Article title: HONEY AS A THERAPEUTIC AGENT, AN INSIGHT INTO ITS ANTIMICROBIAL PROPERTIES.

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Review Article

HONEY AS A THERAPEUTIC AGENT, AN INSIGHT INTO IT'S ANTIMICROBIAL PROPERTIES.

Abstract

Traditionally, honey has been used as both food and medicine since ancient times worldwide. Due to its nutritious content and sweet flavor, honey has been in great demand worldwide with China being the leading producer. People apply honey on the wound without having any knowledge of **its** antibacterial properties. Honey has proven to contain some antibacterial properties such as hydrogen peroxide, acidity, low moisture content, pH, etc. Bacteria are ubiquitous and their life has a close association with humans in their diet, food processing, etc. Some bacteria eg *Staphylococcus aureus*, consist of the normal flora of humans making them partially harmless but some can be harmful and in turn cause infections. Clinically, antibiotics such as tetracycline, penicillin, amoxicillin lincomycin, etc. have been used in the treatment of bacterial infections but some bacteria eg Methicillin Resistant *Staphylococcus aureus* have shown resistance to some antibiotics. Medical practitioners have opted for the use of honey in treating bacterial infections due to its antibacterial properties. Researches have proven that honey can kill or inhibit almost every bacteria and is very effective in wound treatment as compared to antibiotics. In light of this most medical practitioners prefer the use of honey in treating bacterial infections.

1. Introduction

Honey is a sweet supersaturated liquid produced by bees such as *Apis mellifera*, insects from the order Hymenoptera. It has been used all over the world for food and medicinal purposes. The honey composition is complex and variable, and it contains at least 181 different substances (Alvarez-Suarez et al., 2010). Some of the differences in the composition of honey are due to the differences between regions (floral sources) but seasonal differences can also be considered. According to “Food and Agriculture Organization of the United Nations”, (2019) honey has a composition of 38% fructose, 31% glucose, 17% water, 8% disaccharide, 2% other sugars, and 4% other substances.

According to the World Health Organization (WHO) statistics, up to 80% of the population in some developed countries have used natural products in their primary health care and one example is honey. Natural product used in medical treatment has become a popular approach in modern times. This natural product which includes honey serves as a therapeutic agent in the field of medicine. The antimicrobial properties of honey have been documented in numerous studies (Aurongzeb & Azim, 2011), (Wilczynska, 2010). In recent years, medical authorities reported increased infections and the emergence of strains resistant to certain antibacterial compounds mainly due to the misuse of these substances (Aggad & Guemour, 2014). Honey's potential to assist wound healing has been demonstrated repeatedly (M. D. Mandal & S. Mandal, 2011) and has been among the best alternatives with broad-spectrum against bacterial infections. A possible reason behind its activity relies on its ability to generate hydrogen peroxide by the bee-derived enzyme glucose oxidase (Nolan, Harrison, & Cox, 2019). The antibacterial activity of honey has been known since the 19th century. Recently, the potent activity of honey against antibiotic-resistant bacteria has further increased the interest for the application of honey, but incomplete

knowledge of the antibacterial activity is a major obstacle for clinical applicability (Nwankwo, Ezekoye, & Igbokwe, 2014).

1.1 Honey Production

The consumption of honey all over the world has increased rapidly especially for diabetic patients. The annual world honey production is estimated at 1.4 million tonnes (Mamo, 2018). The highest production of honey is in Asia, accounting for about 40% of the world's production (Mutinelli, 2011). Also, China is the largest producer of honey with about 0.3 million tonnes annual production. The production of honey is shared among the best ten honey producing countries which include China, New Zealand, Argentina, Belgium, etc.

Figure 1: World ten leading producers of honey

1.2. Nutritional composition of honey

Honey has been used for millennia in traditional medicine for its potential antibacterial, anti-inflammatory, and antioxidant properties (Sforcin, Bankova, & Kuropatnicki, 2017). Dr. Fessenden said that “honey’s many benefits are interrelated, much like the cells of a honeycomb, and at the very least, there are no known medical reasons not to enjoy honey as part of a healthy diet and lifestyle for adults and children over the age of twelve months” (Mamo, 2018). Honey is primarily made up of carbohydrates and water, with several traces of minerals and vitamins. Niacin, calcium, copper, riboflavin, iron, magnesium, potassium, and zinc can be found in honey.

