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REVIEW ARTICLE

Wound Care in the Wilderness: Is There Evidence for Honey?

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Honey is one of the most ancient remedies for wound care. Current research has shown promising results for its use in wound care. This review is intended to inform readers of the physiological properties of honey and the evidence that exists to support its clinical use. When compared with evidence for current wound treatment, honey has proven to be a safe, effective, and sometimes superior treatment for various wounds. There are currently US Food and Drug Administration–approved medical-grade honey products available in the United States. Although there have been no clinical trials exploring the use of honey in wilderness environments, it may be a safe, improvisational wound treatment. More robust studies are needed for definitive conclusions of its efficacy and safety.

Key words: honey, wound, burns, topical, wound care

Introduction

Honey has been used for millennia for wound care. One of the world's oldest surgical texts, the Edwin Smith papyrus, dates back to 1600–2200 BC and describes treating a head wound with an oil-and-honey–soaked linen bandage.[1] Records from ancient Greece and Egypt, the Ayurvedics of India, Hippocrates, Aristotle, and the Qu'ran all refer to the healing effects of honey.[2–5]

In the late 19th century honey began to transition from a folk remedy to a scientific inquisition. Honey's antimicrobial qualities were first documented in 1892 by B.A. Van Ketel, a Dutch scientist, and further research in the United States and Europe noted its worth in treating infected wounds.[6] However, with the new discovery of contemporary antibiotics in mid-20th century, medical use of honey fell out of favor.[7] Honey and its role in wound care have experienced a resurgence in recent research, and particular attention has been focused on its role in treating wounds contaminated with antibiotic-resistant organisms. There is a substantial amount of modern research published to help guide honey's role in wound healing and help one to better understand its unique properties.

In 2007, the US Food and Drug Administration (FDA) approved the first honey-related wound product—a sterile, single-use wound care dressing impregnated with 95% honey, 5% sodium alginate. It was approved in the United States for use in minor traumatic or surgical cuts and burns, and on select ulcers.[8] Various dressings, gels, ointments, and hydrogel dressings have since been marketed (Table 1).[7]

We found no clinical trials exploring the use of honey in prehospital or wilderness environments; however, it may be a safe and effective provisional wound treatment, especially in situations in which antibiotics are indicated but not available. In particular, honey has been advocated as an extemporizing antibiotic strategy in high-risk animal bites for which antibiotics are indicated within an hour of injury.[9] There is in vitro evidence that honey, independent of systemic or topical antibiotics, can sterilize wounds.[10] Evidence supporting the use of topical antibiotics for minor wounds is weak, and it has been connected with antibiotic resistance and other adverse reactions (eg, allergic contact dermatitis).[11] Taking this into consideration, honey may be a useful addition to a wilderness medical kit. It can be used as an improvised treatment for multiple austere medical problems, and, if needed, provide a food source.

Methods

OVID, PubMed, MEDLINE, CINAHL, and Cochrane Database of Systemic Reviews were searched using a variety of combinations of the following terms: "honey," "wound care," "wound," and "wound healing." Titles and abstracts from the initial literature search were

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Table 1. Medical-grade honey products available

Products	*Description*
Elasto-Gel manuka wound dressing	FDA approved, sterile polymer dressing impregnated with manuka honey
MANUKAhoney, MANUKAbalm, MANUKAderm, MANUKApli, MANUKAtex	FDA approved (MANUKAtex), wound dressings, gels, ointment containing manuka honey
Medihoney dressings with active manuka honey	FDA approved, 100% manuka honey topical ointment
OTC API-MED, Medihoney Primary and Medihoney 100% honey dressings with active manuka honey	FDA approved, manuka honey impregnated dressings
L-Mesitran Hydro, L-Mesitran Border, L-Mesitran Net, L-Mesitran Active, L-Mesitran Soft	FDA approved, hydrogel dressings and wound care gel containing honey
API-MED active manuka honey absorbent dressing	FDA approved, dressings impregnated with 95% manuka honey and 5% sodium alginate
MANUKA IG	FDA approved, wound dressing containing 100% manuka honey

FDA, US Food and Drug Administration.

selected and reviewed to explore the benefits and possible negative outcomes of topical honey; references from these articles were reviewed and searched further for pertinent publications not initially found in online searches. Natural Medicines Comprehensive Database was also referenced.

