Honey: its medicinal property and antibacterial activity

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ABSTRACT

Indeed, medicinal importance of honey has been documented in the world’s oldest medical literatures, and since the ancient times, it has been known to possess antimicrobial property as well as wound-healing activity. The healing property of honey is due to the fact that it offers antibacterial activity, maintains a moist wound condition, and its high viscosity helps to provide a protective barrier to prevent infection. Its immunomodulatory property is relevant to wound repair too. The antimicrobial activity in most honeys is due to the enzymatic production of hydrogen peroxide. However, another kind of honey, called non-peroxide honey (i.e., manuka honey), displays significant antibacterial effects even when the hydrogen peroxide activity is blocked. Its mechanism may be related to the low pH level of honey and its high sugar content (high osmolarity) that is enough to hinder the growth of microbes. The medical grade honeys have potent in vitro bactericidal activity against antibiotic-resistant bacteria causing several life-threatening infections to humans. But, there is a large variation in the antimicrobial activity of some natural honeys, which is due to spatial and temporal variation in sources of nectar. Thus, identification and characterization of the active principle(s) may provide valuable information on the quality and possible therapeutic potential of honeys (against several health disorders of humans), and hence we discussed the medicinal property of honeys with emphasis on their antibacterial activities.

1. Introduction

Antimicrobial agents are essentially important in reducing the global burden of infectious diseases. However, as resistant pathogens develop and spread, the effectiveness of the antibiotics is diminished. This type of bacterial resistance to the antimicrobial agents poses a very serious threat to public health, and for all kinds of antibiotics, including the major last-resort drugs, the frequencies of resistance are increasing worldwide[1,2]. Therefore, alternative antimicrobial strategies are urgently needed, and thus this situation has led to a re-evaluation of the therapeutic use of ancient remedies, such as plants and plant–based products, including honey[3–5].

The use of traditional medicine to treat infection has been practiced since the origin of mankind, and honey produced by Apis mellifera (A. mellifera) is one of the oldest traditional medicines considered to be important in the treatment of several human ailments. Currently, many researchers have reported the antibacterial activity of honey and found that natural unheated honey has some broad—spectrum antibacterial activity when tested against pathogenic bacteria, oral bacteria as well as food spoilage bacteria[6,7]. In most ancient cultures honey has been used for both nutritional and medical purposes. The belief that honey is a nutrient, a drug and an ointment has been carried into our days, and thus, an alternative medicine branch, called apitherapy, has been developed in recent years, offering treatments based on honey and other bee products against many diseases including bacterial infections. At present a number of honeys are sold with standardized levels of antibacterial activity. The Leptospermum scoparium (L. scoparium) honey, the best known of the honeys, has been reported to have an inhibitory effect on around 60 species of bacteria, including aerobes and anaerobes, gram—
Natural honey of other sources can vary as much as wounds

Staphylococcus aureus (antimicrobial activity against pathogenic bacteria such as pale honey as being wounds, which has recently been shown to speed up the growth of new tissue and work as an anti-inflammatory agent. The honey has been used from ancient times as a method for the treatment of wounds or stomach ulcers [10].

The honey has been used from ancient times as a method of accelerating wound healing [11], and the potential of honey to assist with wound healing has been demonstrated repeatedly [12,13]. Honey is gaining acceptance as an agent for the treatment of ulcers, bed sores and other skin infections resulting from burns and wounds [14,15]. The healing properties of honey can be ascribed to the fact that it offers antibacterial activity, maintains a moist wound environment that promotes healing, and has a high viscosity which helps to provide a protective barrier to prevent infection [6]. There are many reports of honey being very effective as dressing of wounds, burns, skin ulcers and inflammations; the antibacterial properties of honey speed up the growth of new tissue to heal the wound [16]. The medihoney and manuka honey have been shown to have in vivo activity and are suitable for the treatment of ulcers, infected wounds and burns [6,17].

The honey, when applied topically, rapidly clears wound infection to facilitate healing of deep surgical wounds with infection [18]. The application of honey can promote the healing in infected wounds that do not respond to the conventional therapy, i.e., antibiotics and antiseptics [18], including wounds infected with methicillin-resistant S. aureus [19,20]. Moreover, it can be used on skin grafts and infected skin graft donor sites successfully [21].