Table 1. Nutritional composition of honey

	Per 100 g	Per 20 g serving
Energy	288 kcal/1229 kJ	58 kcal/246 kJ
Fat (g)	0	0
Carbohydrate (g)	76.4	15.3
Fructose (g)	41.8	8.4
Glucose	34.6	6.9
Protein (g)	0.4	0.08
Water (g)	17.5	3.5
Other constituents		

Source: eufic (2020).The health benefits of honey and its nutritional value.

*Based on analysis of 8 samples of assorted types.

1.3. Medicinal and therapeutic uses of honey

1.3.1. Honey had been used as an antimicrobial agent to treat a wide range of infections including Pressure ulcers, Burns Diabetic foot ulcers, and leg ulcers, infected wounds resulting from injury or surgery. However, honey is mostly used when antibiotics and antiseptics are ineffective in the treatment of bacterial ((K. S. Kumar, Bhowmik, Biswajit, & Chandira, 2010).

1.3.2 Properties of honey relevant to its antibacterial activity

Several factors have been shown to contribute to the antibacterial activity of honey, these are high viscosity, high sugar concentration, and low water content, which helps to provide a protective barrier to prevent infection. Also, the mild acidity and hydrogen peroxide content has obvious antimicrobial effects.

1.3.3. Hydrogen peroxide is a potent antimicrobial agent, produced mainly during glucose oxidation catalyzed by the action of the bee enzyme, glucose oxidase, which is introduced into honey during nectar harvesting by bees (Bizerra, 2012). The rate of production of glucose oxidase and its destruction by catalases determines the hydrogen peroxide concentration in the honey. According to Bang et al., the production of hydrogen peroxide in some honey samples can increase continuously over time to a point depending on the dilution used (N. A. Albaridi, 2019). It was originally believed that hydrogen peroxide is the only factor responsible for the antibacterial effect of diluted honey, and this antibacterial activity of honey could be completely removed by the addition of catalase (Najla A Albaridi, 2019).

1.3.4. Acidity of honey. According to the National Honey Board, the acidity of honey ranges from a pH of about 3.4 to about 6.1, with an average of 3.9 (Yadata, 2014). The minimum pH values

for the growth of some common pathogenic species are *Escherichia coli* (4.3), *Salmonella spp* (4.0), *Pseudomonas aeruginosa* (4.4), *Streptococcus pyogenes* (4.5) (M. D. Mandal & S. J. A. P. j. o. t. b. Mandal, 2011). Thus in undiluted honey, acidity is a significant antibacterial factor.

Honey contains several different acids, including about 18 amino acids, many different inorganic acids, as well as aliphatic and aromatic acids. The aromatic acids greatly contribute to the flavor of honey.

1.3.5. Low water activity. Water activity is the partial vapor pressure of water in a substance divided by the standard state partial vapor pressure in water. In the field of food science, the standard state is most often defined as the partial vapor pressure of pure water at the same temperature. Water activity (a_w) of honey ranges from 0.562 and 0.62, which means it provides a very low water availability to support the growth of any microorganisms, lower than the range where the growth of bacteria is completely inhibited (a_w 0.94–0.99) (Najla A Albaridi, 2019).

Since osmosis normally occurs because of the high sugar content. Undiluted honey can stop the growth of bacteria completely due to the high content of sugar. When there is a high sugar concentration of honey, it exerts osmotic pressure on the bacterial cells which causes water to be transported out of the bacterial cells through osmosis. Cells become dehydrated and unable to grow and proliferate in hypertonic sugar solution. This antibacterial action will be reduced when honey is diluted by body fluids at the site of infection. *Staphylococcus aureus* has a high tolerance of low water activity therefore the antibacterial activity of honey must be attributed to other factors (Najla A Albaridi, 2019), (Molan, 1992).

