

An overview on therapeutic applications of honey in contemporary medicine

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Abstract

Honey has been utilized since antiquity for its nutritional and medicinal properties. Although fructose and glucose make up the majority of honey, it also contains fructo-oligosaccharides, several amino acids, vitamins, minerals, and enzymes. The plants that bees feed on determine the content of honey. Flavonoids, phenolic acids, ascorbic acid, tocopherols, catalase (CAT), superoxide dismutase (SOD), reduced glutathione (GSH), Millard reaction products, and peptides are found in practically natural honey, though. The components of honey have been documented to demonstrate antioxidant, antibacterial, anti-inflammatory, antiproliferative, anticancer, and antimetastatic properties. Many evidences suggest the use of honey in the control and treatment of wounds, diabetes mellitus, cancer, asthma, and also cardiovascular, neurological, and gastrointestinal diseases. Honey has a potential therapeutic role in the treatment of disease by phytochemical, anti-inflammatory, antimicrobial, and antioxidant properties. The study aims to explore the non-conventional functions of honey and also the therapeutic potential of in alleviating various diseases.

Keywords: Honey; Natural components; anti-oxidants; Therapeutic benefits

Introduction

Honey is a remarkable natural sweetener that has garnered a great deal of attention not only for its delightful flavor but also for its renowned therapeutic properties across a multitude of traditional medicinal systems. Throughout the ages, it has been extensively utilized in the process of wound asepsis by various ancient civilizations, showcasing its incredible versatility. Its effectiveness and beneficial qualities as a healing agent were undoubtedly acknowledged and recognized, particularly following the advent and discovery of modern medicine, which has further confirmed its valuable contributions. In the modern era, honey has found a prominent place within evidence-based practices, traditional systems, or even complementary medicinal approaches. This integral role has been established marvelously with a wealth of scientific proof that supports its use. Many contemporary medicinal formulations have now prescribed honey due to its remarkable attributes after quite a lengthy period in some practices of certain healing systems. Presently, it is widely believed that honey is unlikely to cross the expiry date of the existing composition and that it never really possessed any such limited shelf life, contrary to popular belief. Moreover, the therapeutic applications of honey can be envisaged for almost all types of health conditions, showcasing its versatility and efficacy. This ranges from minor ailments to more significant health issues, demonstrating its broad-spectrum utility. However, it is important to note that commercial and official honey products could also be encountered in the successful management of some diseases, thereby highlighting honey's ongoing relevance in both traditional and contemporary medicinal practices around the world. (Yupanqui et al.2022) (Mărgăoan et al.2021)(Tashkandi, 2021)(Iftikhar et al.2022)

Self-medication could involve taking honey as a natural sweetener. Nonetheless, it is vulnerable to having those healing characteristics which could be directly or indirectly attributed to one or many unknown compounds or phyto-constituents present in honey. Again, self-medication could happen with pure honey, but as a medicinal formulation, it could be found in combination with food or some drugs.

Indeed, the literature contributes to the possible drugs with which honey is concurrently used. Presently, there are two reviews available on the same topic. More important than consumption are honey's properties or useful teas in health conditions. Moreover, nowadays, people all over the world are interested in the use of natural products in the treatment of diseases because of the facts that have already been mentioned. The fact is given as a piece of information that candidate drugs from traditional systems are being suggested, for which research and importance have already been recognized (Ranneh et al.2021)(Hasan et al.2021).

2. Chemical Composition of Honey

Honey is a complex mixture composed of at least 180 substances, approximately 80% of which are sugars; enzymes such as glucose oxidase, invertase, and catalase; amino acids, proteins, and their respective components; vitamins B1, B2, B3, B5, B6, C, H, and K; minerals and trace elements; minor components such as pigments; volatile compounds of which 600 have been identified in floral honeys; and water. Honey has long been consumed as food and used as an important medical or curative substance to aid dietetics. The biological activity of honey is due to its unique chemical composition and also attributed to two unique factors involved in its production – unique bee enzymes and unique phytochemicals from the nectar of plants used by bees to manufacture honey. Honey contains vitamins including thiamine, riboflavin, pyridoxine, nicotinic acid, biotin, ascorbic acid, and folic acid. It also contains ascorbic acid and other organic acids, catalase, glucose, fructose, glucose oxidase, human α -amylase, and lactose, which produce hydrogen peroxide when in contact with wound fluids, and 2,3,5,4'-tetrahydroxystilbene. Antioxidant enzymes and substances such as catalase, ascorbic acid, flavonoids, glutathione, and carotenoids are involved. The sugar content of honey ($\leq 80\%$) is comprised of fructose and glucose with various amounts of disaccharides, maltose, and other complex carbohydrates. The proportion of individual carbohydrates from honey varies depending on several factors such as the following: • Floral source: flowers and honeydew from different plant species can

