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# ANTIBACTERIAL ACTIVITY OF DIFFERENT GLOBAL HONEY SAMPLES AGAINST STANDARD ORGANISMS

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Abstracts – Bee honey has been used for centuries as wound dressing its effectiveness was attributed to its bactericidal effect. The purpose of this study was to demonstrate in vitro the antibacterial activity of 32 different Global honey samples (crude raw and commercial honey) against 10 standards organisms. Thirty two honey samples (raw and commercial honey) collected from different countries with different floral origin were tested *in vitro* for antibacterial activity against 10 standard organisms using cup plate diffusion technique. All tested bacterial strains showed marked sensitivity to honey. Honey was proved to be an effective bactericidal agent. Raw and commercial honeys exhibited strong antibacterial activity. Significant antibacterial activity of different floral honeys was proved against wide range of Gram positive and Gram negative bacterial standard organisms. The emergence of antibiotics resistance and interest in alternative medicine, encouraged the usage of honey as wound dressing without side effects.

## INTRODUCTION

Honey is a viscous saturated sugar solution produced by honey bees from plant nectar as well as honeydew. Composition of honey varies according to the plant species on which the bees forages but the main constituents are the same as in all honeys (Wenston, 2000).

Honey has been used as a medicine since ancient times. Honey was widely used in folk medicine throughout the world (Dold *et al.*, 1937) was the first to demonstrate the antibacterial activity of honey, who gave the name "inhibine " to the active substance (s) in honey which inhibit bacterial strains. The concept of "inhibine " was attributed to the hydrogen peroxide present in honey due to the action of glucose oxidase enzyme normally present in honey, secreted from the hypo pharyngeal glands of bees (White and Schepartz, 1962). Honey was used to treat a number of clinical conditions; treatment of wounds, peptic ulcers , gastritis , eye infection and sore throat. Although honey has been widely used in traditional remedies and in hospital especially in the clinical treatment of surgical wounds (Armistong and Otis, 1995). Unprocessed honey inhibited most of the fungi and bacteria causing wound infection and surgical infection except *Pseudomonas aeruginos*a and *clostridium oedematiens*, (Efem *et al.*, 1992). *Pseudomonas aeruginosa* isolated from burn infection exhibited similar sensitivity to honey (Cooper, 2002). Postoperative wounds, treated with conventional treatment in nine infants with large opened wound showed no respond, while those treated with topical application of honey showed marked clinical improvement (Vardi *et al*., 1998). Mankua honeys have additional antibacterial activity due to its hydrogen peroxide content. Wounds infection treated with Manuka honey was managed due to bacterial inhibition (Willix *et al*.,1992). Honey collected from Ethiopia Samrearea showed better antibacterial activity than Temben and Atsbi districts. All collected honeys showed varied bacteriostatic and bactericidal activities, and none of the isolates was resistant to tested honeys (Wasihum and Kasa, 2016). Variations in the type and level of antimicrobial activity in honey are associated with their floral source. However, while some floral sources appear to be associated with particular levels of hydrogen peroxide activity, variation in this activity among honeys from within the same floral species has also been observed (Allen *et al*., 1991). The antibacterial effect of Danish honeys was mostly due to hydrogen peroxide (Matzen *et al*., 2018). All tested honey types obtained from different areas at Greece exhibited antibacterial activity against

*S.aureus* and *P.aeruginosa*. The MIC of the tested honey types against *S. aureus* ranged from 3.125 to 12.5% (v/v), while MIC of Manuka honey was determined to be 6.25% (v/v). The MIC values of the tested honey types against *P. aeruginosa* ranged from 6.25 to 12.5% (v/v) and the MIC of Manuka honey was determined at 12.5% (v/v) (Stagos *et al*., 2018). The most active were darker honeys, with strong yellow colour component, rich in phenolics, with high conductivity and water content. The honey antibacterial properties depended mainly on peroxide mechanism and were vulnerable to excessive heating, but quite stable during storage in cold. A number of honey samples showed potential as effective antimicrobial agents (Kuœ *et al*., 2016).