The manuka, jelly bush and pasture honeys are capable of stimulating the monocytes, the precursors of macrophages, to secrete TNF-α [22,23]. On the other hand, glycosylated proteins can induce TNF-α secretion by macrophages, and this cytokine is known to induce the mechanism of wound repairing. Furthermore, the ability of honey to reduce ‘reactive intermediates release’ [23] may well limit tissue damage by activated macrophages during wound healing. Thus, the immunomodulatory property of honey is relevant to wound repair.

The support for using honey as a treatment regimen for peptic ulcers and gastritis comes from traditional folklore as well as from reports in modern times [24]. Honey may promote the repair of damaged intestinal mucosa, stimulate the growth of new tissues and work as an anti-inflammatory agent [24,25]. Raw honey contains copious amounts of compounds such as flavonoids and other polyphenols which may function as antioxidants [26]. Clinical observations have been reported of reduced symptoms of inflammation when honey is applied to wounds. The removal of exudate in wounds dressed with honey is of help in managing inflamed wounds [18].

3. Antibacterial activity

3.1. Potential antibacterial agent

The use of honey as a traditional remedy for microbial infections dates back to ancient times [8]. Research has been conducted on manuka (L. scoparium) honey [27], which has been demonstrated to be effective against several human pathogens, including Escherichia coli (E. coli), Enterobacter aerogenes, Salmonella typhimurium, S. aureus [6-27]. Laboratory studies have revealed that the honey is effective against methicillin-resistant S. aureus (MRSA), β-haemolytic streptococci and vancomycin-resistant Enterococci (VRE) [28,29]. However, the newly identified honeys may have advantages over or similarities with manuka honey due to enhanced antimicrobial activity, local production (thus availability), and greater selectivity against medically important organisms [9]. The coagulase-negative staphylococci are very similar to S. aureus [14,30] in their susceptibility to honey of similar antibacterial potency and more susceptible than Pseudomonas aeruginosa (P. aeruginosa) and Enterococcus species [14].

The disc diffusion method is mainly a qualitative test for detecting the susceptibility of bacteria to antimicrobial substances; however, the minimum inhibitory concentration (MIC) reflects the quantity needed for bacterial inhibition. Following the in vitro methods, several bacteria (mostly...
multidrug resistant; MDR) causing human infections that were found susceptible to honeys are presented in Table 1.

### 3.2. Zone diameter of inhibition

The zone diameter of inhibition (ZDI) of different honey samples (5%–20%) has been determined against E. coli O157: H7 (12 mm–24 mm) and S. typhimurium (0 mm–20 mm)[31]. The ZDIs of Nilgiris honeys were found to be (20–21) mm, (15–16) mm and (13–14) mm for S. aureus, P. aeruginosa and E. coli, respectively[32]. Agbagwa and Frank–Peterside[33] examined different honey samples: Western Nigerian honey, Southern Nigerian honey, Eastern Nigerian honey and Northern Nigerian honey, and compared their abilities to inhibit the growth of S. aureus, P. aeruginosa, E. coli and Proteus mirabilis (P. mirabilis) with an average of ZDIs (5.3–11.6) mm, (1.4–15.4) mm, (4.4–13.5) mm and (9.1–17) mm, respectively, and with honey concentrations of 80%–100%. The extracts of raw and processed honey showed ZDI (6.94–37.94) mm, against gram–positive bacteria viz., S. aureus, Bacillus subtilis, Bacillus cereus, as well as gram–negative bacteria like E. coli, P. aeruginosa and S. enterica serovar Typhi[34]. Figure 1 represents the ZDIs for gram–negative and gram–positive bacterial strains due to ulmo and manuka honeys.