directly influence the color, fragrances, and aromas, as well as the flavor and taste of honey because of their different properties. • Season: influences the collection of honeydew/sap and pollen to make honey, nectar flow, and the amount of precipitation as well as the temperature at which it is collected. Overall, the chemical composition of honey can vary greatly by confirmed geographical area (microclimate), time, and processing of total sugars and minerals (iron, sodium, potassium, copper, manganese, calcium, potassium, and phosphorus) in the human body. Lactic and citric acids are the main organic acids found in honey. (Kumari et al., 2021)(Almasaudi, 2021)(Valverde et al., 2022).

3. Antimicrobial Properties of Honey

Antimicrobial Properties of Honey. Honey acts as an antimicrobial agent towards a broad spectrum of pathogens including bacteria, fungi, and viruses. This is achieved through a variety of mechanisms including honey's osmotic effects, production of hydrogen peroxide, and antioxidants. In testing, it has demonstrated effectiveness against both non-resistant and antibiotic-resistant strains of bacteria, particularly in combating wound infections. By doing so, honey is not only establishing its role in contemporary medicine but also its position as an alternative microbial agent. (Yupanqui et al.2022)(Brudzynski, 2021)(Luca et al., 2024)

Bacteria. Today's increasing resistance to antibiotic treatments is a significant healthcare threat. Identified as MRSA in 1999, MRSA was globally disseminated and resistant to an array of antibiotics by 2005. Reports show MRSA is also changing, converting strains that were traditionally associated with hospital-acquired infections to strains that cause skin and soft-tissue infections in healthy people outside the hospital environment. Fortunately, some natural treatments are unaffected by resistance mechanisms; some honeys are one such example. (Akram et al., 2023)

Fungi and Viruses. Partly due to similarities in the behavior of fungi and bacteria, honey's antifungal properties are well researched. There are many different types of fungi that cause

a variety of infections; these range from superficial, mucosal, and systemic infections. Therefore, effective treatment can be difficult; however, honey has been identified as effective against a range of fungi associated with these infections. Viruses are another significant threat to public health, and honey has also demonstrated potential as an antiviral agent. Currently, drug options are limited, with only a small number of active pharmaceuticals available for patients. Further, these are only suitable for a few types of viral infections and are not suitable for widespread use. In this sense, honey is making its case for utilization. Overall, honey has the potential to be a useful component in contemporary medicine. With its unique component profile and broad-spectrum antimicrobial properties, it has potential for use in a range of fields including wound care, where it has demonstrated particular effectiveness. (de et al.2021)(Miller et al., 2021)(van et al.2021)

3.1 Against Bacteria

Among the most valuable properties of honey, of importance in the therapeutic context, is its antibacterial nature. It is well documented that it is effective against Gram-positive bacteria and Gram-negative bacteria. That is why honey is finding applications chiefly in the treatment of wounds and infections. Good results were obtained when heather honey was topically applied to mild-to-moderate superficial and partial-thickness burns in children. A beneficial influence of heather honey on recalcitrant infected post-surgical wounds following radical debridement after osteosynthesis was also reported. In order to explore the mechanisms associated with such activity, many researchers have also investigated the antimicrobial properties of honey and its inhibitory spectrum against various microorganisms. (Aljaghawani et al.2021) (Stavropoulou et al.2022)

Evidence of the high efficacy and a broader spectrum of bactericidal activity of honey preparations has been presented in comprehensive reviews, concentrating on multiple studies of the susceptibility of pathogens to most commercially available medicinal honeys. Moreover, the lack of bacterial resistance to honey is of great interest regarding the widespread use of topical medicinal agents based on honey

since antibiotic resistance is a severe and widespread problem among patients undergoing conventional antimicrobial therapies. Clinical trials are being conducted with various honey preparations that are used to treat, among others, burn patients, especially children. By standardizing the methods for collecting and processing therapeutic honeys, it will be possible to ensure that such honeys have optimal antibacterial activity and can be safe as antimicrobial agents. (Almasaudi, 2021)(Hossain et al.2022)