Honey tested against MRSA and MSSA were found to be sensitive with a zone of inhibition of 36.2±0.2 mm and 40.16±0.152 mm, respectively (Gruvu *et al*., 2017). Misuse of antibiotics is one of the reasons for the increasing rates of resistance, especially in rural areas (Okeke *et al*., 1999). An emergence of drug resistance like vancomycin and daptomycin leading to search for still newer drugs for combating the drug resistance in Staphylococci (Srinivas *et al*., 2015). Honey is well known as a natural drug for almost all kinds of diseases, on folk medicine and natural remedies which are cheap that have been known for their therapeutic effects over the past decades (Bagde *et al*., 2013). Honey has well established function as an effective antibacterial agent with a broad spectrum of activity against Gram-positive and Gram-negative bacteria (Irish *et al*., 2011). The application of honey can promote the healing of infected wounds that do not respond to the conventional therapy, i.e., antibiotics and antiseptics (Ahmed *et al*., 2003). Including wounds infected with methicillin-resistant *S. aureus* (Natarajan *et al*., 2000; Dunford and Molan, 2000). Tualanghoney has variable but broad-spectrum activities against many different kinds of wound and enteric bacteria. There also many reports of honey being very effective as dressing of wounds, burns, skin ulcers and inflammations (Lusby *et al*., 2005). It has been shown that undiluted and diluted honey at 75, 50, 30, and 10% inhibited the growth of *S.aureus* and *S.epidermidis* (Basualdo *et al*., 2007; Bucekova *et al*., 2018, confirmed that the obtainedresults demonstrated that antibacterial activity of honey dew honey was equivalent to medical-grade manuka and kanukahoney and was abolished by catalase. The high osmotic nature and naturally low pH (3.2–4.5) (Kwakman and Zaat, 2012), ability to produce hydrogen peroxide, which plays a key role in the antimicrobial activity of honey (Kacaniova *et al*., 2011) are factors attributed honey to have potent bactericidal and bacteriostatic activity against pathogenic bacteria Although $H_2O_2$ is an important factor in the inhibition of bacterial growth, polyphenolic compounds and their interaction with $H_2O_2$ are the key factors responsible for high antibacterial activity of honey dew honey. The chemical composition of honey is attributed to all healing properties. Honey contains water, carbohydrates, fructose, glucose, maltose, sucrose, proteins, amino-acids, vitamins andminerals. Vitamins contained in honey are: thiamine, riboflavin, niacin, panthotenic acid, pyridoxine (B6) and ascorbic acid (C). Honey contains also minerals like: calcium, copper, iron magnesium, manganese, phosphorus, potassium, sodium and zinc (David, 2007). All tested honey samples exhibited potent antibacterial activity against the 11 multidrug resistant bacterial strains, isolated from urinary tract (Bouacha *et al*., 2018).

## MATERIALS AND METHODS

### Bee Honey Samples

Thirty two different raw bee honey samples were obtained from Global countries, as well as commercially sold honey samples from the local market different brands, of different floral origin. Honey samples were stored in glass container at room temperature samples were labeled according to the source, location, pH, date of collection and floral origin as shown below Fig. 1.

### Standard Organisms

The following 10 standard organisms , Microbiology Reference Laboratories were obtained, the American Type Culture Collection (ATCC), 12301 Drive, Rock Ville, MD 20852, USA.

*Enterobacter aerogenes* : ATCC: 13048, *Enterococcus faecalis*: ATCC: 29212.

*Escherichia coli*: ATCC: 259, *Klebsiella pneumoniae*: ATCC: 70060

*Pseudomonas aeruginosa*: ATCC: 27853, *Serratiamar cesscens*: ATCC: 8100.

*Staphylococcus aureus*: ATCC: 29213,*Staphylococcus epidermidis*: ATCC: 12228.

*Staphylococcus Methicillin Sensitive*: ATCC: 29213 and *Staphylococcus Methicillin* Resistant: ATCC: 23591.

