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Commentary

Can Honey Combat Life Threatening Bacterial Infections to Humans?

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Abbreviations

CLSI: Clinical and Laboratory Standards Institute; MDR: Multidrug Resistant; MIC: Minimum Inhibitory Concentration; NCCLS: National Committee for Clinical Laboratory Standards; SNPs: Silver Nanoparticles; ZDI: Zone Diameter of Inhibition

Introduction

The incidence of human infection with enteric bacteria is common in India [1], and the commonest bacterial isolates reported were *Salmonella enteric* serovar Typhi [1], *S. enterica* serovar Parayphi A [2], *Escherichia coli, Proteus species,* and *Klebsiella pneumoniae* [3]. The isolates, from different clinical samples from patients, had multidrug resistance [1,3], as determined by disk diffusion method and MIC value determination following the NCCLS/CLSI criteria. The MDR isolates had transferable R-plasmids [3,4]. The cholera outbreak, due to the infection of *Vibrio cholerae* O1 biotype El-Tor serotype Ogawa, has also been reported [5]. Currently, β-lactamase producing clinical bacterial isolates (*S. Typhi, E. coli, K. pneumonae* and *P. vulgaris*) has been reported [6].

In order to combat the bacterial antibiotic resistances, as depicted above, several strategies have been developed: synergistic activity between antibiotics [7], antibacterial activity of indigenous plant extracts alone and in combination with antibiotics [8-10], and studies on antibacterial activity and antioxidant activity of natural and commercially available honey samples [11-13]. In addition, curd lactobacilli strains were characterized for their probiotic property and antibacterial activity [14]. The probiotic nature of *Lactobacillus rhamnosus* GG was reported [15], and found to be effective for diarrheal patients (infants). The current communication justifies the usage of honey against bacterial infections to humans.

Honey Chemistry and Bioactivity

Honey is a sweet and flavorful natural product that is valued for its high nutritional property and its contribution to human health for many decades [16]. It (honey) was the first bee product used by mankind in ancient times [17]. A large number of substances have been reported to be present in honey, and is considered an important part of traditional medicine [12]. Among different compounds, a number of components are known to act as antioxidants (phenolic components, flavonoids, ascorbic acid, etc.) and antibacterials, such as H_2O_2, high sugar contents and lactic acid [16]. The reducing (due to phenolics and sugars) and stabilizing (due to protein contained in honey) capacity of honey make it potential to be used in nano-biotechnology in order to synthesize as well as stabilize metal nanoparticles, including silver nanoparticles (SNPs) [18].

Antioxidative Capacity

Malaysian acacia honey contained high concentration of phenolic compounds (341.67 mg of gallic acid equivalent/kg) and flavonoid content (113.06 mg of catechin equivalent/kg), and had excellent antioxidant activity (43.89 %) in DPPH system [19]. Based upon the DPPH scavenging activity, the tualang honeys (59.89%) [20] and Indian honeys (57.5%) [21], had good antioxidant potential. Alzahrani., *et al.* [22] reported from Saudi Arabia, that the manuka honey had high content of polyphenols, with 899 mg gallic acid/kg, whereas lavender honey had the lower, with 111.42 mg gallic acid/kg. Thus, with different compositions of active compounds in honey samples from different locations, differences in honey properties are to be expected, and hence studies with local untested honey are mandatory [13].

Antibacterial Activity

It has been reported that the functional activity of honey as a nutrient, as a medicine and as a liniment has been approved in present days based upon the traditional practices, and thus apitherapy (an alternative branch of medicine) has been developed in recent years, offering treatments based on honey and other bee products against many diseases including bacterial infections, and at present a number of honeys are sold with standardized levels of antibacterial activity [12]. Manuka honey, as has been reported from Saudi Arabia, was the most effective against *Staphylococcus aureus (S. aureus)* with MICs of 6% and 7%, respectively, whereas wild carrot honey was the most effective against *P. aeruginosa,* with a MIC of 12%; the lavender honey was the least effective against all tested strains [22]. As per the report of Mandal., *et al.* [11], honey sample, harvested from *Apis indica* hive during spring from Purulia, West Bengal (India) had antibacterial activity against *E. coli, Pseudomonas aeruginosa* and *S. enterica* serovar Typhi. The locally available (khadikraft) honey (Chennai: India) showed growth inhibitory activity against *P. aeruginosa* and was found to be better than all of the imported varieties of therapeutic honeys, as determined by agar dilution method [23]. Further, the locally produced honeys possess excellent antibacterial activity compa-

rable to the commercial honeys, as has been documented by Mandal and Mandal [12], and therefore, it is necessary to study other locally produced untested honeys for their antimicrobial activities. The combined antibacterial activity of commercial honeys and antibiotics has also been reported earlier [13].