2.0 Bacteria

2.1. Bacteria are microscopic, single-celled organisms that live in enormous numbers in almost every environment in the world. They have no nucleus or membrane-bound organelles making their cell structure simpler than other organisms. Some bacteria have an extra circle of genetic material called a plasmid. The plasmid often contains genes that give the bacterium some advantage over other bacteria. For example, it may contain a gene that makes the bacterium resistant to a certain antibiotic. Bacteria are classified into five groups according to their shapes: spherical (cocci), rod (bacilli), spiral (spirilla), comma (vibrio), or corkscrew (spirochaetes). They can exist as single cells, in pairs, chains, or clusters. Examples of bacteria include *Escherichia coli*, *Staphylococcus aureus*, *Campylobacter*, *Bacillus cereus*, *Pseudomonas aeruginosa*, *shigella*, etc.

2.2 Selected pathogens and its reaction to antibiotics and honey

2.2.1. Antibiotics are medicine – therapeutically used to inhibit or prevent the growth of microorganisms such as bacteria, fungi, or protozoa. Antibiotics are divided into different subgroups such as β -lactams, amphenicols, tetracyclines, macrolides, aminoglycosides, fluoroquinolones, and others (Johnson, Jadon, Mathur, Agarwal, & environment, 2010). β -lactams are used to treat bacterial infections by attacking the cell walls of bacteria. e.g. penicillins, ampicillin, cloxacillin, amoxicillin. Amphenicols function by blocking the enzyme peptidyl transferase on the 50S ribosome subunit of bacteria e.g. chloramphenicol, thiamphenicol, azidamphenicol, and florfenicol. Teteracylines are used for the treatment of bacterial brood

diseases e.g. oxytetracycline, chlortetracycline, tetracycline. Macrolides are potent against a wide variety of gram-positive and negative bacteria used for the treatment of infectious diseases in cattle, sheep, swine, and poultry e.g. tylosin, erythromycin, lincomycin.

Mundo *et al* discovered that the antimicrobial activity of honey was more with *Pseudomonas* and *Acinetobacter* spp, both with resistance to some antibiotics like gentamicin, Ceftriaxone, Amikacin, and Tobramycin than other bacteria tested (Olaitan, Adeleke, & Iyabo, 2007). Undiluted honey has been found to stop the growth of *Candida* spp while *Clostridium oedemantiens*, *Streptococcus pyogenes* remained resistant (Mot, Nichita, Tîrziu, Mq , & ere_, 2016). Some species of *Aspergillus* did not produce aflatoxin in various dilutions of honey while honey has been found to stop the growth of *Salmonella*, *Escherichia coli*, *Aspergillus niger*, and *Penicillium chrysogenum* (Moğ et al., 2016).

2.2.1. *Staphylococcus aureus* is a Gram-positive coccus with the round cells, approximately 1mm in diameter, form grape-like (Greek staphyle) clusters indicative of the ability to divide in more than one plane. *Staphylococcus aureus* can be commensal bacteria and human pathogen (Shu et al., 2013). About 30% of the human population is colonized by *Staphylococcus aureus* (Tong, Davis, Eichenberger, Holland, & Fowler, 2015). They are capable of both aerobic and anaerobic respiration and most strains ferment mannitol anaerobically. *S. aureus* can cause a range of illnesses, from minor skin infections, such as pimples, impetigo, boils, cellulitis, folliculitis, carbuncles, scalded skin syndrome, and abscesses, to life-threatening diseases such as pneumonia, meningitis, osteomyelitis, endocarditis, toxic shock syndrome, bacteremia, and sepsis (A. Kumar, Bisht, Joshi, Singh, & Talwar, 2010). Antibiotics used to treat *Staphylococcus* infections include cefazolin, cefuroxime, cephalexin, nafcillin (Nallpen), oxacillin (Bactocill), dicloxacillin,

vancomycin, clindamycin (cleocin), rifampin, and telavancin (vibativ). However, the notorious among this group is methicillin-resistant *Staphylococcus* (MRS) which can resist a wide variety of antibiotics.

