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Sweet success? Honey as a topical wound dressing

The antimicrobial properties of honey may help in the treatment of recalcitrant wounds.

ABSTRACT: Honey has a time-honored, albeit underrecognized, role as a wound-healing agent. In vitro studies have determined that honey demonstrates wide-ranging antimicrobial activity as a result of several putative antimicrobial components. Efficacy has been corroborated by many clinical anecdotes and some evidence from controlled trials. Commercial medicinal products have now become available outside of Canada. Where conventional treatments have failed, judicious use of honey can be recommended for topical wound dressing.

The medicinal use of honey for the treatment of wounds is ancient.[1] Despite this, there is very little awareness of honey's use in general practice. Physicians can benefit from knowing more about successful treatment using honey and the history and current aspects of such treatment.

Case report

An 89-year-old female presented to a medical centre with ongoing drainage from a back lesion in December 2004. She was otherwise in good health and was receiving daily L-thyroxine, enalapril, and rabeprazole. The upper posterior thoracic mass had been slowly increasing in size over many years but had not been treated because of its slow growth. Over the previous week, the patient had been cared for in an ambulatory facility where the lesion was deemed to be a sebaceous cyst abscess. An incision for drainage was made, and an antibiotic was prescribed.

The patient returned for dressing changes, but the open wound continued to release copious amounts of drainage. A culture taken at the initial visit yielded a pure growth of anaerobic *Peptostreptococcus*, and the Gram-stained smear included polymorphonuclear cells. The patient had been prescribed cloxacillin before the culture results were obtained, and was advised to continue with this agent. The drainage was unabated, and daily dressing changes were necessary. A repeat culture in early January yielded a pure growth of *Klebsiella pneumoniae*. Cephalexin was therefore prescribed. The drainage site was explored, debrided, and irrigated with moxifloxacin in solution.

Repeat routine cultures 2 and 4 weeks later were devoid of bacteria. Culture of the wound for fungi and atypical mycobacteria were also negative. Despite the latter, a purulent drainage continued, and referral was made to the plastic surgery service. In mid-March 2005, a surgeon performed further debridement and closed the wound with primary intention. Pathology of the contents confirmed an epithelial inclusion cyst. For the next 3 weeks, the wound remained closed with apparent superficial healing, but once again by mid-April, the wound spontaneously opened and continuous drainage ensued, again necessitating regular dressing changes. A review of the wound by the surgical service led to regular application of topical silver sulfadiazine cream along with daily dressing changes. The intensity of the drainage varied, but the wound re-

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mained open, and the recommended treatment was continued for the next several months.

On 22 October 2005, the silver sulfadiazine applications were discontinued, and pasteurized commercial honey was used instead with each dressing change. By 25 October 2005, more than one-half of the wound had closed. By mid-November, the entire wound was crusted and closed. No further drainage occurred. Through follow-up in June 2006, the wound continued to be healed.

Antimicrobial properties of honey

The production of honey by bees is affected by pure or mixed floral origins. The sugars that make up honey include large quantities of fructose and glucose, and lesser quantities of maltose and sucrose. Natural honey may possess low-level contamination with sessile forms of microbes, including mold, yeast, and bacterial spores, but these will not become vegetative in the harsh environment that honey provides.

Honey has several antimicrobial qualities and components (Table 1).[2] In its undiluted state, honey's high osmolarity creates a hygroscopic effect on microbes, thereby interfering with growth and metabolism. Such hygroscopic activity has led some to use granulated sugar or other sugar concentrates for the same purpose. Nevertheless, the antimicrobial action of honey well exceeds a simple osmotic effect, and an equivalent osmolarity of various sugars does not match honey's antimicrobial capability.

Table 1. Possible antimicrobial qualities and components of honey.

- High osmolarity
- Low pH
- Ability to generate hydrogen peroxide
- Flavonoids
- Phenolic acids
- Trace antibiotics
- Lyzozyme
- "Inhibines" (yet undefined organic compounds, including other compounds with antioxidant activity, which may provide antimicrobial activity)

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Natural honey has a low pH level of 3 to 5, which in itself inhibits microbe growth. A number of natural compounds may act as antioxidants (e.g., flavonoids, phenolic acids), and the presence of lysozyme is antagonistic to some bacteria. Trace amounts of antibiotics may also be found in some preparations, although in Canada, there are required standards for controlling the presence of antibiotics.[3] Apiaries are permitted to use antibiotics to control the problem of American foulbrood (a bee infection with a bacterial cause) or similar infections that can significantly curtail commercial production.