Mechanism of Action

Honey is an acidic, hygroscopic, hyperosmolar sugar solution produced by honeybees from plant nectar.[12–14] It is composed of water, sucrose, glucose, fructose, amino acids, wax, pollen, pigments, minerals, and enzymes, including invertase, which converts sucrose into simpler glucose and fructose, and glucose oxidase, which oxidizes glucose and produces gluconic acid.[15] This enzymatic process contributes to the production of hydrogen peroxide. The gluconic acid lowers pH to ranges from 3.2 to 5.5, making an acidic environment inhospitable to microbe growth. The low pH also inhibits protease activity, which uninhibited will adversely affect growth factors and protein fibers essential to the healing process.[16,17] In addition to its enzymatically produced acidity and peroxide generation, honey has been described as an antimicrobial and antioxidant that produces proinflammatory cytokines, decreases biofilm formation, inhibits bacterial cell cycle production, decreases pain perception, reduces malodor, and decreases exudates (Table 2).[7] Although not all mechanisms are completely understood, every year further research illuminates honey's efficacy as a useful auxiliary in wound healing.

Free radicals from excessive and prolonged inflammation can cause tissue damage and prevent healing. Honey-exposed cells have been shown in histological studies to have higher levels of antioxidants present and decreased numbers of inflammatory cells.[18] In cell cultures, honey has been shown to stimulate B and T lymphocytes and phagocytes and release of modulator cytokines tumor necrosis factor-1 (TNF-1), interleukin 1 (IL-1), and IL-6. It also provides macrophages with the essential glucose needed for hydrogen peroxide production and energy production.[19,20] In vitro studies show honey may be able to modulate the activity of immunocompetent cells, such as monocytes.[21,22] Honey is thought to decrease edema, thereby decreasing hydrostatic pressure, allowing better wound circulation and delivery of oxygen and essential nutrients to the wound.[17]

Honey is effective in providing a protective barrier and maintaining a moist environment that is inhibitive of bacterial growth colonization, in addition to preventing adhesion of dressings to wounds.[23,24] Its viscosity and hyperosmolarity dehydrate bacteria.[25] The osmotic pressure from honey draws out lymphatic fluid from the base of wounds, which aids in removal of necrotic and devitalized tissue.[20,23] The sugary wet environment may improve local nutrition and epithelialization, and the acidity provides an optimal medium for fibroblast activity.[14] A 2010 animal study showed that honey stimulates angiogenesis at wound sites, bringing vital oxygen and nutrients necessary for healthy granulation tissue.[26]

In addition to honey's hygroscopic hyperosmotic dehydrating effects inhibiting bacterial growth, it also has been shown to have both bacteriostatic and bactericidal activities across a broad spectrum of significant wound bacteria.[27,28] Applying an occlusive dressing with 0.5 mL of standardized Dutch medical-grade honey to healthy skin for 48 hours showed reduced bacterial skin

Table 2. Summary of honey's effects on wound healing, classically described as three stages: inflammatory, proliferative, and remodeling

Phases of wound healing		
Inflammatory	*Proliferative*	*Remodeling*
Increases cytokine production: TNF-α, IL-1, IL-6	Removes debris, necrotic and devitalized tissue	Increases hygroscopic effect
Increases H_2O_2	Increases epithelialization	Increases remodeling
Increases antioxidant activity	Increases granulation tissue	Speeds remodeling
Increases cell nutrients	Increases fibroblast activity	Decreases scar formation
Decreases pH	Increases angiogenesis	Decreases contractures
Decreases microbial burden	Decreases edema	
Decreases biofilm	Decreases exudates	
Decreases pain		

IL, interleukin; TNF, tumor necrosis factor.

colonization 100-fold versus increased colonization under a dressing without honey.[10] One of the attributes of honey's antimicrobial qualities is its ability to produce hydrogen peroxide at a level that is both antibacterial and nontoxic to cells.[14] Levels of hydrogen peroxide in topical honey are estimated to be 1000 times lower than in medical rinse solutions, which is thought to promote growth of new cells, such as fibroblasts, important in early wound healing.[29,30] However, even in the presence of catalase (which inactivates hydrogen peroxide), honey is still an effective antimicrobial.[31,32]

