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Te Whare Wānanga o Waikato

Department of Biological Sciences

Waikato Honey Research Unit

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Honey as an Antimicrobial Agent

1. Introduction

That honey has antibacterial properties has been known for more than a century 1. Although it has been used as a medicine since ancient times in many cultures 2,3, in its ancient usage there was no recognition of its antibacterial properties - it was just known to be an effective remedy. This is not surprising considering that it is only since the latter part of the last century that it has become known that many ailments are the result of infection by microorganisms. Now it can be seen that the effectiveness of honey in many of its medical uses is probably due to its antibacterial activity. It is well established that honey inhibits a broad spectrum of bacterial species. There are many reports of bactericidal as well as bacteriostatic activity. There have also been reports of honey having antifungal activity. These numerous reports of the antimicrobial activity of honey have been comprehensively reviewed 4: the collation of data shows that honey is active against a wide range of bacterial and fungal species, many of which cause infections. However, there are ailments which may be treated with honey which have not had the infectious agents tested for their sensitivity to the antimicrobial activity of honey. Also, there has not been much distinction made in the different types of antimicrobial activity in honey to which the various microbial species are sensitive. For serious consideration to be given to the use of honey as a therapeutic agent it is necessary that these aspects be further investigated.

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2. Antimicrobial Properties of Honey

The numerous reports of investigations which have established the nature of the antimicrobial factors in honey are cited in a comprehensive review of this subject 4,5. A brief summary of what has been established is given here.

2.1 Explanation of Antibacterial Activity

2.1.1. Osmotic effect

Honey is a saturated or super-saturated solution of sugars, 84% being a mixture of fructose and glucose. The water content is usually only 15-21% by weight. The strong interaction of these sugar molecules with water molecules leaves very few of the water molecules available for microorganisms. This "free" water is what is measured as the water activity (aw): mean values for honey have been reported from 0.562 to 0.62. Although some yeasts can live in honeys that have a high water content, causing spoilage of the honey, the aw of ripened honey is too low to support the growth of any species, no fermentation occurring if the water content is below 17.1%. Many species of bacteria have their growth completely inhibited if the aw is in the range 0.94-0.99. These values correspond to solutions of a typical honey (aw of 0.6 undiluted) of concentrations from 12% down to 2% (v/v). On the other hand, some species have their maximum rate of growth when the aw is 0.99, so inhibition by the osmotic (water-withdrawing) effect of dilute solutions of honey obviously depends on the species of bacteria.

2.1.2. Acidity

Honey is characteristically quite acidic, its pH being between 3.2 and 4.5, which is low enough to be inhibitory to many animal pathogens. The optimum pH for growth of these species normally falls between 7.2 and 7.4. The minimum pH values for growth of some common wound-infecting species is: *Escherichia coli*, 4.3; *Salmonella sp*., 4.0; *Pseudomonas aeruginosa,* 4.4; *Streptococcus pyogenes,* 4.5. Thus in undiluted honey the acidity is a significant antibacterial factor. But if honey is diluted, especially by body fluids which are well buffered, the pH will not be so low and the acidity of honey may not be an effective inhibitor of many species of bacteria.

2.1.3. Hydrogen Peroxide

The major antibacterial activity in honey has been found to be due to hydrogen peroxide produced enzymically in the honey. The glucose oxidase enzyme is secreted from the hypopharyngeal gland of the bee into the nectar to assist in the formation of honey from the nectar.

The hydrogen peroxide and acidity produced by the reaction:

$$\textbf{glucose} + H_2O + O_2 \textbf{ --> gluconic acid} + H_2O_2$$

serve to preserve the honey. The hydrogen peroxide produced would be of effect as a sterilising agent only during the ripening of honey. Full-strength honey has a negligible level of hydrogen peroxide because this substance is short-lived in the presence of the transition metal ions and ascorbic acid in honey which catalyse its decomposition to oxygen and water. The enzyme has been found to be practically inactive in full-strength honey, it giving rise to hydrogen peroxide only when the honey is diluted. This is because the acidity produced in the action of the enzyme drops the pH to a point which is too low for the enzyme to work any more. On dilution of honey the activity increases by a factor of 2,500 - 50,000, thus giving a "slow-release" antiseptic at a level which is antibacterial but not tissue-damaging.

