Products & Procedures under the microscope

With Gaynor Wooldridge
Chair of the Medicines and Procedures Panel (MaPP)
at the Institute of Chiropodists and Podiatrists

Introduction

Bees are incredible. Honey bees (Apis Mellifera) are nature's chemists. They are able to change the watery sugar collected as nectar (83% water), into the supersaturated power food that we know as honey (18% water). If we were to perform this magical action of super saturation, we would need 181 components, including heat, enzymes and other chemicals to achieve our goal (Riddle, 2016).

In this article, we will discuss a brief history of the use of honey, by humans, for it's medicinal, it's biological and it's activities on wound healing; we will also assess how we, as podiatrists, can incorporate medical honey into our management of foot ulcers (including diabetic wounds), acute and chronic wounds (superficial or deep), and post surgical wounds that present either in clinic or a domiciliary environment.

The History of Honey as a Medicine

Honey has been used by humans since ancient times. Geiling (2013) reports that modern archaeologists excavating ancient Egyptian tombs have often discovered unexpected pots of honey still preserved, and cave paintings dating from Stone Age (approximately 8000 years ago), depict a man climbing a cliff face on rope ladders to harvest honey (Topal et al. 2021, fig 1). It was the Egyptians, however, who almost certainly were the first people to apply honey to wounds. Honey, grease (animal fat to form a barrier) and lint (vegetable fibre to drain the wound) were the main components of the most common plaster used by the Egyptians, with honey used as an effective antibacterial. (Shah, 2011).

FIG.1

> *"The god Re wept, and the tears from his eyes fell on the ground and turned into a bee"*
>
> *From an acient Egyptian papyrus*

The first human beekeepers were foragers of wild honey, and not keepers of bees. Domesticated beekeeping became a common practice starting around 2,500 BC, again in Egypt and possibly earlier in China.

The use of honey in wound management has enjoyed a resurgence over the past few years, after falling out of favour in the 1940s (Clardy et al. 2009). This is largely due to the growing problem of antibiotic-resistant bacteria, and the combined difficulties in the management of chronic wounds that may become infected with methicillin-resistant Staphylococcus aureus or Pseudomonas (Lay-flurrie et al, 2008). Minden-Birkenmaier and Bowlin (2018) scrutinised the plethora of in vitro and in vivo evidence that demonstrated that honey debrides wounds, kills bacteria, penetrates biofilm, lowers wound pH, reduces chronic inflammation and promotes fibroblast infiltration.

So what exactly is honey that makes it so special?

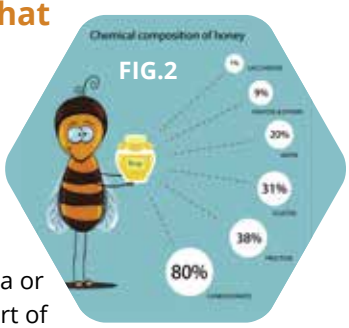

FIG.2

The chemical make-up of honey ($C_6H_{12}O_6$) is primarily sugar. Sugars contain very little water in their natural state (hygroscopic), but they can suck in moisture if left unsealed (Avarez-Suarex et al. 2014); very few bacteria or microorganisms can survive in this sort of environment. It is also extremely acidic, with a pH between 3 and 4.5, which kills off almost any bacteria and organisms that may attempt to colonise it (Nolan et al. 2019). An acidic pH also encourages blood to release oxygen, vital for wound healing, and reduces the presence of proteases that can impair wound healing (Du Toit and Page, 2009).

Sugar has an osmotic effect. The sugar naturally present in honey draws water out of damaged tissues, reducing swelling and encouraging the flow of lymph to enable wound healing. Sugar also draws water out of bacterial cells, preventing them from multiplying (Nair et al. 2020). Honey has been shown to also have an antibacterial effect on colonised wounds, such as methicillin-resistant Staphylococcus aureus (MRSA) and vancomycin resistant Enterococci (VRE) (Molan and Rhodes, 2015).

Medical Honey:
the taste of sweet success?

Lets get back to the bees, those scientists in the natural world, and where it all begins! Honey starts with nectar. Honey is a viscous substance with a very low water content, whereas flora nectar is approximately 80%. Bees are able to change the complex sugars found in nectar, into simple sugars by producing invertase, an enzyme in their salivary glands; this process is known as hydrolysis (Riddle, 2016).

ACTIVITY

Place a piece of potato in 100mls of water

Place a piece of potato in 100mls of water with 2 tablespoons of honey

Leave both overnight Remove both, dry potatoes and weigh

What does this tell us about osmosis?