2.2.2 *Escherichia coli* is a Gram-negative, facultative anaerobic, rod-shaped, coliform bacterium of the genus *Escherichia* that is commonly found in the lower intestine of warm-blooded organisms (endotherms) (Zeljko, Drazgalski, & Mayorga, 2018). Most *E. coli* strains are harmless, but some serotypes (EPEC, ETEC, etc.) can cause serious food poisoning in their hosts and are occasionally responsible for food contamination incidents that prompt product recalls (Tijjani, Arzai, & Sadiq, 2012). Antibiotics used to treat *E. coli* infections include trimethoprim/sulfamethoxazole, nitrofurantoin, or a fluoroquinolone (McKinnell, Stollenwerk, Jung, & Miller, 2011).

2.2.3 *Pseudomonas aeruginosa* is a Gram-negative, monoflagellated, aerobic rod bacterium of the *Pseudomonadaceae* family (a member of the Gammaproteobacteria) (Conrin, 2020). *P. aeruginosa* contains 12 other members in its family. *P. aeruginosa* causes infection in the urinary tract, respiratory system, dermis, soft tissue, bacteremia, bone and joint, gastro intestine, and blood, particularly in patients with severe burns, tuberculosis, cancer, and AIDS (Wu, Jin, Bai, & Jin, 2015). *Pseudomonas* infection can be treated with a combination of an antipseudomonal beta-lactam (eg, penicillin or cephalosporin) and an aminoglycoside. Carbapenems (eg, imipenem, meropenem) with antipseudomonal quinolones may be used in conjunction with an aminoglycoside.

Table 2: List of some bacterial species sensitive to honey or honey products and diseases they cause.

Bacteria species	Disease caused
<i>Escherichia coli</i>	diarrhea, septicemia, urinary infections, wound infections
<i>Pseudomonas aeruginosa</i>	urinary infections in wound infections
<i>Salmonella typhi</i>	Typhoid
<i>Staphylococcus aureus</i>	Abscesses, boils, carbuncles, impetigo, wound infection
<i>streptococcus pyogenes</i>	Ear infections, impetigo, puerperal fever, rheumatic fever, scarlet fever, sore throat, wound infections
<i>E. coli, Salmonella, Shigella, Vibrio, Helicobacter Pylori</i>	Peptic ulcer
<i>Proteus spp.</i>	Septicemia, urinary infections
<i>Mycobacterium tuberculosis</i>	Tuberculosis
<i>Klebsiella pneumoniae</i>	Pneumonia
<i>Shigella spp</i>	Dysentery

According to (Kwakman et al., 2011), medical-grade honey enriched with antimicrobial peptides such as synthetic Bactericidal Peptide 2 (BP2) has rapid bactericidal activity against *Pseudomonas aeruginosa*, *Staphylococcus epidermidis*, *Enterococcus faecium*, *Burkholderia cepacia*, and methicillin-resistant *S. aureus* (MRSA)

3.0 Methodology

A critical organized review of microbiological literature on therapeutic agents, an insight into antimicrobial properties of honey on *Staphylococcus aureus*, *Escherichia coli*, and *Pseudomonas aeruginosa* was conducted. It focused specifically on major and minor issues on the topic including information having a bearing on the topic. Articles in high impact journals were downloaded and used for the study. We search for studies conducted using the following phrases: antimicrobial activity of honey, therapeutic agents, staphylococcus aureus, Escherichia coli, pseudomonas aeruginosa, the impact of the therapeutic agent, and infections caused by the bacteria (*Staphylococcus aureus*, *Escherichia coli*, and *Pseudomonas aeruginosa*).