2.1.4. Phytochemical Factors

The evidence for the existence of other antibacterial factors is mainly that the peroxide-generating system does not account for all of the observed antibacterial activity, but there have also been some reports of isolation of antibacterial substances from honey that are not hydrogen peroxide. Furthermore, it has ben found that heating honey, which inactivates the glucose oxidase, causes loss of activity against some species whilst it is retained against others. Although the stability of the enzyme varies in different honeys, there have been reports of honeys with stability well in excess of this variation, showing that there must be an additional antibacterial factor involved. The most direct evidence for the existence of non-peroxide antibacterial factors in honey is seen in the reports of activity persisting in honeys treated with catalase to remove the hydrogen peroxide activity. Several chemicals with antibacterial activity have been identified in honey by various researchers: pinocembrin, terpenes, benzyl alcohol, 3,5-dimethoxy-4-hydroxybenzoic acid (syringic acid), methyl 3,5-dimethoxy-4-hydroxybenzoate (methyl syringate), 3,4,5-trimethoxybenzoic acid, 2-hydroxy-3-phenylpropionic acid, 2-hydroxybenzoic acid and 1,4-dihydroxybenzene. However, the quantities of these present were far too low to account for any significant amount of activity.

2.2. Variation in Antibacterial Activity

In almost all reports on the medical use of honey as an antibacterial agent no consideration is given to the selection of type of honey for therapeutic use. Aristotle, c.350 B.C. **6**, and Dioscorides, c.50 A.D. **7**, recommended that honey collected in specific regions and seasons (and therefore presumably from different floral sources) be used for the treatment of particular ailments, but in modern medicine clinical practitioners have not heeded these views nor the laboratory findings of large differences in the antibacterial potency of different honeys. It was recognised more than 40 years ago that there are differences in the antibacterial activity of different honeys, and a method was devised to determine the "inhibine number" of honeys as a measure of their antibacterial activity. The "inhibine number" is the degree of dilution to which a honey will retain its antibacterial activity, representing sequential dilutions of honey in steps of 5% from 25% to 5%. Studies measuring the "inhibine number" of honeys report activity to range over the five-fold difference in concentration in the dilution series, and studies using a wider range of dilutions report the minimum inhibitory concentrations of the honeys tested to range from 25 to 0.25%, >50 to 1.5%, 20-0.6%, and 50-1.5%. The data showed activities to be fairly well spread over these ranges. A study of 345 samples of New Zealand honeys **8** found a large number with low activity (36% of the samples had activity near or below the level of detection), the rest having almost a Gaussian distribution over a twenty-fold range of activity. The major variations seen in overall antibacterial activity are due to variation in the level of hydrogen peroxide that arises in honey, and in some cases to the level of non-peroxide factors. Hydrogen peroxide can be destroyed by components of honey: it can be degraded by reaction with ascorbic acid and metal ions, and by the action of the enzyme catalase which comes from the pollen and nectar of certain plants, more from the nectar. Also, very large differences have been found between honeys from different floral sources in the thermal stability of their glucose oxidase content, and in the sensitivity of this hydrogen peroxide-producing enzyme to denaturation by light because of a photosensitizing component that comes from some floral sources.

Although it appears that the honey from certain plants has better antibacterial activity than that from others, there is not enough evidence for such definite conclusions to be justified because the data are from small numbers of samples. However, honeys from some sources have been been studied in large enough numbers or have been included in enough different studies for some trends to be noted. Honeydew honey from the conifer forests of the mountainous regions of central Europe has been found to have particularly high antibacterial activity. Also honey from manuka (*Leptospermum scoparium*) in New Zealand has been found to have a high activity, about half of this type of honey having an exceptionally high level of non-peroxide activity **9**.