3.2 Against Fungi

Candida species are the most common fungal organisms that cause infection in humans. To target these pathogens, honey uses many mechanisms, such as inhibition of germ tube formation, damage to the cell wall, suppression of ergosterol biosynthesis, and the ability to produce reactive oxygen species. The minimum inhibitory concentration of honey that can inhibit the growth of *Candida* depended on its species and varied from 2.5% up to 75% from study to study. This indicates the necessity to standardize the experimental methods. In vitro studies frequently describe the synergistic effects of honey and standard antifungal drugs. In some clinical cases, where infection was caused by fungi resistant to traditional therapy, the addition of honey in the treatment protocol restored the success of therapy. Most of these cases concerned topically delivered honey, but some described complementary oral delivery of honey in immunocompromised patients. These results are crucial to consider and indicate honey as a natural remedy for physicians of many specializations, suggesting that the therapeutic use of honey can be proposed not only in classical medicine but also in dental, dermatological, and veterinary fields for the treatment of many mycoses, particularly candidiasis, frequently induced post-surgically. (van et al.2021)(de et al.2021)

Negative effects of pharmaceutical antifungal drugs on the human microbiota indicate the emergence of studies on naturally-based agents; honey seems to be a good candidate, particularly in chronic infection treatment. Consistent results of mutual enhancement in antifungal action by both honey and antifungal drugs suggest that comprehensive studies

using animal models or double-blind, prospective clinical trials are necessary to plan new therapy protocols. Because studies have proven the low MIC value of honey against many *Candida* species, in vitro and in vivo confirmations can be proposed before detailed tests. The only issue is the genetic and phenotypic differences of *Candida* species. The isolated human candidal species were different in susceptibility to hydrolysable tannins affecting wound healing in a dose-dependent manner. However, honey can be very useful and probably the optimal remedy in common drug delivery chaotic directions; it is also useful prophylactically, if used in a moderate dose as a sweetener, to protect mucosa and subsequently to prevent some candidiasis through its antimicrobial properties. (Yupanqui et al.2022)(Tashkandi, 2021)

3.3 Against Viruses

Honey has broad-spectrum antiviral properties. It has activity against a number of viruses, including those that cause upper respiratory infections, such as influenza virus, respiratory syncytial virus, human parainfluenza viruses, rhinovirus, and adenovirus. Two different mechanisms of action against influenza A virus may be suggested for honey: damage to virus structural proteins and inhibition of virus mRNA synthesis. The potential of honey to help with currently circulating viral diseases has not yet been demonstrated, but it has been suggested that sources of antioxidants and phenolic compounds present in honey might enhance immune responses against viral infections that lead to respiratory tract inflammation and catarrh, particularly in alleviating symptoms due to secondary bacterial infections. Medicinal honey is recommended as a last-resort treatment option for cough for the management of upper respiratory symptoms. However, there are no standardized cultivation and clinical studies on honey. (Asma et al.2022)(Sekar et al.2023)

Honey significantly decreases lower respiratory tract symptoms caused by rhinovirus, though whether it affects rhinovirus replication is unclear. Store-bought or genuine Manuka honey composition with the associated level of activity should be considered for future antiviral intervention

studies. Honey may offer the potential to reduce rhinovirus symptom duration. Honey is a good supplement to decrease symptoms of acute cough when already known, and there are several previous studies that have been done. Nevertheless, there are no studies on the use of Indonesian honey against influenza. So, new directions come up with new hope for a breakthrough in this research direction by studying the inhibitory power of honey directly, especially honey in the region of Indonesia against the influenza virus. Several clinical trials indicate that the use of honey can present antiviral activity in various types of viruses, but from many viruses, in Indonesia, clinical trials can be found only in dengue fever. In one clinical trial on the oral honey consumption process, a decrease in the number of the dengue virus was experienced. Most of these trials have focused on the effect of honey as an antiviral synergistic activity with other antiviral drugs. The use of honey is expected to accelerate the healing process and provide protection and immunity to the body. In a new publication of a review, bee honey showed inhibition of 11 viruses through the virus entry phase, 20 viruses in which the replication is inhibited, and 20 viruses in the release of the virus. (Abuelgasim et al., 2021)(Arentz et al.2021)

4. Wound Healing Properties of Honey

Honey is a sweet substance produced by bees and has been used for centuries as a traditional medicine to treat various diseases and injuries. Currently, many studies are underway that have proven its efficiency as an alternative for the treatment of wounds and many other diseases. In this work, we present the state of the art with therapeutic properties of honey according to its potential applications in contemporary medicine. Wound healing properties of honey. Honey has been used for centuries in the treatment of wounds and to encourage tissue regeneration and reduce inflammatory changes, thereby promoting rapid scarring. However, this mechanism was not well understood until late in the 19th century. It was determined that honey, when diluted, has an inhibitory effect on several pathogenic organisms. This observation correlated with the increased use of this product in clinical settings such as surgical wounds, ulcers, and burns.

