Text of a paper presented at the First World Wound Healing Congress, 10-13 September 2000, Melbourne, Australia.: The potential for using honey to treat wounds infected with MRSA and VRE. (Allen, K. L.; Hutchinson, G.; Molan, P.C.)

## INTRODUCTION

Many natural antibacterial substances are being evaluated to find a treatment for wounds infected with bacteria with multiple resistance to antibiotics, the "superbugs", as this becomes a major clinical problem. But most of these natural substances have no proven effectiveness on infected wounds, nor is it known if they have any adverse effects on wound tissues.

Honey is different, as it has an excellent "track record" over 4 000 years of usage as a wound dressing. In recent times it has been "rediscovered", with numerous reports of animal model and clinical studies, case reports and randomised controlled trials showing it rates favourably alongside modern dressing materials in its effectiveness in managing wounds.

Honey has a potent antibacterial activity and is very effective in clearing infection in wounds and protecting wounds from becoming infected. It also has a debriding action, an anti-inflammatory action, and a stimulatory effect on granulation and epithelialisation.

The objective of the study described here was to test the sensitivity to the antibacterial activity of honey of a large number of strains of antibiotic-resistant bacteria isolated from infected wounds.

## BACKGROUND

The evidence for the effectiveness of honey in clearing infection from wounds is in numerous reports published on case studies, animal studies and randomised controlled trials. In many cases honey has cleaned up wounds where conventional treatment was failing.

These reports have been reviewed briefly in: Molan PC, 1999. "The role of honey in the management of wounds." J Wound Care 8 (8): 423-6, and in more detail in: Molan PC, 1998. "A brief review of honey as a clinical dressing." Primary Intention 6 (4): 148-158.

These reports describe infected wounds quickly becoming sterile, mostly within a week. Also, that honey acts as a barrier preventing clean wounds from becoming infected, thus preventing cross-infection.

By soaking honey into absorbent dressings it can be held in place on a wound without running away. An occlusive secondary dressing stops seepage, the osmolarity of the honey protecting the surrounding skin from maceration. (Molan PC, Betts JA, 2000. "Using honey as a wound dressing: some practical considerations." Nursing Times, in press.)

Honey can be sterilised by gamma-irradiation without loss of its antibacterial activity (Molan PC; Allen KL, 1996. "The effect of gamma-irradiation on the antibacterial activity of honey." J Pharm Pharmacol 48: 1206-1209.)

Honey has no adverse effects on tissues, so it can be safely used on wounds and inserted into cavities and sinuses to clear infection.

Any problem of messiness using honey can be overcome by the use of appropriate methods of application.

Honeys produced from different types of flower have different properties. Ancient physicians were well aware of differences in the therapeutic value: Dioscorides (c.50 AD) stated that a pale yellow honey from Attica was the best, being "good for all rotten and hollow ulcers".

Mostly the antibacterial activity is due to hydrogen peroxide, continuously produced by enzyme action when honey is diluted, and remaining well below the level that causes inflammatory effects. Some honeys additionally contain plant-derived antibacterial components: honey from some Leptospermum species has a very high level of such.

EXPERIMENTS

Isolates of epidemic strains of MRSA and VRE, many from infected wounds, were cultured in Trypticase Soy broth overnight. They were then plated out, using a Mast multi-point inoculator delivering 1 µl drops, onto Trypticase Soy agar plates containing various concentrations of honey. The range of concentrations of honey in the agar plates was in steps of 1% (v/v).

As the antibacterial activity of honeys can vary up to 100-fold in potency, for this study we used honeys selected to be in the middle of the range. A pasture honey was used, with antibacterial activity due to hydrogen peroxide, and a manuka (Leptospermum scoparium) honey.

After incubating for 24 hours the growth of the cultures inoculated on the plates was examined. Plates containing no honey were used as controls to verify that the cultures inoculated would grow.

The minimum inhibitory concentration (MIC) of honey for each strain of bacteria was determined by finding the plate with the lowest concentration of honey on which the strain would not grow.

All inoculations, for each concentration of honey, were carried out in triplicate. Mostly the same MIC was found each time. Where there were differences between the replicates the MIC is shown as a range.

RESULTS FOR MRSA STRAINS

| Manuka honey | | | Pasture honey | | |
|---|---|---|---|---|---|
| 1 strain | MIC = | 3% honey | 56 strains | MIC = | 3% honey |
| 79 strains | MIC = | 4% honey | 20 strains | MIC = | 4% honey |
| 3 strains | MIC = | 5% honey | 3 strains | MIC = | 5% honey |
| 1 strain | MIC = | >6% honey | 1 strain | MIC = | 6% honey |
| 1 strain | MIC = | 7% honey | 1 strain | MIC = | >6% honey |
| | | | 2 strains | MIC = | >7% honey |

RESULTS FOR VRE STRAINS

| Manuka honey | | | Pasture honey | | |
|---|---|---|---|---|---|
| 1 strain | MIC = | <5% honey | 2 strains | MIC = | 8% honey |
| 1 strain | MIC = | 6% honey | 6 strains | MIC = | 12% honey |
| 2 strains | MIC = | <7% honey | 2 strains | MIC = | 14% honey |
| 2 strains | MIC = | 7% honey | 15 strains | MIC = | 16% honey |
| 1 strain | MIC = | >7% honey | 3 strains | MIC = | 20% honey |
| 7 strains | MIC = | 7-8% honey | 6 strains | MIC = | >20% honey |
| 24 strains | MIC = | 8% honey | (23 strains were not tested) | | |
| 17 strains | MIC = | 9% honey | | | |
| 2 strains | MIC = | 10% honey | | | |

CONCLUSIONS

The antibacterial potency of honey of average level activity is well in excess of that needed to stop the growth of MRSA and VRE. Since honey is of proven effectiveness in clearing wounds of infection with other bacteria, and it gives many other benefits as a wound dressing material, there is good justification for trying it for the treatment of wounds infected with MRSA and VRE.

Under these laboratory conditions the unusual antibacterial activity of manuka honey is about twice as great as the hydrogen peroxide activity of other honey against VRE, but against MRSA the activity of the two honeys is similar. On wounds, some hydrogen peroxide may be broken down, so honey with hydrogen peroxide activity may be less effective.