Thus it is important that when honey is to be used as an antimicrobial agent it is selected from honeys that have been assayed in the laboratory for antimicrobial activity. It is also important that honey for use as an antimicrobial agent be stored at low temperature and not exposed to light, so that none of the glucose oxidase activity is lost. Although all honey will stop the growth of bacteria because of its high sugar content, when the sugars are diluted by body fluids this antibacterial action is lost. The additional antibacterial components then become important.

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3. Potential Uses of Honey as an Antimicrobial Agent

3.1. Limitations to Usage

The popular literature on health and self-treatment of ailments gives the impression that honey can be taken to cure almost anything, but a rational consideration would suggest that the antimicrobial activity would be insignificant when an oral dose of honey becomes diluted after absorption from the gut into the many litres of fluid in the circulation and tissues of the body. Realistically, the potential for honey as an antimicrobial agent in medicine is in topical application rather than as a systemic agent, although there are some situations such as gastrointestinal infections or mastitis where the honey could remain localised and thus not become too dilute to be effectively antibacterial.

3.2. Honey as an Antiseptic Dressing

3.2.1. Established Usage of Honey as a Dressing

Honey has a well established usage as a wound dressing in ancient and traditional medicine **10**. In recent times this has been re-discovered, and honey is in fairly widespread use as a topical antibacterial agent for the treatment of wounds, burns and skin ulcers, there being many reports of its effectiveness **11-23**. The observations recorded are that inflammation, swelling and pain are quickly reduced, unpleasant odours cease, sloughing of necrotic tissue occurs without the need for debridement, dressings can be removed painlessly and without causing damage to re-growing tissue, and healing occurs rapidly with minimal scarring, grafting being unnecessary. In many of the cases honey was used on infected lesions not responding to standard antibiotic and antiseptic therapy. It was found in almost all of the cases to be very effective in rapidly clearing up infection and promoting healing.

3.2.2. Importance of Antibacterial Activity

Much of the effectiveness of honey as a dressing appears to be due to its antimicrobial properties. The healing process will not occur unless infection is cleared from a lesion: swabbing of wounds dressed with honey has shown that the infecting bacteria are rapidly cleared **13**, **16**, **18**, **20**, **24.** In this respect honey is superior to the expensive modern hydrocolloid wound dressings as a moist dressing. Although tissue re-growth in the healing process is enhanced by a moist environment, and deformity is prevented if the re-growth is not forced down by a dry scab forming on the surface, moist conditions favour the growth of infecting bacteria. Antibiotics are ineffective in this situation, and antiseptics cause tissue damage, so slow the healing process **25**. Honey is reported to cause no tissue damage, and appears to actually promote the healing process. There are also numerous reports of sugar being used as a wound dressing, this also being found to be effective **26-31**. Antibacterial activity is attributed by several authors to the high osmolarity of the sugar or honey **11**, **17**, **22**, **27**, it not being generally recognised that some honeys can have additional antibacterial activity considerably greater than that due to the osmolarity. This additional activity would be of particular significance in situations where the dressing becomes diluted by body fluids, and in regions of a lesion that are not in direct contact with the dressing. *Staphylococcus aureus* is exceptionally osmotolerant: for complete inhibition of its growth the aw has to be lowered below 0.86, which would be a typical honey at 29% (v/v). In the reports of sucrose syrup or paste being used as a wound dressing it is noted that infection with *Staphylococcus aureus* is hard to clear. Measurements that have been reported 27 of the dilution occurring from the uptake of water from surrounding tissues when an abdominal wound was packed with sugar reveal that a saturated sucrose syrup containing undissolved granules becomes diluted in 7.5 hours to a concentration that is 30% of that of a saturated solution. Although the aw of this solution is low enough to prevent the growth of most human pathogens, it is not low enough to seriously restrict the growth of *Staphylococcus aureus*, a species which has developed resistance to many antibiotics and has become the predominant agent of wound sepsis in hospitals **32**. But *Staphylococcus aureus* is one of the species most sensitive to the antibacterial activity of honey. There have been many reports of complete inhibition of *Staphylococcus aureus* by honeys diluted to much lower concentrations **4**, showing the importance of the other antibacterial factors in selected honeys.

