



**A REVIEW OF ALL-INCLUSIVE THERAPEUTIC POTENCY OF PURE HONEY: A
NEW HOPE FOR ANTIBIOTICS ALTERNATIVE**

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ABSTRACT

Honey is a sweet substance created from the nectar of blossom flowers, which is gathered by honey bees and blended in with an emitted compound. Honey was an aged long traditional medicine that was captured in many religious history of the world. It has both pharmaceutical and nutritional value. The therapeutic potency of honey is enormous. It had recorded significant success within the treatment of the many infectious diseases causing agents like fungi, bacterial, parasitic worms and viruses and non-infectious diseases like diabetes, anemia and cancer. No history of antimicrobial resistance to honey as applicable to synthetic antibiotics. The advantage of using honey as a medicinal agent is that it takes care of the many diseases conditions which make it as an independent medicine. Therefore, with these plethora therapeutic evidences, more clinical research should be carried out on honey so that it can be used and accepted clinically as antibiotics alternative since the world is witnessing dynamic treatment failure.

KEYWORDS: Honey, antioxidant, anti-anemic, diabetic and anti –biofilm.

INTRODUCTION

Honey is a perplexing sweet food stuff with settled antimicrobial and cancer prevention agent properties which was accepted to be the nature's miracle and incredible therapeutic benefit for quite while.^[1-2] It's created from the nectar of flowers, which is gathered by honey bees and blended in with an emitted compound.^[3] It has assortment of uses, however, the foremost significant is the application within the treatment of surface injuries, burns and inflammation.^[2]

Natural medicinal plants are utilized for hundreds of years within the treatment of varied sicknesses. Albeit, many are succeeded by traditional pharmaceutical methodologies.^[1] Nonetheless, due to the continued ascent in antibiotics resistance, there has been an expanded requirement for elective treatment techniques^[4], additionally to the very fact that honey possesses powerful bacterial clearance, but even have numerous nourishment benefits, empowers angiogenesis, and quickens wound recuperating.^[3]

Numerous organic compounds are distinguished in honeybee products by a broad arrangement of scientific research, while various discoveries are committed to sum up therapeutic properties and uses as nutraceutical, pharmaceutical and cosmetic ingredients.^[5]

Furthermore, many investigative research about the medical use of honey had proved that it had no record of antibiotics resistance as applicable to other conventional antimicrobials.^[1] Honey isn't only an antimicrobial agent but also function as food supplement to avert other non-infectious diseases of human due to its phytochemical component as reported by Hadagali and Chua.^[6]

Composition of honey

Honey was made of water, glucose, fructose, proteins, vitamins and minerals.^[7] It might be also described as the ordinary sweet substance created by honeybees from the nectar of blossoms or from the exudation of living parts of plants or excretions of plants sucking insects on the living parts of plants, which bees gathered, converted and mixed with specific substances of their own, kept and confined in the honeycomb to mature as reported by Elijah et al.^[8]

Olakunle et al.^[9] reported that Honey predominantly comprises sugar and water. The sugar content is about 96 - 98% of honey dry matter, mostly, are simple sugars, fructose (38.2%) and glucose (31.3%), which represents 85 - 95% of total sugars. These are simple sugars, 6-carbon sugars. Other sugars include disaccharide like maltose, sucrose and few oligosaccharides also are present.

Water is the second most vital component of honey^[9]. Its content is critical, since it affects the storage of honey. The ultimate water present in honey depends on plethora of environmental factors at the time of production like climate and moisture within the hives, but also on nectar surroundings and treatment of honey during removal and storage.^[10]

Gluconic acid is one among the organic acids in honey that constitute 0.57%, which may be a product of enzymatic utilization of glucose. The organic acids are liable for the acidity of honey and contribute largely to its characteristic taste.^[10] The main enzymes found in honey are invertase, amylase and glucose oxidase.^[10] Singh *et al.*^[11] reported that honey also contains numerous other sorts of sugars, acids, vitamins, proteins and minerals. The pure honey contains alkaloids, antraquinone glycosides, cardiac glycosides, flavonoids and reducing Compounds.^[12]

Types of honey

Olatunji *et al.*^[13] reported that, there are two main sorts of honey; apiary and forest honey. Apiary honey is produced by the honeybees in apiaries, *Apis cerana indica* and *Apis mellifera*, which are gathered by the fashionable extraction method whereas, forest honey is produced in forests by rock bee, *Apis dorsata*, or wild nests of *A. cerana indica*, and are gathered by the crude method of compressing the comb.^[14]