Fig. 1. Bee Honey Samples

| Code | Locality | Source | Date of collection | Floral Origin |
|---|---|---|---|---|
| A | Sudan | East- Singa | November 2017 | Neem |
| B | Sudan | East- Singa | November 2017 | Sidr |
| C | Sudan | East- Singa | November 2017 | Sidr |
| $D_1$ | Sudan | Damazine East | November 2017 | Sidr |
| $D_2$ | Sudan | West | November 2017 | Acacia |
| E | Sudan | West Darfour | November 2017 | Sidr |
| F | Sudan | West Darfour | November 2017 | Mountain |
| G | Sudan | South | November 2017 | Acacia |
| H | Sudan | Darfour | November 2017 | Acacia |
| $I_1$ | Saudi Arabia | College of Agriculture | November 2017 | Sun flower |
| $I_2$ | Saudi Arabia | College of Agriculture | November 2017 | Sun flower |
| J | Kashmir | Commercial | November 2017 | Sun flower |
| K | Yemen | Apiary | November 2017 | Sidr |
| $L_1$ | Kashmir | Apiary | December 2017 | Sidr |
| $L_2$ | India | Apiary | December 2017 | Unknown |
| M | Iran | Commercial | December 2017 | Sidr |
| N | Turkey | Commercial | December 2017 | Orange |
| O | Saudi Arabia | Al-Shifa | December 2017 | Flowers |
| P | Australia | Commercial | December 2017 | Flowers |
| Q | Argentine | Commercial | December 2017 | Orange |
| R | Saudi Arabia | Al-Shifa commercial | December 2017 | Orange |
| S | United stated | Goody | December 2017 | Flowers |
| $T_1$ | Germany | Langenese | December 2017 | Flowers |
| $T_2$ | Germany | Langenese commercial | December 2017 | Flowers |
| U | Saudi Arabia | Al-Shifa commercial | December 2017 | Acacia |
| V | Palestinian | Apiary | December 2017 | Citrus |
| $W_1$ | Egypt | Apiary | December 2017 | Alfa |
| $W_2$ | Egypt | Apiary | December 2017 | Alfa |
| X | Jordan | Apiary | 7 December 2017 | Citrus |
| $Y_1$ | Yemen | Apiary | December 2017 | Sidr |
| $Y_2$ | Yemen | Commercial | December 2017 | Sidr |
| Z | Saudi Arabia | Tabuk | December 2017 | Sun flower |

*In vitro* Antibacterial Activity of Bee Honey

Inoculum preparation

Pure culture and standard inoculums size was maintained for antibacterial susceptibility. Control organisms were suspended in a sterile saline to match 0.5 McFarland standard tube, which is commercially available, provide an optical density of $1.5 \times 10^8$ Colony forming units (CFU/mL). The most common diffusion methods are Kirby Bauer disc (1966) (paper disc method) and cup plate technique. The cup plate technique was used for testing honey antibacterial activity due to its high viscosity.

Well plate technique

The standard seeded agar diffusion technique was used (Garrod *et al.*, 1981). Muller Hinton agar used as the culture medium, was reconstituted, sterilized (using autoclave) at 121 °C for 15 minutes allowed to cool at 48 °C and inoculated with 0.1 mL of standardized 24 broth culture of bacterial suspensions that match the turbidity of the 0.5 McFarland standard tube ($1.5 \times 10^8$) (FU/mL). The 10 standard organisms were used. Standard conditions for antimicrobial susceptibility testing methods have been established based on numerous laboratory investigations. Guidelines and recommendations for their use are published by the National Committee for clinical laboratory standards (NCCLS), NCCLS, 940 W. valley Road, suite 1400, Wayne, pa. 19087. The inoculated medium was distributed aseptically in 20 mL volumes into sterile Petri-dishes (95 mm internal diameter) and allowed to set. The solidified seeded agar plate were then stored at 4 °C till use. Four cups (8mm diameter) were cut using 8 mm sterile crock borer, and the cut-disc of agar are removed. 0.2 mL of each honey sample was

carefully added to diffuse. The inoculated plates were incubated at 37 °C for 18-24 hours. The diameter of the resultant growth inhibition zone was measured in (mm). Each sample of honey was tested against each organism in four replicate. The mean of inhibition zone diameter was tabulated.

## RESULTS

All honey samples tested against standard bacterial strains exhibited strong antibacterial activity. The following Gram positive organisms: *S.aureus, S.aureus Meithicillin Resistant MRSA and Staphylococcus aureus Meithicillin sensitive MSSA,* were found to be the most sensitive organisms to the tested honey samples Table 1. The degree of inhibition of the honey sample against *Staphylococcus aureus* (22-34 mm diameter inhibition zone) was higher tha that against *Enterococcus faecalis* (22-25 mm diameter inhibition zone). *Enterococci faecalis* showed the least activity towards honey tested Table 1. Honey samples obtained from Sudan different floral origin was found to be more sensitive against Standard organisms.