Antibacterial qualities differ based on region and flora supply of nectar. Perhaps the most studied is monofloral honey derived from *Leptospermum* trees (manuka) out of New Zealand, which has been shown to have significant antibacterial properties independent of hydrogen peroxide and osmolarity.[25,33,34] Although all forms of honey studied have demonstrated low pH, hydrogen peroxide production, and hyperosmolarity, manuka honey has been shown to contain high concentrations of the enzyme methylglyoxal, which has been shown to be the active component in its antibacterial activity.[35] In vitro studies indicate methylglyoxal is an effective antimicrobial agent against forms of methicillin-resistant *Staphylococcus aureus* (MRSA), and effectively acts in synergy with oxacillin in the treatment of otherwise oxacillin-resistant *S aureus.*[35–37] Furthermore, honey of varying types has shown in vitro antibacterial activity against nearly 60 species of bacteria, including MRSA, vancomycin-resistant enterococcus, and *Pseudomonas aeruginosa.*[18,38–43]

It is unclear how much honey's antimicrobial qualities are unique to honey or are attributable to its hyperosmolarity,[44] although when diluted with water it still inhibits growth of many bacterial species and when compared directly with sugar water of a similar viscosity it was found to be more effective in reducing bacterial contamination and promoting wound healing.[16,45]

Types of Honey

Composition and quality of honey varies by floral source. Honey's pharmacological activity and potency is thought to vary based on region, season, harvesting, processing, storage, and floral source.[19] Some honey can even be harmful. Up to 26% of raw (unprocessed) honey contains *Clostridium botulinum* spores, which can cause significant problems when consumed by children younger than 1 year old; however, its importance in topical wound care is questionable. There are no documented cases of botulism from wounds topically treated with honey.[46] The rare reports of wound botulism are found only in intravenous drug users as a result of using contaminated needles. "Mad honey" from Turkey's Black Sea region is toxic if ingested.[47] This specific honey contains grayanotoxin, which derives from the nectar of plant species *Rhododendron,* and when consumed can cause cardiac dysrhythmias.[48] Although this plant is endemic to various parts of the world, almost all case reports are out of Turkey.

Consumption of honey produced from flowers of oleanders, rhododendrons, mountain laurels, sheep laurels, and azaleas may also result in a variety of unwanted side effects. This is more likely when ingesting unprocessed honey from farmers who have a small number of hives. Commercial processing, with pooling of honey from numerous sources, theoretically dilutes any toxins. Honey derived from the *Leptospermum* tree species, or manuka tree, is a monofloral honey from New Zealand and Australia that has been best studied and marketed as a medical-grade honey. Whereas processed (culinary) honey often undergoes a heat treatment that is thought to

destroy some of the wound-healing components, medical-grade honey, such as the "manuka" honey, is treated with gamma-radiation, sterilizing the honey but keeping enzymes intact.[36,49] However, heat-treated honey's high osmolarity would remain unaltered and with it any contributing antimicrobial activity, and many large studies discussed subsequently demonstrated efficacy with raw, unprocessed, untreated honey. With growing antibiotic resistance, there is an increasing interest in plant species–specific honey, such as manuka, to discover new and effective therapies.

Clinical Literature Review

Much evidence exists for honey-based treatment of wounds of various types, ranging from superficial abrasions to partial-thickness burns. The number and quality of the studies has been increasing in the past decade; however, the wide range of trials and wound types makes it difficult to standardize recommendations and justifies further inquiry into clinical effectiveness of honey and specific wounds.

BURNS: SUPERFICIAL AND PARTIAL THICKNESS

There have been several randomized, controlled trials using honey on minor burns that show accelerated healing time compared with both conventional and nonconventional dressings. Unprocessed, undiluted honey has been compared in clinical trials with silver sulfadiazine, polyurethane film, boiled potato peel, sterile linen dressings, petrolatum-treated gauze, and framycetin/gramicidin dressings. These various studies compared 1246 patients treated for partial-thickness burns and demonstrated a statistically significant decreased average healing time with honey use.[50–54] A 1998 randomized, controlled study compared the use of unprocessed honey with silver sulfadiazine dressings in treating superficial burns.[50] The results showed a statistically significant ($P < .001$) faster epithelialization at 7 and 21 days, and greater histological reparative activity on days 7 and 21 ($P < .005$) for honey. Of the silver sulfadiazine group, 60% had eschar present, and 4 required skin grafting, whereas honey had no eschar and required no skin grafting. A 2001 review by Moore et al of 7 randomized controlled trials of honey's use in burn and postoperative wound management concluded that time to healing was significantly shorter for honey.[44] Bardy et al[55] reviewed 43 studies in 2008; 5 studies found honey to be equally as effective as the comparator, and 3 found honey to be less effective than the comparator treatment. Others did not show any significant difference between standard treatment regimens and honey treatment. However, both Moore et al and Bardy et al found that studies were generally poor in quality owing to small sample sizes, lack of randomization, and absence of blinding.