Honey can equally be distinguished on the idea of nectar source visited by the (fauna) bee.^[15] These comprise floral (sweet deposit from flower) and non-floral (sweet deposit from plant) honeys.^[16]

Honey can either be unifloral or multifloral (more than one blossom sources), contingent upon whether the honey gathered is from the nectar of a comparable bloom or from nectar of different blossoms.^[16] Non-flora honey (honey dew) is shaped by honey bugs that concentrate sugars from living tissues of plants or organic products, and additional discharges of bugs (aphids) that tap the veins of upper plants.^[14]

Source of honey

The honey bee (*Apis mellifera*) is of great importance for humans as a pollinator of both commercial and domestic crops and provider of honey, a high-value nutritional commodity.^[17]

The most considered honey are those delivered by *Apis mellifera*, which are spread wherever on the planet. In Europe there are distinctive local honey bee, *Apis mellifera* subspecies, however there are just a couple of studies looking at the natural properties of different species as there are commonly no distinctions inside the honey delivered by these honey bees.^[17] During an examination of honey created by the neighborhood dark honey bees, *Apis mellifera sp.* had around multiple times higher substance of polyphenolics and preferable

antibacterial activities over an equal honey species delivered by other *Apis mellifera* honey bees.^[18]

History and ancient medication of honey

Honey had been reported as the oldest sweeteners ever exist within the world since existence of man while the genuine date of the origin stays obscure.^[19] Honey use and production features a long and varied history.^[19] The use of honey for healing intentions is entrenched in antiquated remedies likewise as present day wound management.

The most primitive records of the use of honey in medication could be traced back to the Egyptian Papyri as well as Sumerian clay tablets dated from 1900 to 1250 BC where honey was in almost one third of the prescriptions.^[20] The Egyptian used honey for different reason like remedy of sickness of the skin, application on wound and renovation of the dead body. Hippocrates (460-357 BC) found the usefulness of honey in remedy of sores and ulcers of the lips and healed buncles and strolling sores. Aristotle (384-322 BC) noted light honey being an honest salve for sore eyes.^[21]

Saranraj and Sivasakthi^[20] reported that when there is a strong weakness as a result of low glucose levels inside the body, traditional Greeks were believed to have used honey for rapid energy recovery: athletes mixed honey with water in a major athletic drinking event. For the healing of eye and ear infections, the Babylonian applied honey as an ointment for topical application.^[20]

Honey is used by various African tribes to treat snakebites, fever and as a laxative. In addition, honey has been used by the Masai warriors to realize more power and improve their strength, perhaps due to the high sugar content of honey, as stated by Saranraj and Sivasakthi.^[20]

Eating honey prolongs life, according to Aristotle, while Hippocrates says that I eat honey and use it in the treatment of many diseases because honey provides good food and health.^[19] Pedanius Dioscorides, an army Roman surgeon, wrote in his book that honey could be used as a treatment for stomach disease, pus wound, hemorrhoids, and cough prevention treatment, as reported by Nayik *et al.*^[19]

Religious perception of honey

Haile *et al.*^[22] recorded that several religious books contain the record of the use of honey in one way or in the order as mentioned below: the faith of Islam advocated the use of honey as food and medicine, and Surah al-Nahl, which means the Honeybee chapter, was dedicated to honey within the Holy Qur'an. The Prophet Muhammad strongly promoted the use of honey for medicinal and therapeutic purposes throughout the book of hadith.

There are references in Christianity to the Bible's value of bees and honey, including the Books of Exodus,

Psalm, Judges, Mathew, and Proverbs. King Solomon was quoted in accordance with this Christian holy book, the Bible, as follows: eat honey, my baby, because it's sweet.^[22]

Many cultural values support the use of honey and are embraced by all generations, customs and civilizations, both ancient and modern with no barrier^[19] as a powerful therapeutic agent.^[1]

Antioxidant property of honey

Antioxidant is, by definition, any material that postpones, prevents or eliminates oxidative damage to a target molecule.^[23] Oxidation reactions generate free radicals that start multiple reactions in chains that ultimately trigger cell damage or death.^[24]

With the growing demand for food requirements for antioxidants, honey is recognized as an antioxidant basis.^[1] By oxidizing themselves, antioxidants eliminate free-radical intermediates and prevent other oxidation reactions, thereby preventing dangerous chain reactions.^[24]

Lack of antioxidants in food induces oxidative stress, which has contributed to an unbalanced reaction between the free radical assembly and thus our body's normal protective effect resulting in cell damage and genetic composition disruption.^[22] The term oxidative stress may also be defined as lack of balance between the assembly of species of free radicals.^[25]

It is believed that oxidation defense can avoid certain chronic diseases.^[22] The antioxidant properties of honey, as stated by Bogdanov *et al.*^[25], include glucose oxidase, catalase, vitamin C, flavonoids, phenolic acids, carotenoid derivatives, organic acids, maillard reaction products, amino acids and proteins.

