What's special about *Active Manuka Honey*

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The history of manuka honey

In 1981 Kerry Simpson, who was at that time head of Science at Otorohanga College, brought to the attention of Dr Molan that honey is commonly used by people as an antiseptic, and that in New Zealand manuka honey had a reputation as having the best antiseptic properties. He was aware of Dr Molan's research interests in natural antibacterial substances, and persuaded him to look into manuka honey.

A search of research publications revealed that it had been found in 1962 that the antibacterial activity of honey was due to the antiseptic hydrogen peroxide naturally present in it. They thought that maybe manuka honey had something in it which was additional to the antibacterial components of other honey. To test this hypothesis they measured the antibacterial activity of samples of honey with sufficient of the enzyme *catalase* added to destroy all the hydrogen peroxide present. They found that whereas all the other types of honey lost all of their antibacterial activity, the samples of manuka honey retained in full all of their antibacterial activity.

This antibacterial activity that was due to something other than hydrogen peroxide was termed **non-peroxide activity**. There had been publications reporting findings of very low levels of non-peroxide activity in some honeys. Manuka honey was unusual in having high levels of antibacterial activity that was non-peroxide.

Manuka honey is very unusual

Subsequent testing of a large number of different types of honey, in New Zealand and later in other countries, revealed that manuka honey was the only type of honey to have a significant amount of non-peroxide antibacterial activity. A limited quantity of the same type of honey is produced in Australia (where it is called "jellybush honey") from *Leptospermum scoparium* trees (called manuka trees in New Zealand) and other species of *Leptospermum.* These trees grow uncultivated in a few parts of Australia. In New Zealand manuka trees grow uncultivated over large areas of land throughout the country.

It is interesting that the folklore knowledge of the superior antiseptic qualities of manuka honey developed in a relatively short period of time, possibly because it is so different from other types of honey. Manuka honey did not exist before European settlers brought honey bees to New Zealand in 1839.

The bees as well as the trees are responsible for the unusual activity

Although the original Maori inhabitants used the manuka tree as an antibacterial medicine, its antibacterial components do not get into the nectar which the bees collect to make manuka honey. The antibacterial component of the honey, methyglyoxal, forms by a chemical reaction that occurs after the bees have processed the nectar into honey. The component of the nectar from which the methylgyoxal forms, dihydroxyacetone, is a sugar with no antibacterial activity.

There is another component of this unusual antibacterial activity, as yet unidentified chemically, which has been found to occur only in manuka honey. That component doubles the antibacterial potency of the methylgyoxal in manuka honey. Itself this unidentified component has no antibacterial activity – it acts as a synergist to increase the antibacterial action of the methylglyoxal.

Not all that is called manuka honey has the unusual non-peroxide activity

All honeys have an antibacterial activity, due primarily to hydrogen peroxide formed in a "slow-release" manner by the enzyme glucose oxidase present in honey, which can vary widely in potency. Some honeys are no more antibacterial than sugar, while others can be diluted more than 100-fold and still halt the growth of bacteria.

Only some of the honey sold as manuka honey (likewise only some jellybush honey) has the unusual non-peroxide type of antibacterial activity. The rest has antibacterial activity due to hydrogen peroxide just the same as in other (much less expensive) types of honey, and may have little or no manuka nectar in its source.

The term *Active Manuka Honey* was devised to distinguish manuka honey with this non-peroxide type of antibacterial activity from what was being sold as manuka honey that did not have this activity. This term has been in use in publications since 1998.

Confusingly there is now honey being sold as "Active Manuka Honey" where the seller is referring to antibacterial activity that is due to hydrogen peroxide just like in all other types of honey, and not to the non-peroxide type of antibacterial activity that is unique to manuka honey and jellybush honey.

Why is there variation in the activity of manuka honey?

The level of the special non-peroxide activity in manuka honey varies widely from batch to batch. The activity is measured in comparison with a standard antiseptic, phenol (see "Pdf 8: How the antibacterial activity of manuka honey is rated" on http://waikato.academia.edu/PeterMolan). It varies from a rating of below 5 (*i.e.* the equivalent of 5% phenol, the minimum that can be measured), to higher than 30.

Research at the University of Waikato, investigating manuka honey collected from many sites over a large area of New Zealand, has found two reasons for the level of the non-peroxide antibacterial activity in manuka honey varying. It depends to some degree on the variety of manuka the honey is collected from. But mainly it depends on the proportion of manuka nectar in the honey. (Bees collect and combine whatever types of nectar are available to them in their locality.)

All manuka varieties of manuka were found to give honey with non-peroxide activity. Honey sold as manuka honey which does not have a measurable level of the non-peroxide antibacterial activity is thus likely to have been produced predominantly from nectar sources other than manuka. Honey produced from kanuka (*Kunzea ericoides*), sometimes sold labelled as manuka honey, does not have any detectable non-peroxide antibacterial activity.

Why is the non-peroxide antibacterial activity important?

The non-peroxide type of antibacterial activity in manuka honey is not affected by the catalase enzyme present in serum, saliva, blood and the other tissues and of the body. This enzyme will rapidly break down, to a large degree, the hydrogen peroxide which is the major antibacterial factor found in other types of honey. (See Photo 1 below.) If a honey without non-peroxide antibacterial activity were used to treat an infection, the potency of the honey's antibacterial activity would most likely be greatly decreased because of the action of catalase.

