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ANTIMICROBIAL PROPERTIES OF HONEY AND MECHANISM OF ACTION: A REVIEW

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ABSTRACT

The antimicrobial properties of honey have been well documented. The antimicrobial activity in most honeys is due to the production of hydrogen peroxide. However, it has been observed that this antimicrobial activity persists even when hydrogen peroxide activity is blocked. This may be due to the presence of some other constituents or it may be due to natural properties of honey like osmolarity and pH. It has also been observed that honeys vary in their antimicrobial properties depending on the bee type and the source of nectar.

KEYWORDS: Antimicrobial Properties of Honey Have Been Well Documented

INTRODUCTION

The role of antimicrobial agents in management of infectious diseases and wounds is utmost important. However the emergence of antibiotic resistance is a global public health concern now. Today, clinically important bacteria are characterized by multiple antibiotic resistances. [Levy SB et al]. Keeping this in mind, much concern is being given to alternative antimicrobial strategies. Here comes the role of traditional medicine, of which honey has been the pioneer. Honey has been used by humans since Ancient times to treat a variety of ailments through topical application, but only recently have the antiseptic and antibacterial properties of honey been chemically explained [Altmann]. Scientists have revealed that honey has powerful antibacterial properties, and unlike antibiotics, honey has wide range of action, has no side effects, is non-toxic and has no issues of developing resistance. The antimicrobial properties of honey are due to its varied composition: its viscous nature; acidic pH; generation of hydrogen peroxide; non-peroxide antibiotic activity; and the presence of antioxidants.

ANTIBACTERIAL ACTIVITY

To assess the variation in antibacterial activity of honey, numerous varieties of New Zealand honeys were tested in vitro against Staphylococcus aureus in an agar well fusion assay [Allen KL et al, 1991]. It demonstrated significant difference in the antibacterial activity of honey from different floral sources. Kanuka, manuka, heather and ling kamahi were sources likely to produce honey with high antibacterial activity.

Manuka honey (Leptospermum scoparium) has been demonstrated to be effective against several human pathogens including Escherichia coli, Enterobacter aerogens, Salmonella typhimurium, Staphylococcus aureus [Lusby PE et al, 2005; Visavadia BG et al, 2006]. Studies have revealed that honey is effective against methicillin-resistant Staph. Aureus (MRSA), beta-hemolytic Streptococci and vancomycin-resistant Enterococci (VRE) [Allen KL et al, 2000; Kingsley A, 2001].

The multifactorial nature of honey is responsible for its broad-spectrum antimicrobial activity. This includes hydrogen peroxide and non-peroxide components such as Methylglyoxal (MGO), Methylseringate, low pH and an antimicrobial peptide bee defensin-1.

Hydrogen peroxide has been described as the main compound responsible for the antibacterial activity of honey. Hydrogen peroxide is produced by the enzyme glucose oxidase:

$C_6H_{12}O_6 + H_2O + O_2 \rightarrow C_6H_{12}O_7 + H_2O_2$ (glucose oxidase reaction)

The hydrogen peroxide concentration in honey is determined by the rate of its production by glucose oxidase and its destruction by catalases. Thus, hydrogen peroxide levels in various honeys may differ considerably. Honeys with high concentration of hydrogen peroxide have high antibacterial activity. However, honey contains several other compounds which may interact with and affect this oxidizing property. The oxidizing effect of hydrogen peroxide is augmented by other honey components such as transition metals (Fe, Cu) [Bizzera FC et al, 2012].

The pH of honey is commonly between 3.2 and 4.5. This relatively acidic pH level prevents the growth of many bacteria. The non-peroxide antibiotic activity is due to methylglyoxal (MGO) and an unidentified synergistic component. Most honeys contain very low levels of MGO, but manuka honey contains very high levels. The presence of the synergist in manuka honey more than doubles MGO antibacterial activity.