A major antibacterial property of honey, if not the foremost one, is its ability to generate hydrogen peroxide. Bee-derived glucose oxidase in honey converts glucose into glucuronic acid, and in doing so generates hydrogen peroxide as a by-product. In its pure state, honey's glucose oxidase activity is less than in honey dilutions of 30% to 50%. As honey concentration decreases, the glucose oxidase enzyme becomes more functional and this produces, in effect, a constant low concentration of hydrogen peroxide. Therefore, as honey on a wound is diluted by serous drainage, the hydrogen peroxide presence may in fact increase even though pH and osmotic effects diminish.[4] Different honeys vary in their hydrogen peroxide content and in their antibacterial activities.[5] Excess heat treatment of honey may inactivate the glucose oxidase enzyme.

The variation of antimicrobial activity among honeys has led investigators to realize that non-hydrogen-peroxide mechanisms of antagonism can be relevant. This appears to be more so with Manuka honey, the production of which is linked to the tea tree.[6]

The spectrum of direct antimicrobial activity is considerable, but the evidence of beneficial effect in vitro is largely confined to bacteria.[5,7-10] Antibacterial activity affects atypical mycobacteria and most clinical bacterial pathogens, whether Gram-positive or Gram-negative. Notable among the

latter are methicillin-resistant *Staphylococcus aureus* and vancomycin-resistant enterococci, enteric pathogens (such as *Salmonella*, *Shigella*, and *Escherichia coli* O157:H7), coagulase-negative staphylococci, *Helicobacter pylori*, oral streptococci, and anaerobes. Among Gram-negative bacteria, the antibacterial activity has extended to multidrug-resistant organisms. Some investigators have demonstrated an additive effect in vitro by combining honey and a traditional antibiotic. There is limited antimicrobial activity against yeast and molds, although the latter germs do not actively grow in the context of the strong osmotic gradient of honey. Nevertheless, some honey products and extracts have demonstrated antifungal activity. Of note, antimicrobial resistance does not appear to be inducible after repeated exposure.

Treating wounds with honey

There are many conventional wound treatments, some of which are dictated by the nature of the wound.[6,11] Physicians have become familiar with the strengths and limitations for many of these, which include topical chemicals (e.g., silver sulfadiazine cream, zinc compounds, vitamin E), hydrophilic alginates, hydrophilic colloids, and synthetic polymers. It is apparent, however, that many of the time-honored approaches for wound management by secondary intention have never been established by rigorous clinical trials.[12,13] Support for the use of all approaches, including honey, must therefore be tempered by the relative lack of evidence.

Successful wound treatment with honey has been reported anecdotally for the most part. Successes include some dramatic resolutions of large wounds that have not responded to other topical and systemic treatments.[6] Some controlled trials have also supported dressing wounds with honey.[14] Nevertheless, a recent systematic review of honey use is cautious in its recommendations.[15]

A beneficial effect of honey on the nonantimicrobial aspects of wound healing is unclear and still a subject for speculation.[16] Honey may stimulate inflammatory cytokine release from mononuclear cells.[17] In so doing, it may effectively stimulate granulation tissue and immune responses. Some have noticed a beneficial effect of honey to reduce wound odor and debris. Others have observed a reduction in wound swelling and a reduction in scarring. Honey has some practical advantages as a topical wound dressing. The consistency of honey reduces the likelihood that the dressing will adhere to the wound when removed. As well, the cost of honey compared with other commercial products is minimal, even when repeated applications are required.

Table 2. Precautions for the use of honey in wound therapy.

- Use where conventional treatments do not succeed.
- Use under medical supervision.
- Provide careful follow-up.
- Use with caution when deep tissue infection is present (i.e., where ancillary modalities should be used as well).
- Watch for the dilution effect of wound exudates and debris (i.e., regarding the necessary frequency for dressing change).
- Use honey that has some pre-use decontamination (i.e., pasteurization).
- Watch for allergic or irritant reactions on normal skin.

The translation of honey products for medicinal use is evolving. Given the potential effect of heat sterilization on the activity of honey, processing of some products includes gamma irradiation.[18] Commercial dressings with honey as the active ingredient have been designed, are reaching markets, and are being used successfully. For example, the Manuka honey of Australia has been packaged as Medihoney, and details of its use are now emerging in the medical literature.[19] Commercial preparations for medicinal use are generally taking the form of nonadherent dressings or slabs.[20-23] Standards for these products will most likely emerge. There is also potential for honey to be combined with other agents, including antibiotics.[24]

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While there are no studies that show honey may have an adverse impact on wounds, caution should be exercised until standard forms of medicinal honey become available (Table 2). The current medical literature provides many anecdotes suggesting how honey may be used. In the interim, there is justification to use honey when more conventional treatments have failed.

There is justification to use honey when more conventional treatments have failed.

Competing interests

None declared.

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