Review Article
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Honey: A Natural Counter to Antimicrobial Resistance

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ABSTRACT:

With the global threat of antimicrobial resistance (AMR) escalating in magnitude, the need for a sustainable antimicrobial agent has become a key objective for many scientists. Honey has been valued for its varied antimicrobial mechanisms. However, there is a lack of studies that have investigated honey in the context of AMR. The purpose of this review is to examine the mechanisms that contribute to honey's role as an antimicrobial agent suitable to be used alongside modern medicine. Honey's high sugar content, lower pH, presence of organic compounds, and ability to produce hydrogen peroxide have identified honey as a suitable candidate for the global threat of AMR. These characteristics enable the honey to target specific bacteria, such as methicillin-resistant Staphylococcus aureus, Shigella sonnei, and Helicobacter pylori. In conclusion, honey has the potential to be a powerful and natural antimicrobial agent that can be utilized for infection control and the development of future antibiotics.

KEYWORDS:

INTRODUCTION:

Honey has been utilized in medical settings across various civilizations for centuries, spanning from ancient Egypt to the present day. The earliest mention of honey's clinical applications dates back around 2100 BCE to Sumer, an ancient civilization nestled within Mesopotamia (Mandal & Mandal, 2011). Since then, numerous clinical applications have been discovered for honey, including aiding wound healing, treating severe burns, and even serving as a tool in combating cancerous tissue (Al-Waili *et al*., 2011). However, arguably the most important property of honey, especially within the future of the healthcare world, is honey's inherent antibacterial properties.

Bacteria are microorganisms that comprise the whole world around us; from our internal bodies to the outside ground, bacteria exist in nearly all environments that we as humans expose ourselves to. While some are beneficial for our health, others pose serious harm and can ultimately lead to death. Thus, the discovery of antibiotics, drugs used to specifically target and eliminate harmful bacteria, has been one of the greatest revolutions in the history of medicine. Since the discovery of the first antibiotic, penicillin, in 1928, antibiotics have played a significant role in healthcare, with new types and classes being discovered over time (Ventola, 2015). However, the continued use of antibiotics has raised a new, impending obstacle, serving as one of the most prominent threats to global health in the current era: antimicrobial resistance (AMR).

AMR is the phenomenon in which bacteria gain the ability to withstand the effects of known antibiotics. This is accomplished through a variety of mechanisms: investing energy in pumps to pump the antibiotic out of the bacterial cell body, modifying the target organelle of an antibiotic, developing thicker cell wall coatings, and more (Munita & Arias., 2016). Resistant bacteria can then transfer the

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resistant genes through the horizontal transfer of plasmids, thus further proliferating the resistance crisis (CDC, 2019). This crisis is compounded by the declining efforts of pharmaceutical companies to discover new, effective antibiotics (Hurley, 2021), as well as the misuse and overuse of existing antibiotics in both clinical and agricultural settings (Iwu & Okoh, 2020).

While AMR may appear to be an insignificant trend in the healthcare world, it proves to be one of the biggest and most pressing concerns in both current and future global health. Approximately 1.14 million deaths were directly attributable to AMR globally, with an additional 4.71 million deaths associated with AMR. The future outlook looks even more disastrous: AMR is projected to directly cause 39.1 million deaths globally from 2025-2050, with an estimated 169 million additional deaths associated with AMR (Naghavi *et al*., 2024). AMR has wide-reaching effects that extend beyond healthcare, as it is projected to cause a loss of 3.8% of the world's gross domestic product by 2050 (World Bank, 2017). However, despite these concerns, honey may serve as a revolutionary catalyst in the battle against AMR due to its innate chemical, physical, and biological properties. Honey is a natural solution to this crisis, as it effectively combats resistance and inhibits the growth of various microbes.

This narrative review aims to assess the properties that contribute to honey's effectiveness as an antimicrobial agent, while also exploring the rationale behind each property's efficacy. By evaluating current literature and research, this review aims to highlight the significant potential of honey in the ongoing fight against AMR, particularly as harmful bacteria continue to adapt and evolve more rapidly than we can manage.