To know for certain the clinical significance of the additional antibacterial activity in honey, a clinical trial will need to be conducted to compare dressings of sugar and selected honeys. The little comparative work reported to date indicates that more rapid healing is achieved with honey than with sugar **12**, **15**. Since infection is one of the most common impediments to wound healing **33**, then such results would be expected if the sugar dressing were not able to fully suppress the growth of bacteria as the sugar became diluted. The additional antibacterial activity of honey could be the reason for the remarkable rates of healing reported when honey has been used as a dressing **11**, **13**, **14**.

3.2.3. Effectiveness against Wound-infecting Species of Bacteria

The seven species of bacteria most commonly involved in wound infection have been tested for their sensitivity to the antibacterial activity of honey 34. The two major forms of antibacterial activity were examined separately: a honey with an average level of activity due to hydrogen peroxide and no detectable non-peroxide activity was used; also a manuka honey with an average level of non-peroxide activity, with catalase added to remove any hydrogen peroxide. The results of this study are summarised in Table 1.

Overall there was little difference between the two types of antibacterial activity in their effectiveness, although some species were more sensitive to the action of one type of honey than they were to the other. The results thus showed that these honeys, with an average level of activity, could be diluted nearly ten-fold yet still completely inhibit the growth of all the major wound-infecting species of bacteria. It is notable that the manuka honey, with an average level of activity, could be diluted with 54 times its volume of fluid yet still completely inhibit the growth of *Staphylococcus aureus*, the major wound-infecting species, and a species notorious for its development of resistance to antibiotics.

Bacterial Species	Manuka Honey	Other Honey
Escherichia coli	3.7	7.1
Proteus mirabilis	7.3	3.3
Pseudomonas aeruginosa	10.8	6.8
Salmonella typhimurium	6.0	4.1
Serratia marcescens	6.3	4.7
Staphylococcus aureus	1.8	4.9
Streptococcus pyogenes	3.6	2.6

Table 1. The minimum concentration of honey (%, v/v) in the growth medium needed to completely inhibit the growth of various species of wound-infecting bacteria

There are frequent reports of hospital wards being closed because of the presence of strains of methicillin-resistant *Staphylococcus aureus* (MRSA). Because these strains are resistant to all of the antibiotics in common use it is necessary to protect patients with impaired immunity from exposure to them in case they contract infections which will not respond to treatment. The collection of strains of MRSA at Waikato Hospital have been tested for sensitivity to the two honeys described above **35**. All of the strains were found to be completely inhibited by both honeys at 10% (v/v) in the growth medium, and many of the strains by the honeys at 5% (v/v).

3.2.4. Microbiological Safety

The use of honey as a wound dressing has been argued against because of the risk of it possibly causing wound botulism **36**. Clostridia are widely distributed in nature, but there is a very low incidence of wound botulism. However, honey sometimes contains spores of Clostridium botulinum **37**, so there is a definite risk of introducing the spores into wounds if honey is used as a dressing. If honey could be sterilized for use as a wound dressing this would remove the risk. The glucose oxidase activity which generates the hydrogen peroxide is very labile and would not withstand autoclaving **5**. The non-peroxide activity of manuka honey is stable to much more heating **38**, but there is some loss on autoclaving **39**, and any hydrogen peroxide activity present in addition to the non-peroxide activity would be completely lost. Honey is too viscous for sterilization by filtration through microporous membranes, but sterilization by gamma-irradiation is a possibility. However, there have been no reports on whether or not the antibacterial factors in honey withstand this sterilizing treatment. Therefore a study was recently undertaken to determine the effect of gamma-irradiation on the antibacterial activity of honey **40**. Honey samples were selected for their antibacterial activity, some manuka honeys with a high level of non-peroxide activity and a low level of hydrogen peroxide activity, others honeys with a high level of hydrogen peroxide activity only. They were put through a commercial sterilising plant which subjected all items processed to the standard 25 kGy of gamma-irradiation used for sterilising medical materials. The results of this study, summarised in Table 2, showed that there was no significant loss of either type of antibacterial activity when the honey samples were gamma-irradiated. A control honey very heavily seeded with Clostridial spores had no viable spores present after the same irradiation treatment.