The reviewed articles had either experimental or non-experimental designs in the study. Extensive searches were conducted using Microsoft Academic, Science Direct, Google Scholar, PubMed, and Base-search.net were used to download the articles. Other sources of information included the World Health Organization (WHO), Food and Agricultural Organization (FAO), United Nations (UN), and Institutional Repositories. The key search terms that were used in the review were antimicrobial properties of honey, microbial contamination, bacterial infections, and the impact of therapeutic agents. Three different types of searches were done in an orderly manner using inclusion and exclusion criteria and that of the search terms. Concerning the first search, articles identified in the specified databases and their complete copies obtained and deemed fit for inclusion criteria were considered for further review. Articles that did not meet the inclusion criteria stated above were excluded. Search two was done six days after the first search. This was to capture recently published articles. Articles obtained through cited articles were looked at following the criteria used for search one; 21 articles were found but not all were included in the

study. Search three was done some months later with an increase in the number of search engines and other international bodies with vivid information. Search three resulted in a total of about 1,286 articles, book chapters, and others. Some documents were downloaded two to four times due to the difference in search engines and titles used to upload documents. A total of 389 documents were obtained after carefully removing duplicated documents. Reading titles of the documents, an additional elimination was done. Also, a further reading of abstracts and whole documents and subjecting them to exclusion and inclusion criteria finally resulted in 37 documents. These included review papers, research articles, case studies, and case reports.

4.0 Results

Table 3: Antimicrobial activity of different honey concentrations on pathogenic bacteria

Author(s)	Year	Honey samples	Bacterial strains	Zone of inhibition (mm)				
				Concentration of honey (% v/v)				
				Below 25	26 – 40	41 – 60	80	100
Al- Naama	2009		<i>S. aureus</i>	0	-	0	11	20
			<i>E. coli</i>	0	-	8	12	22
			<i>P. spp.</i>	0	-	8	10	23
Mandal et al	2011	Ulmo honey	<i>MRSA (c)</i>	22	-	30	-	-
			<i>MRSA (s)</i>	26	-	34	-	-
			<i>P. aeruginosa</i>	6	-	14	-	-
			<i>E. coli</i>	6	-	14	-	-
		Manuka honey	<i>MRSA (c)</i>	16	-	24	-	-
			<i>MRSA (s)</i>	9	-	23	-	-
			<i>P. aeruginosa</i>	7	-	16	-	-
			<i>E. coli</i>	6	-	15	-	-
T.Murugan et al	2012		<i>S. aureus</i>	NZ	14	-	-	16
			<i>E. coli</i>	NZ	16	-	-	20
			<i>K.pneumonia</i>	NZ	14	-	-	19
			<i>P.aeruginosa</i>	NZ	13	-	-	16
			<i>P.vulgaris</i>	NZ	18	-	-	20

Hamza, A. et al.	2015		<i>Proteus</i>	20.00	-	26.63	32.38	38.25
			<i>Bacillus</i>	13.94	-	16.75	19.00	25.33
			<i>Pseudomonas</i>	18.00	-	26.13	28.63	33.50
			<i>Staphylococcus</i>	22.69	-	29.13	35.13	37.94
Teke, G.N. & Ngienyike, B.E.	2016	Oku honey	<i>S. aureus</i>	0.0 ± 0.0	8.33 ±0.58	11.3±0.58	12.67±0.58	16.0±1.0
			<i>P. aeruginosa</i>	0.0 ± 0.0	5.67 ±0.58	8.67±2.1	12.68 ± 2.1	15.68±3.7
			<i>K. pneumonia</i>	0.0 ± 0.0	7.33 ±2.3	10.6±2.1	10.6 ± 2.1	16.67±2.1
			<i>E. coli</i>	0.0 ± 0.0	17.3 ±0.58	24.7±0.58	24.67±0.58	26.33±0.58
		Mbengwi honey	<i>S. aureus</i>	0.0 ± 0.0	18.0 ± 1.0	22.33±1.25	25.67±1.52	27.0±1.0
			<i>P. aeruginosa</i>	0.0 ± 0.0	9.0 ± 1.7	13.17±1.8	16.67±0.58	20.33±0.58
			<i>K. pneumonia</i>	0.0 ± 0.0	7.33 ± 3.2	9.33±4.0	11.33 ± 4.0	13.0±4.4
			<i>E. coli</i>	0.0 ± 0.0	13.0 ±2.64	21.68±1.2	23.67 ± 1.2	26.0±2.0
		Ngaound éré honey	<i>S. aureus</i>	0.0 ± 0.0	21.33 ±1.2	24.0±1.0	25.67±0.58	27.67±0.58
			<i>P. aeruginosa</i>	0.0 ± 0.0	10.0 ± 3.5	16.33±2.1	21.0 ± 1.2	24.0±1.0
			<i>K. pneumonia</i>	0.0 ± 0.0	8.0 ± 1.0	11.67±1.2	11.67 ± 1.2	14.0±2.6
			<i>E. coli</i>	0.0 ± 0.0	18.33 ±1.2	24.33±0.58	24.33±0.58	26.33±0.58
Gambo et al.	2018	-	<i>S. aureus</i>	11.23±0.20	-	12.05±0.20	18.03±0.26	20.70±0.25
			<i>P. aeruginosa</i>	12.2 ± 0.23	-	14.2 ± 0.23	15.95±0.26	18.53±0.20