METHODS

This narrative review employs a thematic synthesis of sources to examine the natural antimicrobial properties of honey and its current use as an antimicrobial agent in clinical settings. The sources selected were identified and accessed through the Google Scholar and PubMed databases, all of which are peer-reviewed and published in reputable journals. A variety of factors influenced the types of sources selected; however, sources focusing on the unique innate antimicrobial properties of honey, current clinical applications of honey as an antimicrobial agent, and future benefits of utilizing honey as an antimicrobial agent were specifically chosen.

The selection criteria included articles, journals, and sources published from 2020 to 2025. This literature search included key terms such as "honey", "antibiotic", "antimicrobial", "antimicrobial resistance", "medicinal applications", and "clinical applications". Boolean operators, such as "AND" and "OR", were used to combine search terms. A total of 19 source articles were reviewed; only peer-reviewed journal submissions were selected and further evaluated. To minimize selection bias, multiple reviewers searched for articles on both platforms (Google Scholar, PubMed) and shared both the titles and abstracts with the other reviewers. After articles were selected, the reviewers collaborated and conducted further discussions on the viability of each source and its potential utilization in the narrative review. Although we minimized selection bias to the best of our abilities, the nature of a narrative review suggests that some selection bias may still be present.

DISCUSSION

High Sugar Concentration of Honey

Honey contains various antimicrobial properties, one of which is its high sugar concentration. Honey is primarily composed of fructose and glucose, which play a crucial role in its antimicrobial properties. The overall composition of sugar content within honey accounts for approximately 80% of its total composition (Combarros-Fuertes *et al*., 2020). Although fructose and glucose are the primary sugars within honey, the sugar content of honey also consists of maltose, sucrose, and other minor sugars,

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including rhamnose, trehalose, and erlose (Combarros-Fuertes et al., 2020). This overall abundance of major sugars and minor sugars contributes to the 80% sugar content that is contained in honey. An osmotic effect is created within the honey, drawing out any water that the microbes may need to thrive (Ogwu & Izah, 2025). As these microbes absorb the honey through their cell walls, the high osmolarity creates a hypertonic environment that draws water out of the microbes, shrinking the cells and resulting in cell death due to dehydration (Ogwu & Izah, 2025).

The creation of a hypertonic environment is highly effective in honey's ability to combat antimicrobial resistance, as microbes are unable to thrive in these harsh environments where water is scarce. In addition to the osmotic pressure and hypertonic environment that is created by the high sugar concentration of honey, a strong interaction between the sugars and water molecules occurs within the honey. The higher the sugar concentration, the lower the amount of free water molecules. This free water content determines the moisture content of the honey and allows for the prevention of microbial growth, with honey's water activity ranging between 0.5 and 0.65. This water activity correlates to the moisture of the honey, as the lower the water activity, the lower the humidity (Yupanqui Mieles et al., 2022). Fermentation within honey cannot occur if the humidity level is below 17.1%, as the water activity would be too low to support microbial growth. For example, the water activity needed for microorganisms to develop is as follows: 0.70 for mold, 0.80 for yeast, and 0.90 for bacteria (Yupanqui Mieles et al. 2022). Since the water activity of most honey is within the range of 0.5 and 0.65, the moisture within honey is too low to allow for the growth of microbes. The water activity needed for mold, yeast, and bacteria to thrive is all higher than that of water activity that occurs in honey.

Low pH of Honey

Honey's antimicrobial properties are also derived from its low pH level. Most microorganisms thrive in environments with neutral pH levels, with optimal growth occurring at pH levels ranging from 6.5 to 7.5 (Almasaudi, 2020). The pH of honey is found to be within the range of 3.2 to 4.5, indicating its generally acidic nature. This acidity within the honey is due to the presence of gluconic acid, which is generated from glucose oxidation. This process occurs when the enzyme glucose oxidase catalyzes glucose, breaking it down into hydrogen peroxide (Almasaudi, 2020). The production of hydrogen peroxide through glucose oxidation causes the pH to shift towards the acidic side. There is a direct correlation between the acidity of honey and the floral source used to produce it (Bouacha *et al*., 2018). These different floral sources help contribute to the varying acidity within the honey due to the amino acids that are contained within these floral sources, as well as the amino acids that are contained within the bee. There are about 18 amino acids, many different organic acids, as well as aliphatic and aromatic acids that are contained within the bees and are transferred to the honey when it is secreted from the honeybee (Bouacha et al., 2018). The low acidity of honey is a likely reason why microbes can't develop resistance to honey, as they aren't able to survive when the highly acidic honey is absorbed into their cells. Since the optimal range for microorganism growth is relatively neutral, when an acidic agent is introduced, there is a breakdown of cellular structures, which will eventually lead to the complete degradation of the microorganism cells.