The adherence of bacteria to a wound is an important step in establishing infection and biofilm formation. It has been shown that the presence of biofilms in a wound is related to its chronicity [Merckoll et al, 2009]. In 2009, a study into the effects of honey on planktonic and biofilm-embedded bacteria suggested that honey has a bactericidal effect against the wound pathogens grown in the laboratory as biofilms [Merckoll et al, 2009]. Similarly, biofilms of *S. aureus* and *P. aeruginosa* exposed to honey were inhibited in vitro [Alandejani et al, 2009]. Methylglyoxal has been implicated in the inhibition of biofilms (Jervis-Bardy et al, 2011). Biofilms of methicillin-sensitive S. aureus (MSSA), MRSA, and VRE can be prevented from forming - and established biofilms can be inhibited - in vitro with varying concentrations of manuka honey [Cooper et al, 2011b]. Honey has been shown to be effective in inhibiting six isolates of P. aeruginosa forming biofilms in vitro [Okhiria et al, 2009] and one reference strain of Streptococcus pyogenes [Maddocks et al, 2012]. The downregulation of two genes coding for surface-binding proteins in S. pyogenes following exposure to manuka honey was found to contribute to the prevention of biofilm formation [Maddocks et al, 2012]. These findings need to be validated by clinical studies once a reliable test for the presence of a biofilm has been developed.

Table 1

Antibacterial activity of honey against bacteria causing life-threatening infec

Bacterial strain	Clinical importance
Proteus spps.	Septicemia, urinary infections, woundinfections
Serratia marcescens	Septicemia, wound infections
Vibrio cholerae	Cholera
S. aureus	Community acquired and nosocomial infection
E. coli	Urinary tract infection, diarrhea, septicemia, wound infections
P. aeruginosa	Wound infection, diabetic foot ulcer, Urinary infections

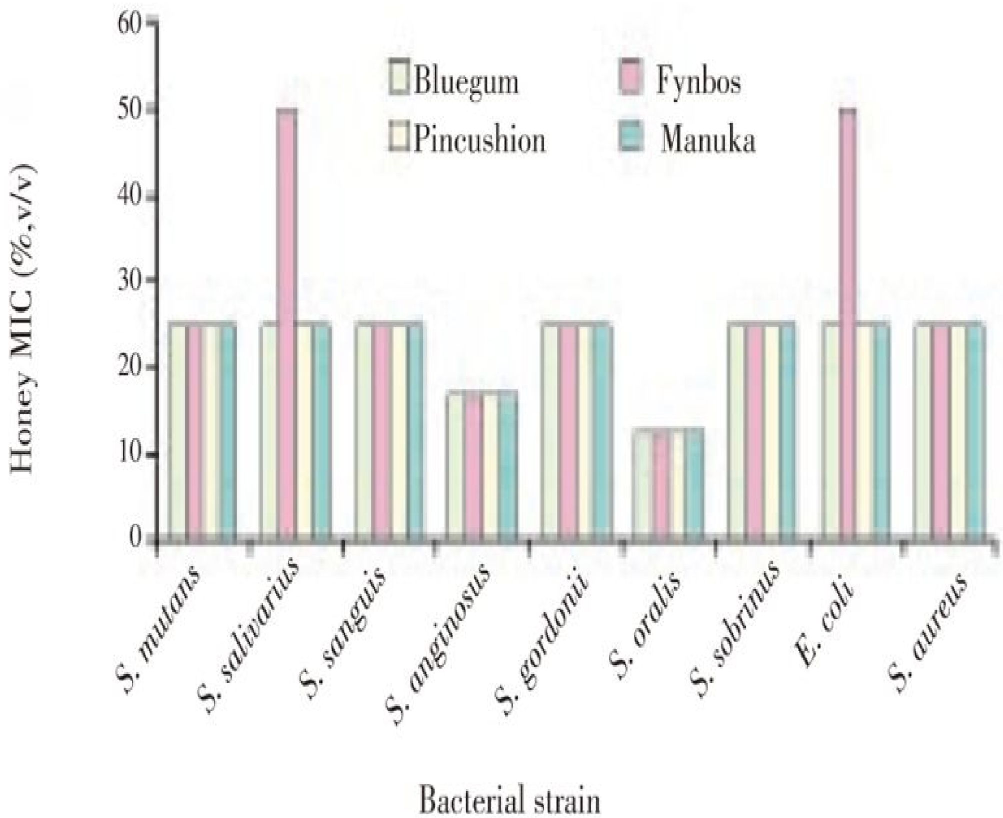

Figure 1: The MIC of Four Different Honeys to Oral Bacterial Strains (Streptococcus, E. Coli, and Staph Aureus)

