## Healing with Manuka honey-Modern Science Supports Ancient Practice.

By Rebecca Schumacher

Honey has been used cosmetically and therapeutically since ancient times and is one of the oldest skin care ingredients currently in use. Archeological records indicate its use therapeutically in Sumaria as early as 3000 BC and in ancient Egypt, in cosmetics, as early as 4500 BC. Writings from Aristotle, Dioscorides, Pliny, The Bible, Koran, Torah and Talmud, include references to the benefits of honey. Honey is classified as an emollient/humectant/ moisturizing product, in the International Nomenclature of Cosmetic Ingredients (INCI). Additionally, honey as been demonstrated to be hygroscopic, antibacterial, and fungicidal. It nurtures the skin and regulates the mildly acid pH of the upper protective layer of the skin. Some of the known active constituents present in honey include: Sugars, primarily fructose and glucose; proteins and amino acids; vitamins, including ascorbic acid, biotin, nicotinic acid, pantothenic acid, pyridoxine, and thiamin; enzymes such as diastase, invertase, glucose oxidase, and catalase; minerals, primarily potassium, magnesium phosphorus, calcium iron and copper; phytocompounds derived from botanical sources and other minor components.[1]

Ancient peoples knew what honey could do, and how to use it, even though they did not know how or why it worked. Modern science, in an effort to create a standardized medical product has begun to explore the how and why behind the benefits of honey. There are currently two primary medical grade honeys available, Monofloral Manuka honey produced from the manuka bush (*Leptospermum scoparium*) in New Zealand (and Gamma irradiated to remove *Clostridium botulinum* spores and other bacteria), and a trademarked honey called Revamil® produced commercially in greenhouses and shrouded in a cloud of industrial secrecy[2]

The antibacterial activity of Manuka honey is measured in an industry standard phenol-equivalent scale expressed as unique manuka factor (UMF). This is measured in a radial diffusion assay with *Staphylococcus aureus* as the target microorganism. There is batch to batch variation in UMF, and this only measures efficacy, and does not identify the constituents which are responsible for the antimicrobial activity. Revamil® is registered only as a medical device for applications in wound healing and not as an antimicrobial agent.2

A comparative, in vitro study by Kwakman, Sebastian and Zaat, sought to identify and quantify the individual components responsible for the anti-microbial action of Manuka and also potentially, Revamil®. They identified 5 unique properties of honey which contribute antimicrobial properties: High osmolarity; hydrogen peroxide; low pH: methylglyoxal; and antimicrobial peptide bee defensin -1. They attempted to isolate each component by rendering the others inert, and also tested them in combination with each other, using a quantitative liquid assay, against S. aureus, B. subtilis, P. aeruginosa, and E. coli. They concluded that each honey has a unique profile of constituents, and a unique microbial action, as a result. But that both honeys do have powerful antimicrobial actions against multiple micro-organisms, and also acknowledge that these components, as well as other, as yet unidentified components present in trace amounts, likely work synergistically to give honey a broad scope of action.2 By identifying these components researchers hope to be able to standardize products for medical applications.

A double-blind controlled in vivo study performed on 59 patients, (standardized for 8 factors, including: Gender, age, mean duration of diabetes, control of diabetes, and smoking) in Saudi Arabia, used Manuka soaked primary dressings in addition to conventional treatment vs conventional treatment only to evaluate rate of healing of diabetic foot ulcers.

Manuka treated patients had statistically better wound healing, fewer amputations, and required dressing changes less often due to decreased amount of wound exudate, at both 6 weeks (65% of manuka patients completely healed vs 15% of conventional patients) and 6 months (100% of manuka patients completely healed vs 45% of conventional patients). [3]

This study indicates a high level of effectiveness in treating diabetic foot ulcers.

But Wait!! We are not only able to demonstrate that honey can kill bacteria and support more rapid wound healing when applied topically!!!

Another controlled study, addresses the antiproliferative effects of Manuka honey on tumor cells, both in vitro and in vivo. The in vitro phase introduced various dilutions of either Manuka alone, or Manuka combined with taxol, (a chemo therapeutic agent), taxol alone as a positive control, or untreated as a negative control. Cell viability was assessed at 24/48/or 72 hours. Results showed statistically significant inhibition by both Manuka and taxol treated groups, as well as an additive effect when Manuka and taxol were combined. In the in vivo phase of this study, mice were implanted with murine melanoma cells. Mice were treated with IV injections of Saline; Manuka/saline; taxol alone or Manuka/Taxol, administered twice per week. Tumor growth and survival were followed for the subsequent 3-4 weeks. At days 20-24 post treatment tumors were cytologically analyzed for "apoptosis" or spontaneous tumor cell death/necrosis. Mice treated with taxol alone or taxol plus manuka exhibited significantly greater inhibition of tumor growth, inhibition of growth occurred sooner than manuka only subjects, however manuka/taxol subjects had the best overall survival, suggesting that manuka may play a role in reducing drug induced toxicity. [4] This study did not continue administration of agents until the tumor was gone but stopped treatment and then followed tumor growth post treatment, leaving me with many questions about longer term treatment, but it does give insight into the possible method of action of Manuka on cell apoptosis. They did work to make sure that there were no toxic effects associated with administering the manuka IV, and results from the Manuka only group were only 3 days behind the taxol treated group. I'd like to see a longer-term study to assess the usefulness of

Manuka IV in cancer treatment since there seemed to be no demonstrable toxicity associated.

Lastly, we review study that demonstrates honey's ability to facilitate wound closure, this is an aspect of wound healing separate from infection control, which we have previous investigated. A key step in wound healing, involves the ability of the keratinocytes lining the wound to transform into actively moving cells which facilitate wound closure. An in vitro study used a scratch wound healing model of proliferating and migrating keratocytes.

This controlled in vitro study evaluated three types of honey: acacia, buckwheat and Manuka, a platelet lysate solution was used a positive control and untreated cells as a negative control to assess the rate of migrating cells in each culture. Experiments were carried out in triplicate with a minimum of eight replications each. Using a chemotaxis assay, it was demonstrated that all honeys significantly increased the number of migrating cells, with buckwheat honey having result similar to the positive control. The other two honeys demonstrated lower rates but were still significantly increased compared to the negative control. [5] The conclusion suggests that different honeys contain different constituents which are affecting re-epithelialization, but that each shows strong wound healing potential.

It would seem that the deeper we look with science the more we are able to confirm what Cleopatra et al. already knew! The benefits of honey are many and powerful! Other studies have shown benefits against tooth decay[6] as well as in the treatment of multiple side effects associated with chemotherapy[7]. Because the active compounds in honey are many and varied, reducing the chances of microbial resistance, the future of Manuka honey as medicine seems GOLDEN.

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