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Honey / Maggots / Leccches What is the evidence?

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Honey

Medicinal functions of honey include stimulation of wound healing and antimicrobial properties. Honey has been show to increase the release of cytokine TNF-alpha from macrophages and TNF-α, IL-1L, TGF-ß, amd MMP-9 ctytokines from keratinocytes. It also stimulates wound re-epithelialization. Through synergistic action of sugar, hydrogen peroxide, methylglyoxal, and defensing-1, it also kills antibiotic-resistant bacteria, such as methicillin resistant Staphylococcus aureus (MRSA). (1) Antimicrobial and antioxidant properties of honey are influenced by the plant species on which the honeybees feed.

Honey's osmotic properties draw fluid from the wound, keeping the wound bed moist while reducing the risk of maceration. Via anti-inflammatory processes, it reduces exudate and inhibits fibrin formation. Results of studies in people are variable. (2) In one randomized, controlled, double blind study, wound healing after toenail surgery was similar with honey coated and conventional paraffin dressings. In another study, wound healing with honey was delayed, compared with conventional iodine dressing, in patients that underwent toenail avulsion surgery. Uncontrolled case series also provided variable results. In one study of people with chronic leg wounds, a 50% reduction in size was seen after one month of treatment with a honey bandage. In other studies, use of honey resulted in no difference in rate of wound healing, as compared with calcium alginate dressing, or increased rate of wound healing, when compared with a conventional hydrogel dressing. In studies of abdominal incision infections, honey resulted in faster time to healing (6 days) as compared with iodine/alcohol antiseptic treatment (15 days). Unfortunately, most studies of use of honey for treatment of infected wounds in people were of low quality. In the case of burns, randomized controlled studies showed that treatment with honey resulted in a significantly shorter time to healing (7-11 days) as compared with silver sulfadiazine (13 days) or polyurethane film (15 days). Systematic reviews conclude that honey induces more rapid healing times in mild-to-moderate superficial and partial thickness burns as compared with conventional dressings. (2)

Other studies in people report honey is successful for treatment of seborrheic dermatitis and dandruff and reduction in duration of diarrhea in children with gastroenteritis. Honey does not reduce the number of symptoms in people with allergic rhinoconjuntivitis. Application of a honey/beeswax/olive oil mixture reduce the number of psoriasis lesions in affected patients. (2)

Overall, evidence that honey is effective in treating wounds in people is relatively weak because of poor controls, multiple variables, lack of standardization, lack of blinded evaluation, and other factors.(3a) Additionally, evidence that Manuka honey and Medihoney are better than other types of honey are not well substantiated. The clearest evidence of superior effectiveness in people is associated with treatment of burns, compared to other topicals, and honey is likely equally as effective for stimulating closure of chronic wounds as several other modalities.

Controlled clinical studies of honey's antibacterial, anti-inflammatory, and wound stimulating effects in animals are lacking. Experimentally, iatrogenic distal leg wounds in horses healed most rapidly when treated with manuka honey. (4) Interestingly, in that study wounds that were contaminated with feces healed faster than those that were not. In another study, different types of honey were tested against 10 bacterial isolates from equine wounds. (5) Of the 28 types of honey purchased, 18 were contaminated with pure cultures of aerobic bacteria or fungi, with *Bacillis spp* being the most common contaminants. Effectiveness of contaminated products was not evaluated. Eight of the 11 uncontaminated products were active against all bacterial isolates, including *Pseudomonas, E. coli,* and MRSA. Gamma irradiation was found to have no significant effects on antibacterial properties and therefore should be considered over heat sterilization for pretreatment of honey products. In studies of rats with experimentally induced peritoneal inflammation, instillation of honey into the abdominal cavity reduced the risk of severe adhesions, as compared with saline lavage or Intergel. (6,7)

Maggots

Like honey, maggot therapy has been used for thousands of years to treat wounds. (1) Popularity of maggot therapy waned with introduction of antibiotics in the 1940's but rose once more with the advent of antibiotic-resistant bacteria, such as MRSA. Maggot therapy is recognized by the US Food and Drug Administration and the UK Prescription Pricing Authority and thus can be officially prescribed. Sterile maggots are currently used in human patients for treatment of bed sores, leg ulcers, diabetic foot wounds, primary burns, osteomyelitis, and postoperative incisional infections. They are particularly useful for chronic wounds that have not responded to conventional therapy. *Lucilia sericata*, the green-bottle blowfly larvae, prefer necrotic over live tissue and therefore are well suited for clinical use. Since maggot secretions are effective against vancomycin-resistant MRSA, they are important complement to current wound therapy. (1)

Maggot therapy provides three advantageous processes in wounds: wound debridement, acceleration of wound healing, and wound disinfection. (1, 2) Maggots clean necrotic tissue from a wound to an extent matched only by microsurgery. This removes material that would otherwise serve as a nidus for infection and inflammation. During debridement, the green-bottle fly larvae secrete proteolytic enzymes, including serine- and metallo- proteinases, which digest bacterial byproducts and necrotic tissue. These enzymes also breakdown components of the extracellular matrix within the wound, such as collagen and fibrin, which allows initiation of healing, and they disrupt biofilms that form around devices and necrotic tissue. Dissolution of these biofilms permits bactericidal activity by antimicrobials and the host's immune system. Maggots also secrete ammonia, which increases wound pH and optimizes protease activity. Interestingly, maggot excretions that are incorporated into hydrogel wound dressings will also stimulate debridement and wound healing. (1)

Although not reported in every study, maggot therapy can accelerate wound healing in some cases. (1) Factors implicated in this effect include the physical movement of the maggots within the wound, excreted chemicals that increase wound pH, and stimulation of fibroblast growth. Maggots also modulate mammalian immune system by inhibiting migration, activation, and pro-inflammatory responses of certain white blood cells, which reduces tissue damage caused by these cells.