A second enzyme, glucose oxidase, found in their "honey stomach" or crop, mixes with the nectar. This is then broken down into two by-products: gluconic acid and hydrogen peroxide (Jones, 2009). This mixture is regurgitated into the cells of the hive, and the bees remove most of the moisture by flapping their wings to dry out the honey substance (Topal et al. 2021).

Minden-Birkenmaier and Bowlin (2018) discussed how the production of gluconic acid results in the lowering of the pH of honey, and hydrogen peroxide enhances its bactericidal efficacy. This low pH of honey enables a series of events, allowing tissue repair to occur.

- A reduction in protease activity in the wound site
- An increase in oxygen release from haemoglobin
- The stimulation of fibroblast and macrophage activity

The production of hydrogen peroxide also stimulates vascular endothelial growth factor (VEGF) and sterilises the wound (Molan and Rhodes, 2015).

The current potential of honey in wound care

A wound can result from either an external or internal insult. Following trauma, healing can be delayed for many varied reasons, and inadequate circulation often robs tissues of necessary nutrients, and potentiates pro-inflammatory cytokines; this can lead to tissue necrosis (Mustoe, 2004). The process of wound healing is classically divided into 4 stages: haemostasis (seconds to minutes), inflammation (3-5 days), proliferation (4-14 days) and remodelling (8 days to one year). There can be a significant overlap of these stages (Janis et al. 2010).

The goal of successful wound care must be to initially remove any offending insult, and then provide the best environment in order to facilitate good wound healing. Controlling the bacterial load of a wound is one of the most important aspects of ensuring an optimal level of healing (Jull et al. 2008).

Tashkandi's review of honey in wound healing (2021) concluded that medical honey is a promising wound healing agent, with a broad spectrum of antimicrobial activity and no known resistant pathogens. They also found that it was effective against clinical bacteria and fungal isolates, plus their associated biofilm. It was shown to be safe and cost effective.

Cooper et al. (2011) also investigated the role of medical honey (Activon, Advancis Medical) and in vitro biofilm of MSSA, MRSA and VRE, and found that they could be prevented and inhibited at concentrations above 10%; these concentrations are available to use within clinical practice.

Our role in wound management

The role of the podiatrist and foot health practitioner within wound healing is an essential one. We are often the first to recognise the presence, or the impending formation, of a wound. More than 60% of non traumatic amputations occur in people with diabetes (Bell, 2009). We are all aware that prolonged chronicity of wounds is usually related to bacterial colonisation. This can progress to the bacterial resistance of systemic and topical microbial agents, or the development of the dreaded biofilm. Our job as health professionals usually involves debridement of non-viable tissue and bacterial biofilms, followed by the application of an appropriate dressing. These are commonly a standard dry dressing, a highly absorbent dressing such as an alginate, or a hydrocolloid (Rossi and Morrazzo, 2021). This procedure often fails, which has lead to an interest in alternative treatment approaches, and a renewed interest in honey (Nair et al. 2020).

Honey-based products show excellent compatibility with tissue cell cultures when compared to silver dressings (Du Toit and Page, 2009).

Fig. 3 A granuloma treated with medical honey (one application) left in situ for one week.

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(continued)

With an increasing number of wounds, decreasing budgets and reduced resource availability, as well as an NHS crisis post COVID, wound care services are under increasing pressure. As front line care providers, and often the potential 'gatekeepers', it is important that we provide a robust delivery of care, and pathways to ensure our patients have the best access to optimum medical interventions.

With the appropriate skills and knowledge it has been shown that podiatrists and foot health practitioners can greatly improve patient outcomes (Kivi, Dwyer and Lance, 2016). The ability for patients to attend primary care practices for dressing changes can be difficult for a number of reasons. Within our clinical environment, the possibility of a patient returning home with a simple, and effective, dressing routine, is definitely exciting and food for thought!

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FIGURES

Fig 1 Stone Age cave painting depicting a man on a ladder, foraging for honey. Found in the "cave of the spider" (cuava de la arana), Valencia, Spain. Shutterstock free image.

Fig 2 The Chemical Composition of Honey. Rybakova, image 6231260. Vectorstock free image. www.vectorstock.com/royaltyfree-vector-chemical-composition-of-honey-vector Accessed 23/5/22

Fig 3 Granuloma at nail sulcus, treated with Activon medical honey. Before and after photos. Permission to use given by patient.

GLOSSARY

Re or Ra The ancient Egyptian deity of the sun

MSSA methicillin-susceptible Staphylococcus aureus

MRSA methicillin-resistant Staphylococcus aureus

VRE vancomycin resistant Enterococcus

With thanks to Advancis Medical, manufacturers of Activon Manuka Honey https://uk.advancismedical.com