A 2002 review found that although the antibacterial activity of honeys (including manuka honey) had been demonstrated in vitro, the number of clinical case studies was small.[14] The review concluded that there was a potential for its use in "the management of a large number of wound types." In 2008, Jull et al[56] performed a systematic review of 19 trials, including 2554 participants. They found that honey, when compared with conventional dressings, reduced healing times in mild to moderate superficial and partial-thickness burns by 4.68 days (95% confidence interval, –4.08 to –5.09).

Molan,[57] in 2006, published an in-depth review of 17 randomized clinical trials ($n = 1965$), 5 other clinical trials ($n = 95$), and 16 animal trials ($n = 533$), in addition to laboratory and in vitro studies. He found a large amount of favorable evidence supporting the use of honey in various types of wound care, particularly when other treatments have failed and few risks are associated with its use. He noted the difficulty in blinding trials when using such an easily identifiable substance like honey.

LACERATIONS AND ABRASIONS

Less is understood about surgical, traumatic, and minor abrasion type wounds. A comparison study of 81 patients' status after undergoing a surgical skin graft demonstrated that honey-treated skin graft sites had decreased epithelialization time and subjective pain when compared with paraffin- and saline-soaked gauze.[58] Patients were not randomized, and further studies are needed to better understand these results. In a randomized, double-blind, controlled trial by Ingle et al,[59] honey dressing was found to be equal in healing time compared with hydrogel dressings in patients who sustained abrasions or minor lacerations. In a randomized, double-blind controlled trial by McIntosh and Thomson[60] and a randomized single-blind controlled trial by Marshall et al,[61] patients who sustained toenail avulsions showed no differences in mean healing times when honey was compared with paraffin gauze and iodoform gauze, respectively. A meta-analysis of these 3 studies confirmed no statistical difference in mean time to healing between honey and conventional dressing in these minor acute wounds.[56]

WOUND INFECTIONS

Honey has been proven to be an effective adjuvant for treating infected burn and surgical wounds. Several studies have shown in vitro effectiveness of standardized

honey in treating multiple strains of *Pseudomonas aeruginosa* collected from burn wound infections.[25,42] A prospective case series of surgical site infections in 9 neonates who failed to heal with conventional treatment, including systemic intravenous antibiotics and topical chlorhexidine solution and fusidic acid ointment, showed significant clinical improvement (eg, decreased edema and necrotic tissue) after 5 days of topical honey application.[62] After 21 days of applying 5 to 10 mL of unprocessed honey directly to the wound twice daily, all wounds were closed, clean, and sterile. In another study, 50 patients with postoperative wound infections were randomly assigned to treatment with honey or ethanol and povidone iodine washes; the honey-treated group healed an average of 11 days faster.[63] Both of these studies used a topical solution of crude, unprocessed honey.

A prospective patient-blinded, randomized, controlled trial of 150 patients compared treatment of superficial and partial-thickness burns with honey and silver sulfadiazine dressings and found faster healing times in the honey group as well as a benefit of honey's antimicrobial activity.[64] At 19 days, 8 wounds (6 of them infected with *Pseudomonas*) of the honey group failed to heal compared with 29 of the silver sulfadiazine group (all of them infected, 27 *Pseudomonas*, 2 *Escherichia coli*). Another study comparing silver dressings with honey demonstrated superior cytocompatability of honey-based products.[65]

OTHER USES

In animal models, topical raw honey applied directly to the eye has been proven safe to use. When used to treat corneal injuries or *Pseudomonas* endotoxin-induced keratitis, honey speeds up endothelial healing while decreasing inflammation.[66] Two studies found it safe and effective in treating bacterial conjunctivitis.[67,68] Honey has been reported to be effective in the treatment of *Candida albicans,* cutaneous leishmaniasis, and rubella virus.[43,69,70] Honey may be helpful for labial and genital herpes simplex virus lesions.[71] When compared with topical acyclovir, multifloral natural honey applied 4 times a day healed faster (5.85 ± 1.57 days for acyclovir compared with 2.57 ± 0.95 days with honey; $P < .05$, $n = 16$), with less pain and less crusting. Honey has shown to be equivalent or more effective when compared with dextromethorphan and diphenhydramine.[72,73] Ingesting 2.5 to 10 mL of honey, when compared with placebo, decreases frequency and severity of cough and improves sleep.[74]