Many studies have confirmed that honey increases the rate of wound healing. Its pharmacological properties are related to its chemical composition, which contains sugars, amino acids, proteins, vitamins, and, above all, key components such as nitrogen, hydrogen peroxide, and polyphenols: flavonoids, phenolic acids, and enzymes. The process of wound healing and regeneration plays an essential role at the molecular level; for example, nitric oxide levels are increased, and the balance between matrix metalloproteinases and tissue inhibitors is regulated. Honey maintains moisture and prevents the growth and colonization of bacteria and other pathogenic microorganisms. (Boukraâ, 2023)(Yupanqui et al.2022)

5. Clinical Applications of Honey in Medicine

Honey has been found to be a valuable alternative and complementary medicine for diseases such as respiratory conditions: bronchial asthma, chronic cough, cystic fibrosis, and bronchitis, as well as gastrointestinal disorders: indigestion, diarrhea, Crohn's disease, ulcerative colitis, constipation, and GERD. It also has value in managing chronic and long-term conditions; though research in the area is scarce and needs more studies to cover a variety of clinical fields of medicine. In this chapter, many clinical trials and reports on healing wounds and burns with honey are underway around the world. Much of this work is a combined research effort between conventional medical practice and holistic practice. Researchers argue that the expectation is to show the effectiveness of honey beyond just healing wounds; it is about holistically healing a person as a whole.

Use of Honey in Managing Respiratory Conditions: A typical application of honey in clinical practice is addressing various respiratory conditions, including bronchial asthma, chronic cough, cystic fibrosis, and bronchitis. Many clinical trials and case reports have been recorded in this area.

Use of Honey in Managing Gastrointestinal Disorders and Conditions: Honey is used clinically to address various conditions and disorders, including indigestion, inflammation, chronic inflammation, Crohn's disease, ulcerative colitis, constipation, GERD, gastric pain, and other problems.

Use of Honey in Managing Skin and Dermatological Conditions: Honey is used

clinically in a few instances involving skin diseases. These conditions include herpes complications, lip lesions, and skin moisturizers. Several clinical cases in eczema and psoriasis are also reported. There are other clinical applications in oral care with honey, managing diarrhea, and using honey prior to general anesthetic therapy. (Aw et al.2021)(Jaber et al.2021) (Tashkandi, 2021)(Ízol, 2023)

5.1 Respiratory Conditions

5.1.1. Chronic Cough

Honey can be used to treat cough. Clinical studies have shown that a single dose or a two-day administration of honey can enhance the health of patients who suffer from chronic cough and could not find any relief from medications. Being safe, honey can be used in the entire population. Honey reduced the severity of cough, the frequency of cough, and the discomfort associated with it. Therefore, it has been suggested as a potential substitute for industrial HCl (either used alone or in combination with other medications). The natural anti-inflammatory and emollient properties, which are attributed to the presence of flavonoids and antioxidants in honey, make it very suitable for the treatment of irritation in the respiratory tract. Almost all honey types are recommended in the treatment of cough, whether dark or light, though it has been suggested that honey with a darker color possesses more qualities. (Poursaleh et al.2022)(Sadr et al.2023)

Contrary to the well-known syrups sold as OTC medications for cough, honey has a sweet taste and, because of its better viscoelasticity, it sticks to the throat for a long time and prevents the tickling sensation in the throat. The daily consumption of honey can also prevent throat infections. A daily intake can have a productive result in patients suffering from cough diseases, even allergic rhinitis. Uncontrolled drug users with allergic rhinitis and cough stated that receiving honey in water gave them relief and improved various parameters like frequency of cough, intensity, and quality of sleep. This is popularly called the “honey remedy.” Other respiratory ailments that can be treated by honey, besides chronic bronchitis, include chronic bronchitis and laryngospasm in infants. (Ahmed et al.2023)

5.2 Gastrointestinal Disorders

It is well documented that honey has important therapeutic effects on gastrointestinal complaints such as gastritis and peptic ulcers, as well as other gastrointestinal disorders such as diarrhea and irritable bowel syndrome. Multiple mechanism research has mainly focused on hydroxymethylfurfural, phenolic compounds, and flavonoids in honey, as well as the synergistic effect of honey with other natural products related to inflammation. Multiple studies investigating the influence of promoting a healthy gut used honey as a positive-tasting prebiotic. This review presents a summary of the latest literature, explaining the role of the dosage forms of honey most commonly used for GI disorders, including the respected clinical advantages and long-standing beliefs about honey in promoting gut health. The antioxidant profile of honey is discussed alongside reported evidence of a direct free radical scavenging effect in clinical studies related to GI complaints. (Gośliński et al.2024)(Kim et al., 2024)