In a similar study, Arawwawala and Hewageegana^[26] reported that Honey showed high antioxidant potential and that its activity is highly correlated with the total phenolic material. Nolan *et al.*^[1] also stated in a related study that the existence of polyphenolics in honey is responsible for destroying free radicals and inhibiting oxidation, and is suggested to be involved in peroxide generation.

Anti-anaemic property of honey

The world's most common nutritional deficiency condition is anaemia. It is a disease that arises when the red blood cells in the body's tissues do not hold enough oxygen.^[27] It is characterized by a haemoglobin rate decrease of 13 g / dl in males or 12 g / dl in females.^[28] Within the iron-rich oxygen-carrying pigment form, hemoglobin can be a protein.^[29]

Al-Waili^[21] reported that different positive effects on haematological parameters and blood concentrations of metabolic catalysts are linked to the regular intake of

natural honey. The use of natural honey in apitherapy has been shown to improve anaemic symptoms, thus providing patients with support. Compared to controls, one dietary enhancement study by Ajibola *et al.*^[30], verified an improved haematological benefit in adult rats fed with Nigerian Jungle honey.

In a related study from another laboratory, improved haematological profiles and increased immunity in rats were also reported to be nurtured as a dietary supplement with 10% New Zealand forest honey.^[31]

Dewi *et al.*^[29] observed that honey extend levels of hemoglobin within the blood from 75% to 80% within the first week of the primary week after healing therapy with honey in their research, Titled: 'The Honey Consumption to Haemoglobin Contests when Menstrual at Teenage of Principles in Situbondo'. Bogdanov *et al.*^[25] reported that there was an improvement in haemoglobin content, better complexion, when babies were fed with honey instead of sucrose.

Anti-inflammatory property of honey

Anti-inflammation is the positive reaction to a procedure that decreases inflammation, according to Hadagali and Chua^[6], and inflammation may be a disease resulting from tissue response to trauma or pathogenic agents. In order to get rid of the injuring stimuli, such as bacteria, damaged cells or irritants, it has a protective method of action by an organism / tissue.^[31]

Melipona marginata is a Brazilian species of endangered stingless bee. With exceptional physicochemical properties and a special taste, it produces honey. In one experiment, when used on the skin, the honey showed anti-inflammatory effects.^[33] There have also been reports of the therapeutic efficacy of Manuka honey by exposing human monocytes to Manuka honey, the assembly of diverse inflammatory cytokines was assessed.^[34]

In livestock, the administration of Tualang honey to a chemically induced injury on rabbit cornea yielded effects similar to those of normal treatment^[35], demonstrating its potential to treatment of eye disease.

Boosting of immune system

Honey has been reported to stimulate the proliferation and activation of neutrophils in the cell culture of B-lymphocytes and T-lymphocytes.^[34] In a related research, Manyi-Loh *et al.*^[16] documented the stimulation of monocytes in cell cultures to release TNF-alpha, IL-1 and IL-6, the cell cytokines, messengers that activate the different facets of the infection in immune reaction. In addition, honey provides a glucose supply, which is necessary for the respiratory burst of peroxide-producing macrophages, the dominant component of their bacteria-destroying activity.^[36]

Furthermore, it provides glucose metabolism substrates, the most power-generating pathway within macrophages, and thus enables them to function in damaged tissue and exudates where the supply of oxygen is generally poor. Another element that aids in the bacteria-destroying behavior of macrophages is that of acids in honey, as an acid pH inside the phagocytic vacuole is involved in the killing of ingested bacteria.^[36]

Prebiotics potency of honey

Prebiotics are classified as selectively fermented components that activate specific changes in the composition and/or behavior of microorganisms in the food canal (intestine), beneficial to the health and well-being of hosts.^[37]

The primary objective of prebiotics is to promote the spread and function of beneficial bacteria in the intestine, which gives the host a health advantage.^[38]

Honey intake increases the population of bacterial microflora that are important for the health of the gastrointestinal tract, according to the Abeshu and Geleta^[1] review report. The honey fraction of oligosaccharides induces an increase in *bifidobacteria* and *lactobacilli* and exerts a synergistic mode of action of the prebiotic effect and increases the populations of beneficial or non-pathogenic bacteria.^[39,40]