### 3.3. Minimum inhibitory concentration

The MIC assay showed that a lower MIC was observed with ulmo (Eucryphia cordifolia) honey (3.1% – 6.3% v/v) than with manuka honey (12.5% v/v) for MRSA isolates; for the E. coli and Pseudomonas strains equivalent MICs were observed (12.5% v/v)[35]. The MICs for Tualang honey ranged 8.75% – 25%, while those for manuka honey ranged 8.75% – 20% against many pathogenic gram–positive and gram–negative bacteria[9]. The MICs of manuka, heather, khadikraft and local honeys against clinical and environmental isolates of P. aeruginosa were recorded as 10% – 20%, 10%

### Table 1

<table>
<thead>
<tr>
<th>Bacterial strain</th>
<th>Clinical importance</th>
<th>Authors</th>
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<tbody>
<tr>
<td>Proteus spps.</td>
<td>Septicemia, urinary infections, wound infections</td>
<td>Molan[8]</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Agbagwa and Frank–Peterside[33]</td>
</tr>
<tr>
<td>Serratia marcescens</td>
<td>Septicemia, wound infections</td>
<td>Molan[8]</td>
</tr>
<tr>
<td>Vibrio cholerae</td>
<td>Cholera</td>
<td>Molan[8]</td>
</tr>
<tr>
<td>S. aureus</td>
<td>Community acquired and nosocomial infection</td>
<td>Taormina et al[50]</td>
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<td></td>
<td></td>
<td>Chauhan et al[34]</td>
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<td></td>
<td></td>
<td>Sherlock et al[35]</td>
</tr>
<tr>
<td>E. coli</td>
<td>Urinary tract infection, diarrhea, septicemia, wound infections</td>
<td>Chauhan et al[34]</td>
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<td></td>
<td></td>
<td>Sherlock et al[35]</td>
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<tr>
<td>P. aeruginosa</td>
<td>Wound infection, diabetic foot ulcer, Urinary infections</td>
<td>Chauhan et al[34]</td>
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<td>Sherlock et al[35]</td>
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<td></td>
<td></td>
<td>Mullai and Menon[36]</td>
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<tr>
<td>S. maltophilia</td>
<td>Pneumonia, urinary tract infection, blood stream infection, nosocomial infection</td>
<td></td>
</tr>
<tr>
<td>A. baumannii</td>
<td>Opportunistic pathogen infects immunocompromised individuals through open wounds, catheters and breathing tubes</td>
<td></td>
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<tr>
<td>A. schubertii</td>
<td>Burn– wound infection</td>
<td>Hassanein et al[38]</td>
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<tr>
<td>H. parahaemolyticus</td>
<td></td>
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<td>Micrococcus luteus</td>
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<td>Cellulosimicrobium cellulosans</td>
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<td>Listonella anguillarum</td>
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<td>A. baumannii</td>
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<tr>
<td>H. pylori</td>
<td>Chronic gastritis, peptic ulcer, gastric malignancies</td>
<td>Ndip et al[37]</td>
</tr>
<tr>
<td>Salmonella enterica serovar Typhi</td>
<td>Enteric fever</td>
<td>Mulu et al[38]</td>
</tr>
<tr>
<td>Mycobacterium tuberculosis</td>
<td>Tuberculosis</td>
<td>Asadi–Pooya et al[39]</td>
</tr>
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</table>
activity of autoclaved honey against E. coli, P. aeruginosa and S. Typhi in order to establish the potential efficacy of such local honey (not studied before) collected from a village of the West Bengal state, India[5]. Antibiotic susceptible and resistant isolates of S. aureus, S. epidermidis, Enterococcus faecium, E. coli, P. aeruginosa, E. cloacae, and Klebsiella oxytoca were killed within 24 h by 10%–40% (v/v) honey[40]. Thus, more studies are required to establish various local honeys based upon kill kinetics and their effective in vivo application against MDR infections.

Figure 2. MIC of four different honeys (as shown in the figure) to oral bacterial strains (Streptococcus spp, E. coli and S. aureus).

Figure 3. MIC of different honey types for bacterial strains causing wound infections.