The enzyme that produces hydrogen peroxide in honey is destroyed when honey is exposed to heat and light, or stored in warm conditions. But the non-peroxide antibacterial activity of manuka honey is stable, so there is no concern about genuine *Active Manuka Honey* losing its activity in storage.

Photo 1: Hydrogen peroxide is rapidly broken down (to oxygen and water) when it is exposed to the activity of the enzyme catalase present in a small drop of blood on a pricked finger.

The enzyme that produces hydrogen peroxide in honey becomes active only when honey is diluted. But the non-peroxide antibacterial activity is at full strength in undiluted manuka honey, which will provide a more potent antibacterial action diffusing into the depth of infected tissues. (See Photo 2 below.)

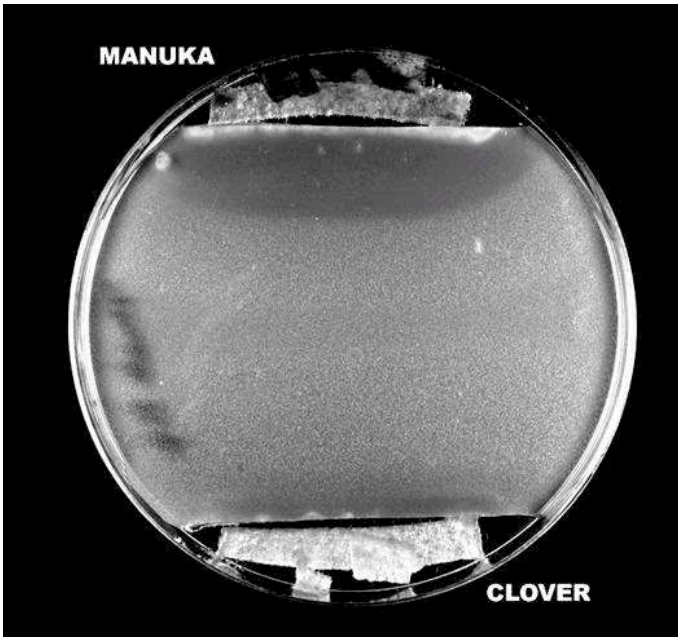

Photo 2: A model of honey dressings at work on an infected wound. The dressing material was impregnated with manuka honey or with clover honey, each honey having the same level of antibacterial activity in a standard laboratory assay of total antibacterial activity. The agar had been seeded with *Staphylococcus aureus* bacteria, which grew to form visible colonies when the plate was incubated.

The enzyme that produces hydrogen peroxide in honey needs oxygen to be available for the reaction, so may not work under wound dressings or in wound cavities or in the gut. Genuine *Active Manuka Honey*, which contains the non-peroxide antibacterial activity, is active in all situations.

The enzyme that produces hydrogen peroxide in honey becomes active only when the acidity of honey is neutralised by body fluids, but then the honey is diluted and so its potency is decreased.

In the stomach the enzyme that produces hydrogen peroxide in honey will not be active because of the acidity of the stomach.

Enzymes are proteins. The enzyme that produces hydrogen peroxide in honeys could be destroyed by the protein-digesting enzymes that are in wound fluids and in the stomach and intestines.

The non-peroxide antibacterial activity of *Active Manuka Honey* diffuses deeper into skin tissues than does the hydrogen peroxide from other types of honey.

Can other types of honey be used to treat infections?

Many medical professionals, in New Zealand and other countries, are using *Active Manuka Honey* (the genuine sort) – and are getting excellent results in patients with infected wounds that have not responded to any standard treatment such as antibiotics.

However, there have been many papers published in medical journals reporting the effectiveness of honey in treating infected wounds where the honey that was used was not manuka honey.

None of the results being obtained clinically should be considered evidence that *Active Manuka Honey* is more effective than other honey – a comparative clinical trial will be needed to establish that. Nevertheless, there are good theoretical reasons (see above) for choosing to use genuine *Active Manuka Honey* with a good level of the non-peroxide antibacterial activity for management of wound infections.

For most of the various brands of registered medical products based on honey that are sold for wound treatment and in ophthalmology the manufacturers have opted to use *Active Manuka Honey*. They use honey with a non-peroxide activity rating ranging from 12 to 16 (equivalent % phenol).

Staphylococcus aureus is the species of bacterium used in the testing to rate the antibacterial activity of honey. Comparing honeys with the same activity rating from this testing, *Active Manuka Honey*, with its non-peroxide, antibacterial activity, is more effective than honey with activity due to hydrogen peroxide against some other types of bacteria. For example, it is about twice as effective as other honey against *Eschericihia coli* and against Enterococci*, species that are* common causes of infection in wounds. It is much more effective than other honey against *Helicobacter pylori*, a common cause of peptic ulcers.

To alleviate any concern over the possible risk of introducing infection by the use of an unprocessed natural product on wounds, at the University of Waikato we investigated ways of sterilising honey without loss of any of its antibacterial activity. We found that honey can be sterilised by gamma irradiation without loss of activity. The honey sold as registered medical products, as plain honey (packed in tubes) and in manufactured wound dressings, is sterilised in this way. (This is a standard way in which medical products are sterilised.)