	Honey 1	**Honey 2**	**Honey 3**	**Honey 4**	**Honey 5**
Untreated, no catalase	20.8±1.1	16.0±0.8	12.7±0.5	13.6±0.5	15.4±0.6
Irradiated, no catalase	13.1±0.7	14.6±0.5	14.9±0.6	21.3±1.0	16.3±0.6
Untreated, with catalase	0.0±0.0	0.0±0.0	12.8±0.4	12.1±0.6	16.3±0.5
Irradiated, with catalase	0.0±0.0	0.0±0.0	13.2±0.4	13.5±0.5	16.5±0.6

Table 2. Comparison of the antibacterial activity of various samples of honey before and after sterilization by gamma-irradiation. The activity is shown as the diameter (mm), ± S.D. (n=16), of the clear zone obtained in an agar well diffusion assay using plates seeded with *Staphylococcus aureus*. Total activity (i.e. 25% w/v honey in water) and non-peroxide activity (i.e. 25% w/v honey in catalase solution) are shown.

3.3. Honey for the Treatment of Mastitis in Dairy Animals

One type of infection in which a localised high concentration of honey could be achieved is mastitis in dairy cows and goats. This can be an expensive and difficult condition to treat. The standard treatment is the introduction of antibiotics into the teat canal of the infected udder, but milk has to be withheld from use until clear of antibiotic residues. Honey could possibly be suitable for the treatment of mastitis if inserted into the infected udder via the teat canal as it is harmless to tissues and would leave no undesirable residues in milk. As a first step in evaluating this possibility, the seven species of bacteria that most commonly cause mastitis in dairy cattle were tested for their sensitivity to the antibacterial activity of honey. Cultures of these were spread on nutrient agar plates containing various concentrations of two types of natural honey and an artificial honey, and the growth of the bacteria was assessed to find the concentration of honey that was necessary to prevent growth of the bacteria. The natural honeys used were a rewarewa honey with an average level of activity due to hydrogen peroxide and no detectable non-peroxide activity, and a manuka honey with an average level of non-peroxide activity and no detectable peroxide activity. The artificial honey was used to assess the sensitivity of the bacteria to the osmotic action and acidity of honey.

The results of this study **41** are summarised in Table 3. It can be seen that the growth of all seven species was completely inhibited by a 1 in 10 dilution of the natural honeys, in some cases a 1 in 20 dilution being sufficient. The manuka honey was noticeably more effective. Since only one species was inhibited by the artificial honey at a 1 in 10 dilution, it can be seen that the other antibacterial factors in natural honeys are important, and honeys should be selected for a high level of these if they are to be subjected to trial in the treatment of clinical mastitis.

Bacterial Species	Manuka Honey	Rewarewa Honey	Artificial Honey
Actinomyces pyogenes	1-5%	1-5%	5-10%
Klebsiella pneumoniae	5-10%	5-10%	>10%
Nocardia asteroides	1-5%	5-10%	>10%
Staphylococcus aureus	1-5%	1-5%	>10%
Streptococcus agalactiae	1-5%	5-10%	>10%
Streptococcus dysgalactiae	1-5%	5-10%	>10%
Streptococcus uberis	1-5%	5-10%	>10%

Table 3. Minimum inhibitory concentration of honeys (% v/v in nutrient agar) for cultures of various mastitis-causing bacteria streaked on the agar plates.