4. Mechanism and factors affecting antibacterial activity

4.1. Mechanism of antibacterial activity

The beneficial role of honey is attributed to its antibacterial property with regards to its high osmolarity, acidity (low pH) and content of hydrogen peroxide (H₂O₂) and non-peroxide components, i.e., the presence of phytochemical components like methylglyoxal (MGO)[41,42]. The antimicrobial agents in honey are predominantly hydrogen peroxide, of which the

- 20%, 11% and 10%–20%, respectively[36]. The MICs of A. mellifera honey ranged (126.23 – 185.70) mg/mL and of Tetragenica angustula honey (142.87 – 214.33) mg/mL against S. aureus[37]. The Egyptian clover honey MIC was 100 mg/mL for S. typhimurium and E. coli O157:H7[31]. The Nilgiri honey MICs were 25%, 35% and 40% for S. aureus, P. aeruginosa and E. coli, respectively[32]. MIC values of honey extracts were found in the range of (0.625–5.000) mg/mL, for S. aureus, B. subtilis, B. cereus, and gram-negative bacteria (E. coli, P. aeruginosa and S. typhi)[34].

By visual inspection, the MICs of Tualang honey ranged 8.75% – 25% compared with those of manuka honey (8.75% – 20%) against wound and enteric microorganisms: Streptococcus pyogenes (S. pyogenes), coagulase–negative Staphylococci, MRSA, Streptococcus agalactiae, S. aureus, Stenotrophomonas maltophilia (S. maltophilia), Acinetobacter baumannii (A. baumannii), S. Typhi, P. aeruginosa, Proteus mirabilis, Shigella flexneri, E. coli, Enterobacter cloacae (E. cloacae)[9]. Six bacterial strains from burn wound patients, namely, Aeromonas schuberti (A. schuberti), Haemophilus parphrophoeumlyticus (H. parphrophoeumlyticus), Micrococcus luteus (M. luteus), Cellulosimicrobium cellulans (C. cellulans), Listonella anguillarum (L. anguillarum) and A. baumannii had MICs of Citrus, Clover, Nigella and Eljahaly honeys 35%–40%, 35%–40%, 35%–40%, 25%–30%, respectively, as has been reported by Hassanein et al. The honeys were inhibitory at dilutions down to 3.6% – 0.7% (v/v), for the pasture honey, 3.4% – 0.5% (v/v), and for the manuka honey, against coagulase–negative Staphylococci[10]. The MICs of various types of honeys for various pathogenic bacterial strains have been determined by many authors[39]; in this article for oral bacterial strains and bacterial strains causing wound infections, honey MICs are depicted in Figure 2 and 3.

3.4. Time–kill study

The kill kinetics provides more accurate description of antimicrobial activity of antimicrobial agents than does the MIC[2]. In our earlier study, we explored the time–kill

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Honey is largely due to H2O2 production: 25% (v/v) solution of H2O2 is toxic to many bacteria. The minimum pH values for growth of some pathogenic bacteria are: *E. coli* (4.3), *Salmonella* spp. (4.0), *P. aeruginosa* (4.4), *S. pyogenes* (4.5)[46], and thus in undiluted honey the acidity is a significant antibacterial factor. The antibacterial property of honey is also derived from the osmotic effect of its high sugar content and low moisture content, along with its acidic properties of gluconic acid and the antiseptic properties of its H2O2[47]. A recent study examining the antimicrobial properties of honey in vitro found that H2O2, MGO and an antimicrobial peptide, bee defensin-1, are distinct mechanisms involved in the bactericidal activity of honey[48].

### 4.2. Factors affecting antibacterial nature of honey

Molan and Cooper[49] reported that the difference in antimicrobial potency among the different honeys can be more than 100-fold, depending on its geographical, seasonal and botanical source as well as harvesting, processing and storage conditions. The antibacterial nature of honey is dependent on various factors working either singularly or synergistically, the most salient of which are H2O2, phenolic compounds, wound pH, pH of honey and osmotic pressure exerted by the honey. Hydrogen peroxide is the major contributor to the antimicrobial activity of honey, and the different concentrations of this compound in different honeys result in their varying antimicrobial effects[8]. It has further been reported that physical property along with geographical distribution and different floral sources may play important role in the antimicrobial activity of honey[50]. Several authors reported that different honeys vary substantially in the potency of their antibacterial activity, which varies with the plant source[6,7,51]. Thus, it has been shown that the antimicrobial activity of honey may range from concentrations < 3% to 50% and higher[6,10,51]. The bactericidal effect of honey is reported to be dependent on concentration of honey used and the nature of the bacteria[4,52]. The concentration of honey has an impact on antibacterial activity; the higher the concentration of honey the greater its usefulness as an antibacterial agent[31]. Taormina et al[50] reported that the concentration of honey needed for complete inhibition of *S. typhimurium* growth is <25%.