Presence of Organic Antimicrobial Compounds in Honey

A significant part of honey's antimicrobial arsenal is underscored by the several organic compounds it contains, such as enzymes, antioxidants, including phytochemical acids, and essential oils (Ogwu & Izah, 2025). For example, the enzyme glucose oxidase catalyzes the reaction between glucose, oxygen, and water to produce gluconic acid and hydrogen peroxide, which is key for compromising the integrity of microbial cell structures (Ogwu & Izah, 2025). More details on its mechanisms are provided in the section below. Phytochemicals, such

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as flavonoids and phenolic acids, help neutralize free radicals within the body, which, when present in excess, cause oxidative stress and contribute to tissue damage (Machado et al., 2020). Flavonoids neutralize free radicals and can reduce the risk of chronic diseases, such as heart disease and cancer. Phenolic acids, on the other hand, can protect against neurodegenerative diseases due to their anti-inflammatory properties (Ogwu & Izah, 2025). Honey also contains essential oils derived from plants where its components were harvested. Oils from tea, eucalyptus, and oregano, in particular, have been studied for their antimicrobial properties, including disrupting cell walls, interfering with DNA replication, and inhibiting the formation of biofilms, which act as a shield for microorganisms (Ogwu & Izah, 2025). It is worth noting that different varieties of honey will contain different levels of antimicrobial compounds and thus exhibit different effects. Interestingly, the botanical source of the honey determines its properties. A 2023 study, for example, assessed the efficacy of multiple Chilean honey varieties. It was shown that honey from different plants, among the wide variety tested, particularly those known for their medicinal value, such as the ulmo and quillay trees, possessed the greatest antimicrobial effects (Poulsen-Silva et al., 2023). Understanding the various organic compounds present in different medicinal honeys is crucial for guiding their use in combating resistant microbes.

Production of Hydrogen Peroxide within Honey

In addition to the previously mentioned properties that enable honey to effectively combat antimicrobial resistance, another method that contributes to this combativeness is honey's ability to produce hydrogen peroxide, briefly mentioned in the previous sections. Honey contains high enzymatic activity, mainly due to glucose oxidase. During the production of honey, when nectar is being transferred from the bees, this enzyme is secreted into the nectar, enabling the entire process of hydrogen peroxide production to occur (Yupanqui Mieles *et al*., 2022). Since honey does not contain much moisture or water activity, high volumes of hydrogen peroxide are not produced, but enough is present to affect the microbes' cellular structures and functions. The production of hydrogen peroxide damages the cellular structures, DNA, and proteins of the microbes as they absorb the honey, ultimately killing them and preventing further growth. When honey is diluted, the glucose oxidase within the honey becomes activated and begins to act on the glucose, producing hydrogen peroxide. The highest amount of hydrogen peroxide production occurred when honey was diluted by 30-50% (Almasaudi, 2020). This illustrates that the increased dilution of the honey allows more water to be readily available to glucose oxidase, thereby facilitating the production of more hydrogen peroxide. By enabling this dilution process to occur, the overall cellular damage to the microbes increased as the amount of hydrogen peroxide that interacted with them increased.

Real World Applications

Throughout history, honey has been utilized in various ways by people worldwide. Honey has been used for consumption, as a medical tool, and has even been traded for its rarity. In contemporary times, honey has continued to be an invaluable natural resource due to its versatility as both a healing agent and a promoter of general health and wellness.