3.4. Honey for the Treatment of Peptic Ulcers

Honey is a traditional remedy for dyspepsia and peptic ulcers **42**, but there has been no rational basis for its use. The finding that *Helicobacter pylori* is probably the causative agent in many cases of dyspepsia and peptic ulcers raised the possibility that the antibacterial properties may be responsible for its therapeutic action. Consequently, the sensitivity of *Helicobacter pylori* to honey was tested **42**, using isolates of *Helicobacter pylori* from biopsies of gastric ulcers. All five isolates tested were found to be sensitive in an agar well diffusion assay to a 20% (v/v) solution of a manuka honey with an average level of non-peroxide activity, but none showed sensitivity to a 50% (v/v) solution of a honey in which the antibacterial activity was due primarily to its content of hydrogen peroxide. Assessment of the minimum inhibitory concentration by inclusion of manuka honey in the agar showed that the growth of all of a further seven isolates tested was completely inhibited over the incubation period of 72 h by the presence of 5% (v/v) honey.

3.5. Honey for the Treatment of Gastroenteritis

Honey has been found to be effective in treating bacterial gastroenteritis in infants 43. Used in place of glucose in an oral re-hydration fluid, it was found to be as effective as glucose in achieving re-hydration, whilst the antibacterial activity cleared the infection in bacterial diarrhoea. However, there is little information available on the sensitivity of the gastroenteritis-causing species of bacteria to the antibacterial activity of honey, and on which of the antibacterial factors in honey is most effective against them. Therefore honey was tested for its relative antibacterial potency against all the bacterial species that commonly cause gastroenteritis, comparing manuka honey and a honey with the usual hydrogen peroxide activity, also an artificial honey to assess how much of the antibacterial activity was due simply to the acidity and the osmotic effect of the sugar in honey **44**. With some of the species of bacteria the assessment was repeated with additional strains obtained from clinical isolates supplied by medical and animal health laboratories to see if there was any variation in sensitivity between different strains of a species.

Cultures of the bacteria were streaked on nutrient agar plates containing various concentrations of the honeys, and the growth of the bacteria was assessed to find the concentration of honey that was necessary to prevent growth of the bacteria. The honeys used were a mixed pasture honey with an average level of activity due to hydrogen peroxide and no detectable non-peroxide activity, and a manuka honey with an average level of non-peroxide activity. Honey concentrations were in a 5% (v/v) step dilution series initially and then with 1% dilution steps, the honey being diluted with either sterile distilled water (for the pasture honey and artificial honey) or a sterile solution of 0.2% catalase (for the manuka honey). Plates where inhibition of growth was observed were swabbed with a loopful of sterile water and streaked onto freshly prepared nutrient agar plates which did not contain honey. The plates were then incubated to find any surviving bacteria growing into visible colonies if the initial inhibition had been due to prevention of growth (bateriostasis) rather than killing the bacteria (bactericidal activity).

The results, summarised in Table 4, showed that honey with an average level of hydrogen peroxide activity is bacteriostatic at 4-8% (v/v) and bactericidal at 5-10% (v/v). The non-peroxide activity of an average manuka honey is bacteriostatic at 5-11% (v/v) and bactericidal at 8-15% (v/v). Activity (just bacteriostatic) was not seen with artificial honey unless it was at 20-30% (v/v), clearly showing the importance of factors other than sugar and acidity.

Bacterial strain	**Manuka honey with catalase;**			**Pasture honey**		
	PI	BS	BC	PI	BS	BC
Escherichia coli 916	6%	7%	10%	5%	6%	6%
Escherichia coli ex AHL	6%	7%	10%	-	6%	6%
Escherichia coli K88+	6%	6%	-	10%	7%	6%
Salmonella enteritis 3484	7%	8%	10%	4%	-	6%
Salmonella hadar 326	6%	7%	10%	-	6%	6%
Salmonella infantis 93	7%	8%	10%	6%	7%	10%
Salmonella typhimurium 298	6%	7%	8%	-	6%	8%
Salmonella typhimurium 1739	6%	7%	9%	-	6%	7%
Salmonella typhimurium ex WH	-	5%	10%	-	5%	10%
Shigella boydii 2616	6%	7%	10%	-	5%	6%
Shigella flexneri 983	6%	7%	10%	-	6%	6%
Shigella sonnei 86	6%	7%	10%	-	5%	5%
Shigella sonnei ex WH	5%	6%	10%	-	6%	10%
Vibrio cholorae	5%	7%	10%	6%	7%	10%
Vibrio paraheamolyticus	5%	6%	10%	-	4%	6%
Yersinia enterocolitica	10%	11%	15%	7%	8%	9%