Antibacterial activity of SNPs synthesized with honey

The use of honey in the synthesis of SNPs in water has been reported recently [24]. A completely green and fast method for the synthesis of SNPs using honey and sunlight has been reported by Obot., *et al.* [25], from Nigeria. The eco-friendly syntheses of SNPs mediated by various bee products (raw honey, royal jelly, honeydew honey and propolis) have been explored, from Mexico [26]. Haiza., *et al.* [27], from Malaysia, demonstrated that the use of honey, a natural, low cost reducing agent can produce SNPs through green methodology, and thus avoiding the presence of hazardous and toxic solvent and waste materials, and noted SNPs of 11.16 nm are synthesized at ambient conditions using $AgNO_3$ and honey at pH 8.53. As has been reported by Heemasagar., *et al.* [28], from Tamilnadu, India, the SNPs synthesized with plant extracts had antibacterial activity when it was mixed with honey against *E. coli, P. aeruginosa, K. pneumonia,* and *S. enterica* serovar Typhi. Moreover, Venu., *et al.* [29] reported that honey mediated synthesis of SNPs has advantages over other biological methods.

Honey as the source of antibacterial probiotics

Lactic acid bacteria including lactobacilli grow in sugar rich low-pH media. Isolation of lactobacilli, with probiotic potentiality and having antibacterial property, from curd samples has been reported earlier [30,31]. Honey has also been reported to be the source of lactic acid bacteria. Aween., *et al.* [32] isolated *Lactobacillus acidophilus* that showed inhibitory activity against *S. enterica* Typhimurium (ZDI; 23 - 30 mm), *E. coli* (ZDI; 7 - 18 mm and *Enterobacter aerogenes* (ZDI; 10 - 18 mm). The lactobacilli strains, such as *Lactobacillus* sp. and *Lactobacillus vermiform* can be the good candidates for potential application as probiotics in honeybees and also as the natural food preservatives, which, in turn, may be useful in the food industry. It has been reported that the presence of probiotic bacteria *Lactobacillus* spp. in honeybee (*Apis cerana indica*) gut play significant role in the general health maintenance of the host [33]. Hasali., *et al.* [34] isolated four probiotic lactobacilli from Meliponine honey that had antibacterial activity against *Staphylococcus epidermidis* (ZDIs: 25 - 32 mm), *P. aeruginosa* (ZDIs: 13 - 16 mm) and *Listeria monocytogenes* (ZDIs: 14 - 24 mm).

Toxicity and safety profiles

Honey, thus, possesses anti-microbial properties that dampen the growth or persistence of microorganisms. Nevertheless, microbial contamination of honey occurs in two ways: primary sources include pollen, the digestive tracts of honey bees, dust, air, soil and nectar, while the secondary sources are those arising from honey manipulation by people that include air, food handlers, cross-contamination and equipment [35,36]. Iurlina and Fritz [37] found the existence of *Bacillus* spp. (*B. cereus, B. pumilus* and *B. laterosporus*) in honey samples in Argentina. Of all food items tested, only honey contained *Clostridium botulinum,* and thus, honey has been identified as an avoidable source of *C. botulinum* spores [38]. According to Kuplulu., *et al*. [39], honey samples from retail market in Ankara, Turkey, had *C. botulinum* contamination among 12.5 % of samples. Al-Waili., *et al.* [40] reported that in Finland, *C. botulinum* spores were detected in 8 of the 114 Finnish and in 12 of the 76 imported honey samples, while 25 % of the honey products in the US contained *C. botulinum*, and the honey consumption was associated with 15 % of the cases of infant botulism reported to the Centers for Disease Control and Prevention. As has been reported by Adenekan., *et al.,* [41], the honey samples, procured from various regions of Ogun State, Nigeria, were found to be contaminated with bacteria, such as *Clostridium* spp., *Pseudomonas* spp., *Bacillus* spp., and *E. coli*, at different levels and counts. Thus, hygienic quality of the honey samples is not maintained in a scientific way, and hence the situation poses a significant risk on public health. However, no scientific reports on the honey mediated bacterial pathogens are available in this part of the globe, and therefore, determining the microbiological risk factors in indigenous honey available in local niches that people consume would decrease the incidence of the potential diseases.

Concluding Remarks

The honeys are excellent sources of antioxidants with attribution to antibacterial activity. The honey can be utilized in pharmaceutical preparations and in the preparation of functional foods fortified with probiotics (found in honey) for the betterment of public health, in region, particularly in developing countries of the globe, where drug resistant bacterial infection is common. Based upon the antibiotic resistance pattern, the probiotic lactobacilli from honey can also be used in combination with antibiotics in combating bacterial multidrug resistances. However, the antibacterial and antioxidative activity of new untested natural honey samples available in local niches are required to be studied extensively for scientific validation, while the probiotic characterization of lactobacilli from honey samples is an urgent and important task. The biosynthesis of SNPs mediated with indigenous honeys that have not been studied earlier is imperative to explore their capacity to synthesize SNPs having potential antibacterial activity against bacteria capable of causing life-threatening infection to humans. However, safety profiling of natural untested honey, to be utilized as medicine and food, must be done before application.

Conflict of Interest

There was no conflict of interest.

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