Discussion

Honey is a natural product, with difficulty in standardization. However, it appears that raw, undiluted honey used in clinical trials has shown good results, regardless of unifloral or monofloral sources.[75] Although some differences in antibacterial potency have been established, this has not affected honey's effectiveness, particularly in treating superficial and partial-thickness burns. Honey's antioxidant, high-viscosity, hydrogen peroxide, acidity, and hygroscopic qualities appear to be present in all forms of honey studied.[31] Standardization may be important to better study honey, but may not necessarily affect outcomes in some wound treatments. However, only select honey products are approved by the FDA for clinical use. Some recommend using only medical-grade honey given the theoretical risks of infection using raw honey, although these risks are likely overstated as previously discussed.[76] Adverse effects of treatment, in general, are few. No deaths or anaphylaxis have been reported, including studies involving unprocessed honey.[56]

Many of these studies referenced here were methodologically weak, did not specify the type or concentration of honey, and could be further complicated by the fact that many were performed by the same researcher. Specifically, although honey has been proven superior to silver sulfadiazine dressings as previously discussed, multiple studies found insufficient evidence to support use of silver sulfadiazine in wound dressing, and noted that there is some weak evidence showing increased infection and delayed healing with silver sulfadiazine, so there are limitations to conclusions based on this comparison.[77,78]

Stronger, more-robust studies, in addition to better treatment standardization. may be justified to more clearly define honey's role in wound care. But wound care overall has a paucity of strong literature supporting current treatments, including randomized, controlled trials, and therefore clinicians should compare the evidence supporting traditional treatments with the evidence of honey's effectiveness when selecting appropriate wound care. In several systematic reviews, evidence was lacking to support the use of topical antimicrobial and antiseptic agents and dressings to promote healing in arterial ulcers, minor burns, and venous ulcers, and in promoting postoperative wound healing by secondary intention.[79–81] The stigma of honey as an "alternative" and "complementary" treatment may prevent many from considering it as a viable treatment.

Conclusions

Although honey has not been shown to be a definitively superior wound treatment, it has proven its effectiveness, safety, and utility. The limited evidence demonstrates it is at least equivalent to the standard treatments. Because of its potential as both a multiuse therapy (Table 3) and

Table 3. Summary of honey's clinical uses and antimicrobial activity

Clinical uses	*Microbe activity*[*]
Burns, superficial and partial-thickness	MRSA
Surgical, traumatic wounds	*Escherichia coli*
Infected surgical/burn wounds	*Pseudomonas*
Animal bites	*Staphylococcus aureus*
Conjunctivitis	*Candida albicans*
Cutaneous leishmaniasis	Rubella virus
Labial/genital HSV lesions	Herpes simplex virus
Corneal abrasion	Vancomycin-resistant enterococcus
Keratitis	
Chronic wounds: diabetic ulcer, pressure ulcers, venous ulcers	

HSV, herpes simplex virus; MRSA, methicillin-resistant *Staphylococcus aureus.*

[*] Demonstrated in human, animal, or in vitro studies; highlights from more than 60 different microbes.

as a nonperishable food source, and owing to its low risk profile, honey may be superior to other single-use items when building a medical kit or planning for expeditions. In resource-poor environments, honey may be a viable, renewable, local resource available for treatment of wounds.

Likely the most ancient of wound treatments, honey is being reintroduced as a viable option for various wound types. Honey's biologic qualities have been extensively explored. Although not all mechanisms are completely understood, there is clear evidence demonstrating in vitro antimicrobial, anti-inflammatory, and antioxidant activity. To better understand honey's clinical role, clinicians would benefit from larger, better-designed randomized, controlled trials. There is convincing evidence, particularly when compared with the evidence that exists for conventional treatments, showing honey is safe and can improve wound granulation and epithelialization, reduce odor and exudate, sterilize wounds, decrease bio-burden, and shorten healing times in various wounds. For these reasons, in addition to its many other potential uses, honey could be an effective and practical adjunct in a variety of settings—in a wilderness medical kit, carried on expeditions, and in resource-poor environments.

Disclaimers

The views expressed are those of the authors and do not reflect the official policy of the Department of the Army, the Department of Defense, or the US Government.

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