Table 4. Minimum inhibitory concentration of honeys in nutrient agar plates (% v/v) giving partial inhibition (PI), bacteriostatic activity (BS) and bactericidal activity (BC) against various strains of bacteria which cause gastroenteritis.

3.6. Honey for the Treatment of Tineas

Honey has been reported to have antifungal activity, but not many species of fungi have been tested. An important group of fungi which regularly infect humans are the dermatophytes (Deuteromycotina). Cutaneous or superficial mycoses, caused through host infection by these fungi, are one of the most common diseases of humans. Only a small number of species of these, from the genera

Epidermophyton , *Microsporum* and *Trichophyton*, regularly infect humans **45**. Superficial fungal infections are amongst the most difficult diseases to successfully treat, antibiotics which successfully combat bacterial diseases being largely ineffective against fungi. A common predisposition to some fungal infections is poor host immunity, thus bacterial infections may also be present quite often. So a treatment which has both antifungal and antibacterial activities would be most beneficial. Therefore the effectiveness of honey against the dermatophyte species which most frequently cause superficial mycoses (tineas such as ringworm and athletes foot) was investigated **46**.

For this investigation two sorts of natural honey were used: a mixed pasture honey with an average level of antibacterial activity due to hydrogen peroxide production, and a manuka honey with an average level of non-peroxide antibacterial activity. An artificial honey was also used, to assess how much of the antibacterial activity was due simply to the acidity and the osmotic effect. The honeys were tested against clinical isolates of seven species of dermatophytes. An agar well diffusion assay was used, the contents of the wells being replaced with freshly prepared honey solutions at 24 hour intervals over the 3 - 4 days of incubation. The honeys were diluted with either sterile distilled water or a sterile solution of 0.2% catalase, a 5% (v/v) step dilution series being used for testing.

The results are summarised in Table 5. No inhibitory activity was detected with any of the seven species with the pasture honey at any concentration up to the highest tested, 50% (v/v), when catalase was present, nor with the artificial honey even at 100%. This showed that it was the the hydrogen peroxide in the pasture honey, and the non-peroxide activity in the manuka honey, that were inhibiting the growth of the fungi. Although the concentrations of honey needed to inhibit some of the dermatophytes are higher than needed to inhibit bacteria, less dilution of the honey is likely with a tinea than with infected wounds, burns and ulcers where there would be serum exudation. It could be that manuka honey may be more effective, even though the dermatophytes are less sensitive to its activity than they are to hydrogen peroxide, if there is insufficient dilution of honey on tineas for the enzymic production of hydrogen peroxide to be activated. Which type of honey is most effective, and the practical usefulness of honey as a topical antifungal salve, will only be known if comparative clinical trials are conducted.

Bacterial Species	**Pasture honey**	**Manuka honey**	**Manuka honey with catalase**
Epidermophyton floccosum	5-10%	5-10%	20-25%
Microsporum canis	10-15%	20-25%	20-25%
Microsporum gypseum	15-20%	45-50%	50-55%
Trichophyton rubrum	2.5-5%	5-10%	15-20%
Trichophyton tonsurans	15-20%	20-25%	20-25%
T. mentagrophytes var. interdigitale	10-15%	20-25%	40-45%
T. mentagrophytes var. mentagrophytes	10-15%	15-20%	20-25%

Table 5. Minimum inhibitory concentration of honeys in agar wells (% v/v) giving a clear zone around the wells in an agar well diffusion assay against seven species of fungi which cause tineas.

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