Gram-negative bacteria *Pseudomonas aeruginosa* the most resistant organism to the commonly used antibiotics was found to be sensitive to all honeys tested, although *Klebsiella pneumoniae, Enterobacter aerogenes* and *Serratiamar cesscesn* showed marked sensitivity to different honey samples. Nevertheless in the case of the Gram-negative organisms *Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa* and *Serratiamar cesscens,* the inhibitory effects of the honey samples were very close or identical as indicated by the very slight or no differences in growth inhibition zones Table 1. The

Table 1. Antibacterial activity of 32 global honey samples against 10 standard organisms.

| Bacterial strains / Honey samlesples | *E.faecalis* | *S. aureus* | *S. epidermidis* | *MSSA* | *MRSA* | *E.coli* | *E. aerogenes* | *P. aerouginosa* | *K. pnuimonae* | *S. marecessens* |
|---|---|---|---|---|---|---|---|---|---|---|
| | Inhibition zone in mm | | | | | | | | | |
| A | 25 | 34 | 32 | 33 | 32 | 24 | 24 | 25 | 25 | 25 |
| B | 22 | 34 | 33 | 32 | 31 | 23 | 23 | 24 | 25 | 24 |
| C | 23 | 34 | 31 | 33 | 32 | 22 | 22 | 24 | 24 | 23 |
| $D_1$ | 23 | 34 | 31 | 33 | 32 | 22 | 24 | 24 | 24 | 23 |
| $D_2$ | 20 | 35 | 33 | 32 | 31 | 23 | 24 | 24 | 24 | 24 |
| E | 22 | 33 | 34 | 31 | 31 | 22 | 23 | 22 | 24 | 25 |
| F | 20 | 34 | 32 | 33 | 32 | 23 | 22 | 25 | 24 | 23 |
| G | 24 | 35 | 34 | 33 | 33 | 24 | 23 | 24 | 25 | 24 |
| H | 23 | 33 | 34 | 33 | 32 | 22 | 23 | 25 | 24 | 22 |
| $I_1$ | 22 | 35 | 33 | 31 | 34 | 21 | 23 | 22 | 25 | 23 |
| $J_2$ | 22 | 24 | 33 | 32 | 32 | 33 | 22 | 24 | 25 | 24 |
| K | 22 | 35 | 32 | 33 | 31 | 22 | 22 | 24 | 25 | 23 |
| $L_1$ | 22 | 22 | 33 | 34 | 33 | 32 | 22 | 25 | 25 | 24 |
| $L_2$ | 24 | 23 | 34 | 32 | 32 | 22 | 23 | 25 | 24 | 24 |
| | 25 | 34 | 32 | 32 | 33 | 22 | 22 | 25 | 23 | 22 |
| M | 25 | 33 | 32 | 34 | 33 | 22 | 23 | 24 | 24 | 23 |
| N | 23 | 34 | 33 | 33 | 34 | 23 | 23 | 25 | 22 | 23 |
| O | 24 | 33 | 32 | 33 | 33 | 33 | 24 | 23 | 14 | 22 |
| P | 23 | 33 | 33 | 34 | 33 | 24 | 33 | 24 | 23 | 24 |
| Q | 22 | 32 | 34 | 32 | 34 | 24 | 24 | 25 | 24 | 25 |
| R | 22 | 32 | 22 | 32 | 34 | 23 | 23 | 23 | 23 | 25 |
| S | 23 | 34 | 32 | 32 | 34 | 24 | 24 | 24 | 24 | 23 |
| $T_1$ | 24 | 34 | 34 | 33 | 32 | 24 | 23 | 24 | 22 | 22 |
| $T_2$ | 23 | 32 | 33 | 34 | 34 | 25 | 23 | 24 | 23 | 24 |
| U | 23 | 33 | 35 | 32 | 33 | 23 | 22 | 23 | 24 | 23 |
| V | 24 | 35 | 33 | 33 | 34 | 24 | 23 | 24 | 23 | 23 |
| $W_1$ | 24 | 34 | 34 | 34 | 34 | 23 | 23 | 22 | 24 | 22 |
| $W_2$ | 23 | 35 | 35 | 32 | 33 | 23 | 22 | 23 | 24 | 23 |
| $Y_1$ | 24 | 33 | 33 | 32 | 33 | 23 | 24 | 22 | 24 | 22 |
| $Y_2$ | 23 | 32 | 33 | 32 | 33 | 24 | 23 | 23 | 23 | 23 |
| Z | 24 | 33 | 32 | 33 | 34 | 24 | 23 | 23 | 22 | 24 |
| | 22 | 32 | 34 | 34 | 33 | 33 | 23 | 23 | 24 | 24 |

influence of geographical source of bee honey on its antibacterial activity was more pronouced against *Staphylococcus aureus* than all other organisms tested as reflected by its wide range of inhibition zone.

Out of 32 honey sample tested for antibacterial activity 12 commercial honey samples different brands (super market honey), were used. Commercial samples exhibited antibacterial activity against the standard test organisms Table 1.