![Figure 4. The pH values of different honeys having antibacterial activity](image)

Honey is characteristically acidic with pH between 3.2 and 4.5, which is low enough to be inhibitory to several bacterial pathogens[45]; Figure 4 depicts the pH values of different honeys. The minimum pH values for growth of some common pathogenic bacteria are: *E. coli* (4.3), *Salmonella* spp. (4.0), *P. aeruginosa* (4.4), *S. pyogenes* (4.5)[46], and thus in undiluted honey the acidity is a significant antibacterial factor. The antibacterial property of honey is also derived from the osmotic effect of its high sugar content and low moisture content, along with its acidic properties of gluconic acid and the antiseptic properties of its H2O2[47]. A recent study examining the antimicrobial properties of honey in vitro found that H2O2, MGO and an antimicrobial peptide, bee defensin-1, are distinct mechanisms involved in the bactericidal activity of honey[48].

### 5. Conclusion

Microbial resistance to honey has never been reported[53], which makes it a very promising topical antimicrobial agent against the infection of antibiotic-resistant bacteria (e.g., MDR *S. maltophilia*) and in the treatment of chronic wound infections that do not respond to antibiotic therapy. Hence honey has been used as a last-resort medication. Manuka honey has been widely researched and its antibacterial potential is renowned worldwide. The potency of honeys, such as Tualang honey, against microorganisms suggests its potential to be used as an alternative therapeutic agent in certain medical conditions, particularly wound infection.

Lusby et al[6] reported that honeys other than the commercially available antibacterial honeys (e.g., manuka honey) can have equivalent antibacterial activity against bacterial pathogens. The growth of bacterial species
that cause gastric infections, such as *S. typhi*, *S. flexneri* and *E. coli*, are inhibited by Tualang honey at the low concentrations. The Tualang honey has been reported to be effective against *E. coli*, *S. typhi* and *S. pyogenes* [54], and thus, when taken orally in its pure undiluted form, this honey may help speed up recovery from such infections. Honey is effective when used as a substitute for glucose in oral rehydration and its antibacterial activity shortened the duration of bacterial diarrhoea.

Currently, the emerging antimicrobial resistance trends in burn wound bacterial pathogens are a serious challenge [55]. Thus, honey with effective antimicrobial properties against antibiotic–resistant organisms such as MRSA and MDR *P. aeruginosa*, *Acinetobacter* spp. and members of the family *Enterobacteriaceae*, which have been associated with infections of burn wounds and in nosocomial infections, is much anticipated [55, 56].

Overall, the unpredictable antibacterial activity of non–standardized honey may hamper its introduction as an antimicrobial agent due to variation in the *in vitro* antibacterial activity of various honeys. At present a number of honeys are sold with standardized levels of antibacterial activity, of which the best known is manuka (*Leptospermum scoparium*) honey as well as Tualang (*Koompassia excelsa*) honey. The medical–grade honey (Revamil, medihoney), which has the potential to be a topical antibacterial prophylaxis because of its broad–spectrum bactericidal activity, or to be a treatment for topical infections caused by antibiotic–resistant as well as antibiotic–sensitive bacteria, should be considered for therapeutic use. Moreover, mountain, manuka, capillaro and eco–hones have exhibited inhibitory activity against *H. pylori* isolates at concentration 10% (v/v) [57], demonstrating that locally produced honeys possess excellent antibacterial activity comparable to the commercial honeys. Therefore it is necessary to study other locally produced but yet untested honeys for their antimicrobial activities.

**Conflict of interest statement**

We declare that we have no conflict of interest.

**References**