Medicinal use of honey in diabetic management

Diabetes, is a group of metabolic disorders and diseases characterized by high blood sugar levels over prolonged period. This is as a result of either pancreas not making enough insulin, or cells of the body improperly responding to the insulin produced as reported by Awuchi *et al.*^[41] Type 1, Type 2, and the Gestational diabetes are the three major types of diabetes.^[41]

Type 1 diabetes results from the failure of the pancreas to produce sufficient insulin due to an autoimmune response caused by the loss of beta cells. Type 2 diabetes starts with insulin resistance, a condition in which insulin does not respond properly to cells. The third most common type of gestational diabetes is gestational diabetes, which occurs when a pregnant woman with no prior history of diabetes mellitus (MD) experiences elevated blood sugar levels. Diabetes control focuses on maintaining very close to normal blood sugar levels, without triggering a low blood sugar level.^[41]

Researchers have shown that in normal volunteers and type I diabetics, honey continuously produces a lower glycemic effect relative to glucose and sucrose, and that honey or sucrose may not have additional acute hyperglycemic effects on the isoglucidic amount of bread in type II diabetics at breakfast. In type I diabetic patients, honey has lower glycemic and incremental indices as opposed to glucose and sucrose.^[41]

One study showed that a substantial reduction in blood sugar levels and other related parameters was induced by various doses of honey (as low as 5 ml / kg)^[43], perhaps honey is an honest alternative to sucrose as a natural sweetener for diabetic patients, even at low doses (5 ml / kg).

In all, honey and its components were found to possess several health benefits, including weight improvement.^[26]

Honey as an antibacterial agent

The antimicrobial activity of honey against a wide range of microorganisms, including multi-antibiotic resistant strains, has been shown by numerous reports and clinical studies.^[44,45] Both gram positive and gram negative bacteria are prevented by honey. Mohapatra *et al.*^[46] reported that alcohol extracts of honey had an inhibitory effect on bacterial species such as aerobes and anaerobes, Gram positive and Gram negative.

Honey has strong antimicrobial effects against pathogenic and non-pathogenic microorganisms.^[44] The action of honey can be bacteriostatic or bactericidal depending on the concentration that is used.^[16] In-vitro studies are particularly sensitive to honey solution for *Campylobacter spp* isolates.^[47]

Honey extracts of methanol, ethanol, and ethyl acetate exhibit in-vitro antibacterial activity against Gram-positive (*Staphylococcus aureus*, *Bacillus subtilis*, *Bacillus cereus*, *Enterococcus faecalis*, and *Micrococcus luteus*) and Gram-negative (*Escherichia coli*, *Pseudomonas aeruginosa*, and *typhoid bacillus*) bacteria, according to Mohapatra *et al.*^[46]

Arawwawala and Hewageegana^[26] in similar study, reported that honey have antibacterial activity against the subsequent bacterial species: *Bacillus anthracis*, *Corynebacterium diphtheriae*, *Haemophilus influenzae*, *Klebsiella pneumoniae*, *Listeria monocytogenes*, *tubercle bacillus*, *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*.

Bansal *et al.*^[48] reported that *Helicobacter pylori* are found to be sensitive to honey with a median level of antibacterial activity as a results of the presence of peroxide at a 20% concentration.

Several bacterial infections have developed resistance to clinically introduced antibiotics. Wound pathogens, including those with high levels of innate or acquired antibiotic resistance, were killed by honey below 15 percent using a medical-grade honey, which can be a concentration that will be retained in the wound

environment.^[1] It was not possible to induce resistance to honey under conditions that easily induced resistance to antibiotics.^[49]

At different concentrations, methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-sensitive *enterococci* (VSE) isolated from contaminated wounds have been shown to be sensitive to honey according to the report of Cooper *et al.*^[50] Honey exhibits a synergistic activity against MRSA Jenkins *et al.*^[51], where sub-lethal concentrations of manuka honey (6% w/v) have a major impact on improving the susceptibility to Oxacillin of methicillin-resistant *Staphylococcus aureus* and reversing tolerance to the medication.