NZ: No zone, - Not included

Table 4: Antimicrobial activity of raw honey samples on pathogenic bacteria

Author(s)	Year	Samples	Bacterial strain	Zone of inhibition (mm)
Rajeswari et al.	2010		<i>Staphylococcus aureus</i>	20.67 ± 0.577
			<i>Pseudomonas aeruginosa</i>	15.67 ± 0.577
			<i>Escherichia coli</i>	13.33 ± 0.577
Kumarasmy, D. & Mahendran, S.	2015	S1 – S6	<i>Staphylococcus aureus</i>	9.36 ± 0.41
			<i>Streptococcus pyogenes</i>	9.05 ± 0.41
			<i>Escherichia coli</i>	8.25 ± 0.32
			<i>Pseudomonas aeruginosa</i>	8.43 ± 0.30
		W1 – W6	<i>Proteus mirabilis</i>	8.65 ± 0.27
			<i>Staphylococcus aureus</i>	10.18 ± 0.34
			<i>Streptococcus pyogenes</i>	10.53 ± 0.4
			<i>Escherichia coli</i>	9.75 ± 0.37
			<i>Pseudomonas aeruginosa</i>	9.65 ± 0.35
			<i>Proteus mirabilis</i>	9.6 ± 0.29

Table 5. Antibacterial activity of honey concentration on selected pathogenic bacteria

Honey Conc. (%)	Zone of inhibition (mm)		
	<i>S. aureus</i>	<i>E. coli</i>	<i>P. aeruginosa</i>
0 - 20	0.00	0.00	0.00
21 - 40	12.50	4.40	9.64
41 - 60	18.50	9.60	16.50
61 – 80	18.63	6.01	15.17
81 - 100	22.55	11.60	22.01

Figure 2. Inhibitory zone of honey on selected pathogenic bacteria

5. Antioxidant activity of honey

Antioxidants bind to the Transcription Factors and prevent harmful effects like cancer, cardiovascular diseases, inflammatory disorders, neurological degeneration, wound healing, infectious diseases, and aging (Milner, Romagnolo, Connor, & Lee, 2010). It is also proven that the therapeutic potential of honey is always associated with antioxidant capacity against reactive oxygen species (Chua, Rahaman, Adnan, & Eddie Tan, 2013). Oxidative stress results from a lack of balancing chemical reaction between the production of free radicals and the natural protective

effect of our body resulting in cellular damage and disruption of genetic structure (Kunwar & Priyadarsini, 2011).

6. Antimicrobial activity of honey

Honey has been reported to have antibacterial activity against various bacterial species including *Bacillus anthracis*, *Corynebacterium diphtheriae*, *Haemophilus influenzae*, *Klebsiella pneumoniae*, *Listeria monocytogenes*, *Mycobacterium tuberculosis*, *Pasteurella multocida*, *Yersinia enterocolitica*, *Proteus* species, *Pseudomonas aeruginosa*, *Acinetobacter* spp., *Salmonella diarrhea*, *Salmonella typhi*, *Serratia marcescens*, *Shigella dysentery*, *Staphylococcus aureus*, *Streptococcus faecalis*, *Streptococcus mutans*, *Strep. Pneumoniae*, *Streptococcus pyogenes*, and *Vibrio cholera*. An antifungal action has been reported for honey against *Aspergillus*, *Penicillium*, as well as all the common dermatophytes and *Candida albicans*. Honey has shown antiviral effects also (Ahmed et al., 2018). According to (Israili, 2014), the topical application of honey on recurrent attacks of herpes lesions concluded that topical honey application was safe and effective in the management of the signs and symptoms of recurrent lesions from labial and genital herpes compared to acyclovir cream. Besides, honey has also been reported to have inhibitory effects on rubella virus activity (Gul, Farooq, Khan, Rehan, & Anees, 2015).