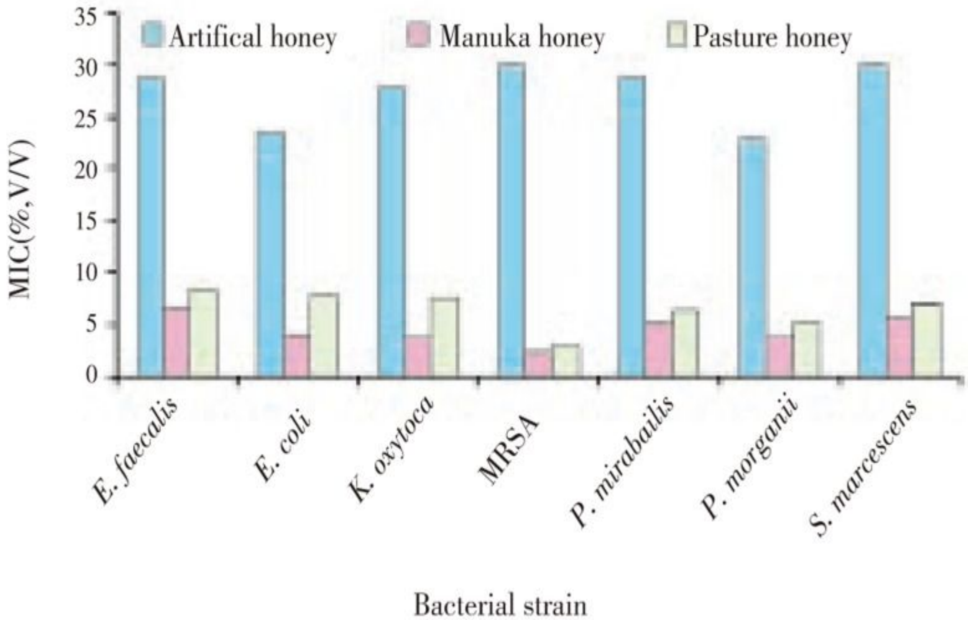

Figure 2: MIC of Different Honey Types for Bacterial Strains Causing Wound Infections

Figure 3: The pH Values of Different Honeys Having Antibacterial Activity

The difference in antimicrobial potency among various honeys can be more than 100-fold, depending upon source, season as well as harvesting and processing conditions [Molan and Cooper, 2000]. The antimicrobial nature of honey is dependent on various factors acting independently or in a synergistic manner. The most important of these are Hydrogen peroxide, phenolic compounds, wound pH, pH of honey and osmotic pressure. Antimicrobial activity of honey may range from concentrations <3% to >50% [Wilkinson JM et al, 2005; French VM et al, 2005].

In Gram+ve bacteria, manuka honey has been shown to inhibit cell division in Staph. Aureus (Henriques et al, 2010) and in MRSA (Jenkins et al, 2011) It was seen that cells formed at the end of cell cycle were complete with cell walls, but were incapable of dividing into daughter cells. Multiple changes in cellular proteins have also been observed in S. aureus exposed to manuka honey (Packer et al, 2012). In Escherichia coli, manuka honey exerts its effect by affecting the gene expression. (Blair et al, 2009). In P. aeruginosa, manuka honey caused changes in the bacterial cell wall that led to instabilities, resulting in cell lysis (Henriques et al, 2011; Roberts et al, 2012). Buckwheat honey has been shown to inhibit MRSA, VRE, E. coli and Bacillus subtilis by extensive degradation of DNA elicited by the generation of hydrogen peroxide on exposure (Brudzynski et al, 2012).

CONCLUSIONS

Microbial resistance has never been reported for honey [Dixon B, 2003]. This makes honey a very promising antimicrobial agent for future use. However, the unpredictable antibacterial activity of non-standardized honey may hamper its introduction as an effective antimicrobial agent. Further studies are required to define the exact role of honey as an antimicrobial agent and to study the antimicrobial effect of locally produced honeys and its comparative effectiveness with respect to currently used medical grade honey.

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