## DISCUSSION

The largest portion of dry matter in honey consists of sugars 79%, which are responsible for much of its physical nature, viscosity and hygroscopicity.

The percentage of various components may vary depending on the plant origin, geographical location seasonal collection, processing, storage and age of honey. Floral origin facilitate satisfactory discrimination between different types of honey, accordingly different honey color ranged from white, golden to black honey were obtained. However, different aroma, taste, and pH can be obtained. Accordingly certain honey types are preferred (Crane, 1975).

In the present study a total of thirty two different Global natural unprocessed and commercially sold honey different brands (supermarket) and honey samples different botanical and geographical sources were used for *in vitro* antibacterial activity against 10 standard microorganisms. All honey samples tested against standard bacterial strains exhibited strong antibacterial activity Table 1. The following Gram positive organisms: *Staphylococcus aureus, Staphylococcus aureus, Methicillin Resistant MRSA* and *Staphylococcus aureus Methicillin Sensitive MSSA*, were found to be the most sensitive organisms to the honey tested, MRSA showed high susceptibility to honey. This is support the findings of (Gruvu *et al*., 2017), who demonstrated that honey tested against MRSA and MSSA were found to be sensitive. MRSA has been a frequent cause of nosocomial infection and a major cause of serious infection, as well as had a pattern of resistance, not only to methicillin but also to the aminoglycoside and cephalosporin.

Development of antibiotic resistant strains of coagulase negative *Staphylococci* has complicated the management of infections associated with the use of invasive medical devices. In the present study *Staphylococcus epidermedis*, are very similar to *S.aureus* in their susceptibility to honey as shown by Table 1.

Gram- negative bacteria *Pseudomonas aeruginosa* the most resistant organism to the commonly used antibiotics was found to be sensitive to all honeys tested, although *Klebsiella pneumoniae, Enterobacter aerogens* and *Serratia marcesscencen*, showed marked sensitivity to different honey samples Table 1. In the present study, *P. aeruginosa* demonstrated highest susceptibility towards different honeys tested. Sample $D_2$ obtained from west of Sudan floral origin –sidr was found to be the most active sample against *P. aerouginosa*, as *Pseudomonas* was known as multidrug resistant organism to the most commonly used antibiotics, antiseptic and disinfectant, it considered the important pathogen in chronic wounds and burns infection. Also it was considered the most common etiological agent of nosocomial infection. A number of clinical trials have been published using honey against *Pseudomonal* infection. Different values have reported good result with honeys as antibacterial (Cooper *et al*., 2002), emphasized on honey floral origin by demonstrating high activity of Manuka honey against *P. aerouginosa*.

In the present study an outstanding sound geographical and botanical origin of honey has been emphasized. Honey collected from tropical countries: (Sudan) - floral origin Neem, sidir and acacia demonstrated the highest level of antibacterial activity Table 1. This support the findings of (Wasihum and Kasa, 2016), who demonstrated variations in the type and level of antimicrobial activity in honey collected from different districts in Ethiopia which were found associated with their floral source. However, while some floral sources appear to be associated with particular levels of hydrogen peroxide activity,

Development of antibiotic – resistant strains of coagulase negative *Staphylococci* has complicated the management of infections associated with the use of invasive medical devices. In the current study *Staphylococcus epidermidis* are very similar to *S. aureus* and *S. aureus methicillin sensitive MSSA* in their susceptibility to honey as shown by Table 1.

The present findings proved that 12 Commercial honey samples different brands exhibited antibacterial activity against the standard test organisms, this proved that commercial honey has the same activity as the raw honey.

This in agreement with findings reported by (Nzeako *et al*., 2001), who obtained favorable results using six brands of commercial honey tested against standard organisms: *S. aureu, E. coli* and *P.*

*aerouginosa. Pseudomonas* was found to be the most sensitive organism to honey tested.

Honey has well established function as an effective antibacterial agent with a broad spectrum of activity against Gram-positive and Gram-negative bacteria (Irish *et al*., 2011). The application of honey can promote the healing of infected wounds that do not respond to the conventional therapy, i.e., antibiotics and antiseptics (Ahmed *et al*., 2003).

Honey had been successfully used to treat infections not responding to common antiseptics and antibiotics therapy.

The findings of the present study suggest that honey is useful in the control and treatment of infected wounds, by inhibiting wide range of Gram –positive and Gram -negative bacteria. Thus honey is highly recommended as wound dressing to mange wound.

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