Maggots secrete or excrete a variety of substances with antimicrobial properties. (1) Factors within these products are active against Gram-positive, Gram-negative, and methicillin-resistant bacteria; viruses; fungi; and even cancer cells. Some of the factors, such as alloferon, stimulate human natural killer lymphocytes *in vitro* and induce interferon production *in vivo*. Alloferon has been shown to be clinically active against herpes simplex and human papilloma viruses and is sold as the product Allomedin, which is used to treat cold sores, genital herpes, and gingivitis. Other factors, such as 5-S-GAD, generate hydrogen peroxide and are active against bacteria, inhibit angiogenesis in some cancers, protect retinal ganglial cells from apoptosis associated with glaucoma, and prevent cataract formation. (1)

Several descriptive clinical studies of maggot therapy have been published in people. (2) In one study, use of maggots in 30 patients with chronic wounds (arterial or venous stasis ulcers, diabetic or pressure ulcers, or chronic surgical wounds) resulted in decrease in wound bacterial counts and healing of 83.2% of the wounds. In a case series of 34 chronic leg wounds (>12 weeks duration), 85% of wounds healed, usually within 7-10 days. In another study of 70 patients with chronic leg wounds, 86% had 66% to 100% reduction in wound size. About a third of these patients perceived an increase in pain during the treatment period. Outcomes for larval therapy are worse in patients with greater wound depth, old age, or septic arthritis. A randomized, controlled comparisons of patients with venous or arterial ulcers treated with maggots or conventional hydrogel dressing found no difference in rate of healing; however, maggot treatment resulted in complete wound debridement 2.3 days faster than hydrogel treatment. Again, the patients receiving maggot therapy significantly reported higher pain scores. (2)

In veterinary medicine, most reports of maggot therapy are either experimental or case series; controlled studies of large numbers of animals are still lacking. (8,9) Maggot therapy has been used in horses for treatment of septic navicular bursitis, hoof infections, complicated laminitis, suprasinous bursitis, ulcers, cartilage necrosis, septic joints, and rattle snake bites. In donkeys, sheep, dogs, cats, and rabbits, it has been used for wound debridement and infection control. (8)

Leeches

Within their saliva, leeches secrete pure anti-coagulating substances hirudin and calin, along with hyaluronidase, which facilitates spread of the anticoagulant through the wound, and a variety of chemicals that stimulate vasodilation and prolong bleeding. (10, 11) Other secretions inhibit proteoloysis, dissolve fibrin, and reduce or prevent inflammation. (11) Plastic surgeons use medicinal leeches to salvage flaps, microvascular free-tissue flaps, digit reimplantations, and facial reconstruction sites that suffer from postoperative venous congestion. (10) Leeches have also been used to treat osteoarthritis, tenosynovitis, sialadenitis, and other inflammatory conditions.

The site is prepped with warm, heparinized saline to encourage vasodilation. Alcohol and iodine may potentially

interfere with attachment. A barrier, such as a moist gauze with a hole in it, is placed over the wound to limit leech migration. The leeches are carefully placed on the wound and left there until they are fully distended, usually 30 to 60 minutes. The leeches will detach themselves when full; alternatively, common salt can be sprinkled on their heads. Forcible removal is avoided because it may cause regurgitation. If the wound bleeds persistently, place pressure over the site. Leeches are disposed of as clinical waste. (10)

Potential complications associated with leech application include infection, often evidenced by local cellulitis or abscess formation. In people, the incidence of leech associated infection ranges from 2 to 20% and can result in extensive tissue loss and septicemia. (10) The most common pathogen is Aeromonas, a resident flora of leeches. Aeromonas produces beta-lactamases, so first generation cephalosporins and pencillins are likely to be ineffective. Options for prophylactic treatment include fluoroquinolones or animoglycosides. Sites should not be prepped with alcohol or hypertonic saline, either of which could cause the leech to regurgitate into the wound and possibly infect the site. Leeches may also result in persistent bleeding, anemia, and local or systemic allergic reactions. Leeches may also migrate (e.g., under flaps, into airways) and therefore should be watched while they are in place. Leeches have the potential to transmit viral infections and should therefore not be reused in people. (10) Most patients require multiple treatments to reduce venous congestion; since leeches can consume 10 times their weight in blood, transfusions may be necessary over the course of the treatment.

As with other adjunctive therapies, controlled clinical trials for leech therapy in people are lacking. (11) In one study, leech therapy resulted in survival of 8 free tissue transfers considered unsalvageable; most patients required 6 or 7 days of treatment with 215 leeches used per patient. At least half of patients receiving leech therapy for chronic sialadenitis/sialadenosis. In 113 patients with advanced osteoarthritis of the stifle, leech application resulted in statistically significant reduction of pain scores, long term reduction in joint stiffness, and improved mobility. In another randomized control trial, a single course of leech therapy effective relieved pain and improved function and quality of life for at least 2 months in women with carpometacarpal thumb osteoarthritis. (13) The reason for the response in patients with osteroartrhitis is not known.

Leech therapy has anecdotally been used in veterinary medicine for treatment of congested flaps, grafts, penis, and paws; drainage of auricular hematomas; treatment of cats with saddle thrombus; relief of pressure or pain in horses with tenosynovitis, tendinitis, and acute laminitis; and reduction of red cells in cats with polycythemia vera. (14, 15, Google) Leech sellers claim it treats joint malformation, arthritis, disc disease, neuritis, muscle stiffness, eczema, abscesses, mastitis, and lymphagitis. All of these claims are unproven in animals.

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