to leg ulcers.[9]

4. Debriding actions

Debridement is the removal of devitalised or infected tissue or foreign material from a wound. There are many reports that wounds dressed with honey are rapidly debrided to give a clean granulating wound bed.[10] The most likely explanations of the debriding action induced by honey are that it promotes — by its osmotic pull — constant bathing of the wound bed with protease-containing lymph fluid, and because it promotes conversion of inactive plasminogen in the wound matrix to the active form, plasmin. This enzyme functions to break down fibrin clots, which attach slough and eschar to the wound bed.[11] This may, of course, also contribute to its odour-reducing effects.

5. Anti-inflammatory actions

Prostaglandins produced during an inflammatory response produce pain and oedema in the wound area. Histological observations have been reported of reduced acute inflammatory changes and control of infection when honey was applied to wounds compared with silver sulphadiazine.[12,13] Furthermore, an investigation into the effect of honey on the release of cytokines from a monocyte cell line in culture showed stimulation of the release of tumour necrosis factor-alpha (TNF-alpha), interleukin (IL)-1-beta and IL-6, which activate immune responses and are known to play an important role in healing and tissue repair.[14]

6. Granulation promotion

The observed stimulation of TNF-alpha, which is known to stimulate angiogenesis might account for some of the preliminary experimental findings of promotion of angiogenesis after application of low concentrations of honey to wound models.[15] Increased blood supply would help bring nutrients, essential vitamins and minerals to the wound bed and honey would provide a source of energy for macrophages, which could be important in promoting wound healing.

Products available

A standardised sterile product with a European conformity CE mark and approved as a sterile medical device must be used. Using a product that is not certified is not recommended and raises possible effectiveness and litigation issues.

Medihoney® wound gel is 80% honey mixed with plant oils such as castor, palm and coconut for ease of handling especially for superficial wounds. Antibacterial medical honeys are very fluid and run easily at body temperature, making these useful for coating cavities and crevices.

Calcium alginate fibres, extracted from seaweed, have been added to honey to make it less runny and more suitable for wound-application products. Sodium present in wound fluids cause the formation of sodium alginate (a soluble gel) and honey is held in a soft gel, which does not slide off nor stick to the wound. Refer to the *British National Formulary*[16] and *The Drug Tariff*[17] for details of individual products (see Box 1 for a summary).

How to select a dressing[18]

A honey gel or ointment from a tube should

Box 1. Honey-based topical applications available in the UK[16,17]

Honey-based topical application	Pack size
Activon medical grade Manuka honey	25g
Medihoney antibacterial medical honey	20g
Medihoney antibacterial wound gel	10g
Medihoney antibacterial wound gel	20g
Mesitran ointment	15g
Mesitran ointment	50g
Mesitran ointment S	15g
Sanoskin Melladerm gel	50g
Honey Based Dressings	
Algivon medical grade Manuka honey	5cmx5cm
	10cmx10cm

be used on wounds with dry black eschar; these should then be covered with an adhesive foam or film for up to seven days. Absorbent dressings should not be used because they will absorb the honey and the exudates, and prevent the opportunity for debridement. In the presence of exudate a honey-impregnated alginate should be used. If levels of exudate are high then the products can be covered with an absorbent pad. If the levels of exudate are light-to-moderate an adhesive foam or hydrocolloid could be used.

Adverse effects

Pain is sometimes experienced after application of honey, but this is usually transient. It is thought that the osmotic effect of honey and/or its acidity may cause the pain. If pain is unbearable treatment should be discontinued. Honey should not be given to people who have an allergic to honey products. Diabetic patients can be treated with honey applications because there is no elevation in blood glucose levels; however blood glucose should be monitored.

In summary, honey has been reported to clear wound infections rapidly.[7,8,13] In some cases the application of honey has promoted healing in infected wounds that were not responding to conventional therapy.[8] A systematic review was published in 2001, which included seven randomised studies in 264 patients.[19] The review noted that the studies were of limited quality and could be influenced by known sources of bias. In addition, six of the studies were conducted by the same researcher in India. However, the overall conclusion was that the effectiveness of honey was plausible.[15]

Box 2. BioFoam dressings

BioFoam dressings (BFD) are available in the following sizes:

BFD 25 = 2.4cmx 4cm	150 maggots
BFD 50 = 5cm x5cm	300 maggots
BFD 70 = 7cm x 7cm	600 maggots
BFD 120 = 7cm x 12cm	900 maggots
BFD 100 = 10cm x 10cm	600 maggots
BFD 150 = 2.5cm 15cm	300 maggots

There are various forms of honey but no published data comparing available products. The lack of comparative studies among medical grade honey products makes it difficult to establish their place in therapy. The wide range of available products however, provides flexibility, especially in the management of wound infections and malodorous wounds.