Antibiofilm Properties of honey

Biofilms are colonies of bacteria, fungi, or yeasts that are prepared by discharging extracellular polymeric substances to form heterogeneous entities on biotic or abiotic surfaces.^[52] Each cell is shielded from aggressive variables such as immunological defense systems, nutrient limitations and antibacterial agents by these substances.^[53]

Honey, however, has been found to actively inhibit and destroy a number of planktonic bacteria, but honey has the ability to break biofilms, more interestingly. As stated by Nolan *et al.*^[2], honey's antibiofilm properties are due to its capacity to disrupt quorum sensing and penetrate the biofilm itself. Two key components of honey's ability to disrupt biofilms have been accredited: bee defensin-1 and methylglyoxal.^[54]

Honey as antiviral agents

Apart from an outbreak or virus possessing a vaccine or specific antibody, the term antiviral agents have been described in very broad terms as substances that can produce either a defensive or therapeutic effect for the clearly detectable benefit of the infected host virus.^[55]

Honey has been confirmed to have anti-Rubella virus antiviral activity and is topically used to treat recurrent herpes simplex lesions.^[7]

Hailal *et al.*^[22] confirmed that honey has in-vitro antiviral activity against Rubella virus, herpes and anti-HIV-1 as tested was due to methylglyoxal present in honey. Manuka honey has been reported to have high inhibitory activity against the influenza virus from various sources.^[56]

Pasture honey are also utilized as anti-infective (especially antiviral) activity, due to hydrogen peroxide. Hailal *et al.*^[22] reported that raw honey can eliminate herpes as compared to acyclovir. The possible mechanism of action that the honey enters the virus and inhibits its replication also at appropriate concentration neutralizes the virus.^[22]

Antifungal effects of honey

An antifungal agent, or fungicide, is a biocidal chemical compound or biological organism used to kill or inhibit fungi or fungal spores.^[57] Antifungal activity of honey was tested, but not many fungi species are tested. Its antifungal activity against dermatophytes which cause humans mycoses, *Epidermophyton*, *Microsporum* and *Trichophyton* had been reported.^[58] Shariati *et al.*^[59] had similar report in their work on dermatophyte strains from 3 genres, *Trichophyton*, *Microsporum* and *Epidermophyton* by agar dilution technique method. These species of fungi are known to be causative agent of dermatophytes.^[59] Dermatophytes are classes of hemogenic keratinolytic fungi that have the ability to invade human and animal keratinized tissues and cause dermatophytosis infection.^[59]

The conventional treatment of fungal disease is limited, and part of the reason is due to the inadequate spectrum of the currently antifungal drugs, and the expensive treatment and protracted therapy.^[22] In recent years, several studies on the *in vitro* susceptibility of superficial mycoses to antifungal of honey had been carried out.^[60] In a related study, multifloral honey samples were evaluated for their ability to inhibit the growth of 40 yeast strains. Some of them include *Candida albicans*, *C. krusei*, *C. glabrata* and *Trichosporon*.^[61] The unifloral honey antifungal activity against *Penicillium* species at concentration higher than 10% was reported.^[62]

Anti-helmintic effects of honey

Helminths are parasitic worms. In developing countries, they are the most common human infectious agents and create a global disease burden.^[63] Honey have been examined for anti-helmintic activity using Earth-worms (*Pheretima posthuma*), tape-worms (*Raillietina spiralis*) and round-worms (*Ascaridia galli*).^[22] Various concentrations (100–300 mg/mL) of sweeteners extract have been investigated for anti-helmintics assay.^[22]

As a consequence of its acidic pH level (3.2-4.5), the operation of natural honey against helminthes prevents the spread of parasitic worms and produces an unfavorable environment for its development.^[64]

Precaution of using honey

Natural products are known to cure some ailments without any side effects, for example honey, which is very safe to use. However, Honey as any other natural food can be contaminated from the environment, for instance pesticides, antibiotics and poison plants.^[65] and moreover, few plants are known to produce nectar containing toxic substances.^[41,43]

Toxicity of honey from plants has also been reported.^[66]

There is a health implication for infants' regarding the presence of *Clostridium botulinum* in honey.^[43] Spores of this bacterium can survive in honey, but they cannot build toxin. Thus, in the stomach of infants less than one

year the bacteria spores from honey can survive and change into toxic in immature intestinal tract leading to illness and even death.^[67]

To minimize risks of honey born poisoning (poisonous nectar^[68] and bacterial spores), honey users should purchase their honey from saved source and ensured that decontamination of spore before giving to the children.

CONCLUSION

Application of honey for therapeutic purposes is an aged long development that has been resurfaced as a result of treatment failure owing to antibiotics resistance nowadays in clinical setting. The striking testimony of honey with many laboratory researches was that it has no record of antibiotic resistance. The positive influence of honey on non-infectious diseases is of great importance. Since Honey pose less risk to users except the ones that are contaminated and the one from toxic nectar, it is therefore imperative for the populace to reconsider the use of honey in clinical management as an antibiotics alternative and equally ensured proper sterilization and the validity of the nectar source before use in order to attain maximum benefit.

Conflict of interest

The authors declared that there are no conflict of interest as regarding the medical use of honey.

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