The active constituents of honey and randomized clinical research support the effects, with meta-analysis verifying that honey enhances the eradication rate and reduces the signs of *H. pylori* infection-related symptoms; however, treatment with a high intake of natural honey was seen to remarkably alleviate and strengthen ulcer symptoms. Children have also shown benefits from honey in one study; the intake of lyophilized bee pollen was shown to reduce symptoms after seven weeks, whereas a different type of lyophilized bee pollen was monitored to reduce erosion areas and the occurrence of psoriatic plaques after twelve weeks. It has been revealed to regulate stomach acid secretion and detoxify reactive oxygen species, regulate GI motility, and inhibit potential pathogen growth should gastric pH be raised, but also to nourish the GI lining and promote recovery. Furthermore, honey is reported to be absorbed slowly into the bloodstream and used directly by the body, providing a safe and effective remedy for those who suffer from digestive problems. (Cardos et al., 2021)

5.3 Dermatological Conditions

Honey has been reported as a natural moisturizer that can

help manage various skin problems. It has 20% water content, low pH, and contains amino acids, B vitamins, and other nutrients that help to regenerate the skin. Besides, honey also has antibacterial and anti-inflammatory properties. Because of its beneficial properties, honey has been used to heal some skin problems, like acne and eczema. Acne is a common skin condition characterized by the presence of comedones, papules, pustules, and nodules that can affect the face, chest, and back. Eczema is one of the most common chronic relapsing inflammatory skin diseases, characterized by pruritus, redness, and various skin lesions. (Almasaudi, 2021)(El-Seedi et al.2022)

Clinical studies of honey in dermatology are very limited and not widely conducted. However, in vitro and in vivo studies have shown the promising effects of honey as an adjunct therapy in dermatology. Honey has been used for skincare formulations to improve its properties and make it user-friendly. In formulating a product with honey, the parameters that must be considered are the concentration of honey, derivation, and a proper preservation system against bacteria and fungi. There is increasing evidence that honey is effective in reducing wound inflammation and enhancing the healing of wounds. Even though many clinicians believe that honey is a natural product and does not require patch testing to establish that patients are not allergic, it is better for dermatologists to perform a total allergy test with a skin patch test using honey before routine use. Moreover, it is more practical not just to think of the individual components of honey as having biological activity, but to be aware of the performance of honey as a whole. In conclusion, the application of honey is a modality that has proven to be an attractive dressing for treating wounds. It also has many uses in dermatology. Honey has been used successfully in patients suffering from a variety of wounds and skin diseases. (Tashkandi, 2021)(Ahmed et al., 2022)

6. Conclusion and future directions

In conclusion, this comprehensive review supports the notion that honey can be an effective complementary or, in some cases, alternative strategy for managing a plethora of

health conditions in modern medicine. Of particular note is that honey encompasses antioxidant, anti-inflammatory, antibacterial, and anticancer effects, possesses important immunomodulatory properties, expedites tissue repair, and can be used as a wound dressing to accelerate healing in an array of wound types, including burns. We have received further evidence that manuka honey is the most extensively studied honey type with established antimicrobial and immunomodulatory benefits for use in wound healing and reducing infections, but we have also suggested exploring the medical attributes of various honey types, not just manuka honey. For the majority of other health conditions, due to the dearth of RCTs, evidence is mostly drawn from in vitro, animal, or small clinical studies that suggest outcomes with the use of honey are promising. Our recommendation is to conduct larger, well-designed clinical trials to produce higher-quality evidence and provide clarity in the application of honey for such conditions.

We suggest conducting studies on the effects of different honey types and their consistency. In this respect, our advice is that the development of a standardized protocol for honey harvest, processing, storage, and application in health care is necessary to ensure that the honey contains the same beneficial and bioactive qualities in every batch produced. Researchers, apiarists, and clinicians should collaborate in the latest research findings to determine the most appropriate honey for various therapeutic applications and related health issues as a way of exploring new uses and benefits of honey as a future-generation product in the realm of modern medicine. Additionally, it is significant for further research to establish whether honey can be used for preventive medicine or optimally complemented with existing medication as a general health promotion agent. Furthermore, there is value in future research to instruct health professionals about the medical applications of honey.

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