Maggots

There is a widely held belief that wound healing is impeded by the presence of devitalised, necrotic tissue and wounds containing such material do not heal successfully.[20] Non-viable tissue not only inhibits the growth of epithelial tissue, but also increases the production of exudate, impairs assessment of the wound bed,

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and makes it more difficult to achieve wound closure, thus having an adverse effect on quality of life. The body can remove devitalised or infected tissue by natural processes but large quantities can delay healing and provide an environment for infection. Debridement is thought to provide a foundation for the subsequent healing of wounds. Maggot therapy has been shown to be an effective, fast-acting debriding agent and has the advantage of being beneficial in eliminating infection.[21]

Historically maggots were used for medicinal purposes by cultures such as the Mayan Indians of Central America and the Ngembe tribe of New South Wales Australia.[22] It would however be wrong to dismiss maggot therapy to history.

Maggots of the common green bottle fly known as *Lucilia sericata* are used. Maggots for medicinal use are sterile and therefore will not introduce pathogenic organisms onto the wound. Healing is facilitated by the maggots' natural feeding processes in conjunction with a properly prepared wound. During normal feeding maggots secrete a powerful mix of enzymes that break down wound tissue into a liquid form that the maggots then ingest. By ingesting this mixture the feeding maggots take up and destroy bacteria. Maggots may help combat odour by ingesting the bacteria in the wound.

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There are reports of maggots' activity against antibiotic resistant organisms such as MRSA. For example, investigastors undertook an observational study in which they recruited 13 consecutive patients aged 18–80 years who had had MRSA-colonized chronic diabetic foot ulcers for longer than three weeks. Sterile maggot larvae were applied for four days. The primary endpoint was complete eradication of MRSA from the ulcer following a minimum of two and a maximum of eight larval applications per ulcer. MRSA colonization was eliminated from all but one of the 13 ulcers after a mean of three applications with a mean duration of 19 days.[21]

Preparations available

Maggots are either applied sealed in a dressing pouch (such as the BioFoam dressings listed in Box 2) or by a 'free-range' technique where they are applied loose to a wound and held in place with appropriate dressings. The free-range technique is preferred for deep wounds. Larval calculators are available to determine the number of maggots to be used, and if pre-filled dressings are used a variety of sizes are available. The sealed pouch is held in place by a hydrocolloid dressing and plastic surgical tape. It is important that nothing

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occlusive is used because it will prevent the maggots from breathing.

A study to determine which method of maggot debridement therapy — free-range or contained — was more effective found that significantly better outcomes were achieved with the free-range technique versus the contained technique.[23] With the free-range technique, the mean number of maggot applications and the total number of maggots per treatment were significantly lower than with the contained application technique. Clinical *in vivo* study supports *in vitro* studies in which containment of maggots was found to reduce the effectiveness of maggot debridement therapy.[23]

Maggot therapy may be used for all types of wounds with necrotic or fibrous tissue that requires debridement. It may be helpful in the treatment of infected ulcers by decreasing the bacterial load and possibly decreasing the risk of amputation and sepis. It is important to consider contra-indications including:[23]

- ☐ patients who refuse consent
- ☐ the wound has large (more than 40cm^2) necrotic or sloughy areas
- ☐ wounds that have a tendency to bleed easily
- ☐ wounds that are open to body cavities or near internal organs
- ☐ wounds close to large blood vessels
- ☐ facial wounds
- ☐ any wound where the blood supply is insufficient to permit healing to take place
- ☐ patients taking anticoagulant therapy.

The maggot therapy should be removed after 3–5 days and should be disposed of as clinical waste. If further debridement is required larvae should be reordered and reapplied.[23]

Often a single treatment lasting two or three days is sufficient to achieve complete debridement in wounds that have proved resistant to other conventional wound treatments.[23] The use of maggots in wound management appears to have a sound basis in literature.[23] The incidence of serious or significant side-effects appears to be low.[23] Advantages include that debridement may be quicker than other methods of facilitating healing. By ingesting necrotic tissue and bacteria it has shown to be beneficial in the treatment and management of infection.[23] The most important aspect of wound management is that the patient is being treated holistically and the choice of maggot therapy is based on a comprehensive wound assessment.

Conclusion

There is evidence to support the use of honey and maggot therapy in wound management. As part of the toolkit for treating wounds, making a thorough wound assessment and preparation of the wound bed; good nutrition; exercise and good control of co-existing medical conditions are key to the healing process. ✣

Declarations of interest

The author has no interests to declare.

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