7. Wound healing of honey

A wound is a type of injury that happens relatively quickly in which the skin is torn or punctured (open wound). It destroys tissue, disruption of blood vessels, and extravasations of blood constituents and hypoxia. Various people have used honey in the local application to facilitate wound healing. Ali-Wali et al. state that honey's physical effect, such as acidity and osmotic effect, and its chemical effect, such as the antimicrobial activity of hydrogen peroxide at the wound site,

added to the nutritional, antioxidant and immune-activating property when taken orally, are the prime sources of wound healing property (Abeshu & Geleta, 2016).

Honey is one of the naturally traditional remedies that has been used in the treatment of a wound. It helps promotes faster wound healing through its regenerative tissue growth and epithelization effects, with little or no formation of scars. According to Efem et al., unprocessed honey inhibited most of the fungi (*Aspergillus fumigates*, *Aspergillus flavus*, *Penicillium citrinum*, *Trichopyton rubrum*, *Trichophyton tonsurans*, *Candida albicans*) and bacteria (*Streptococcus pyogenes*, *Enterococcus faecalis*, *Staphylococcus aureus*, *Escherichia coli*, *Klebsiella pneumonia*, *Proteus mirabilis*, *Proteus spp*, *Bacteroides fragilis*, *Clostridium welchii*, *Clostridium tetani*) except *Pseudomonas aeruginosa* and *Clostridium oedematiens*) causing wound infection and surgical infection (Abeshu & Geleta, 2016). Derma Sciences Medihoney® Dressing with Active Manuka honey received FDA approval for providing a moist environment conducive to wound healing (Abeshu & Geleta, 2016). According to the FDA, Medihoney® dressings are indicated for the management of light to moderately exuding wounds like diabetic foot ulcers, venous or arterial leg ulcers, partial or full-thickness pressure ulcers/sores, first and second partial-thickness burns, and traumatic and surgical wounds (Abeshu & Geleta, 2016).

Subrahmanyam studied a total of 104 cases of superficial burn injury to assess the efficiency of honey as a dressing in comparison with a silver sulfadiazine gauze dressing. In the 52 patients treated with honey, 91 percent of wounds were rendered sterile within 7 days, and 87% healed within 15 days. The study has shown that the healing properties of honey helped burn wounds to heal earlier and with fewer complications than conventional treatment (Subrahmanyam, 1991).

8. Conclusion

Honey is a sweet organic natural substance produced by honeybees. It has been used as food, medicine, etc. in ancient and modern times. Interest has been developed in the antibacterial activity of honey is due to increasing clinical problems of antibiotic-resistant for example, with methicillin-resistant *Staphylococcus aureus* or *Pseudomonas spp.* The antimicrobial activity of honey can be attributed to its pH, acidity, low water activity, hydrogen peroxide, etc. Due to the adverse effects of synthetic drugs, researchers have now pay attention to organic natural drugs such as plant-based drugs. The complete elucidation of the mechanisms of activity and synthesis of all components of honey could lead to the generation of optimally antimicrobial synthetic or semisynthetic honey. Undiluted honey shows a wide broad spectrum of bacterial inhibition than certain conventional antibiotics used to treat bacterial infections.

9. Recommendation

- We recommend that further studies should be carried out on the antibacterial activity of honey on other bacterial strains.
- We also recommend that further research should be carried out on the use of honey for clinical wound treatment removing the need for antibiotics.
- We recommend that the spectrometry assay technique should be used more to investigate the antimicrobial activity of honey.
- We recommend that studies should be conducted on how the quality of honey can be ascertained

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