Despite that, it is still important that the distinctions between different varieties of honey are not overlooked. Honey is produced in areas all around the world, from the rainforests of Malaysia to the mountains of Russia. Not all honey is the same; understanding the specific qualities of each honey variety can lead to a more comprehensive understanding of its chemical properties and potential applications in modern medicine. Tualang honey is a variety that originates in the rainforests of Malaysia. It has been praised for its high levels of antioxidants, flavonoids, and phenolic acids, which allow it to maintain its extraordinary properties as an antimicrobial and anti-inflammatory substance.

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Studies have indicated positive initial results in treating specific bacterial strains such as MRSA and Pseudomonas aeruginosa (Azman, 2024). Bashkir honey is a different variety produced by Russian beekeepers. While it is already renowned as one of the most expensive varieties of honey in the world, Bashkir honey has recently been praised for its medicinal properties. Burzyan wild hive bees (a breed exclusive to Eastern Europe) will interact with Linden leaves, which are a species of plant that has some of the highest biological activity levels of any plant in the world. Research conducted by scientists in Russia suggests that Bashkir honey exhibits significant antimicrobial and antioxidant activity due to its rich polyphenolic structure, as well as the bioactive compounds it receives from Linden leaf nectar (Sultanova, 2022). Understanding these differences can enhance medical research and provide healthier alternatives to the overconsumption of pharmaceutical drugs.

In recent times, certain medical-grade honeys have even been approved for clinical use by the FDA. One of the most well-regarded formulas is Medihoney, which utilizes many of the properties of Manuka for topical wound care. The process of getting approval for honey is very arduous, however. These products are subject to various quality control regulations, intended to test whether the substance is suitable for use in clinical and hospital settings. Despite the steadily increasing relevance of honey in clinical settings, the lack of standardization between oral and topical delivery remains a significant systemic challenge. Topical applications for wounds such as burns or ulcers are generally more common and established in many clinical settings (Patil, 2020). Oral consumption, however, lags significantly behind, mainly due to the lack of dosage standardization and a shortage of consistent and reliable data.

While honey has been understudied as a medical tool, considering modern research capabilities, it has still maintained a significant substance in various ways. Honey is being increasingly used among veterinarians to support gut health in animals. The sugars comprising honey feed the beneficial bacteria in your gut (Lactobacillus), which promotes digestion and enhances nutrient absorption (Kyle, 2020). Honey also has a long and rich history of being used to treat various wounds, dating back hundreds of years. It has been used in treatments for burns, ulcers, wounds, and incisions.

The most useful property of honey in modern times is its potential as an antimicrobial agent. Honey is a unique tool in combating microbes due to its multi-pronged approach. While most antibiotics are designed to target microbial cells in a specific way, honey will utilize multiple approaches simultaneously. The acidity of honey disrupts the activity of microbial cells, while other properties of honey are responsible for dehydrating the cells. Compounds within honey, such as Hydrogen Peroxide and glucose oxidase, are natural antiseptics that aid the body. It can even be used to disrupt biofilms in particularly strong microbes (Almasaudi, 2020).

The historical significance of honey in medicine is being redefined by the research being done by modern scientists. Many avenues remain undiscovered, and the full therapeutic potential of honey remains unknown. The unique properties of the various honey varieties highlight the importance of learning about their distinct characteristics and understanding how they can be effectively utilized to address modern medical challenges. Ranging from wound care to antimicrobial resistance, studying honey presents a genuine opportunity to educate the public about alternative treatments. With growing concern about the rise of superbugs and other highly specialized microbes, honey stands out not only as a complementary tool but as a vital substance in the future of healthcare.

CONCLUSION

This study reviewed literature to investigate the potential of honey as an antimicrobial agent. We identified honey's multifaceted antimicrobial mechanisms and a broad spectrum of antimicrobial

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properties. Considerable evidence suggests that honey, a natural substance, exhibits adaptability across various botanical sources, with a centuries-long history of medical relevance. However, there are still limitations in standardizing the composition of honey due to variations in botanical resources, geographic origin, and processing procedure. These variations may affect the consistency and feasibility of standardized medical use cases.

In conclusion, honey serves as a source of natural antimicrobial agents, which can be potentially utilized for infection control and in addressing the AMR crisis. The findings of this review provide a basis for future research that explores the capabilities of honey through clinical trials to evaluate its effectiveness in modern medicine. These efforts will further studies that focus on optimizing delivery methods and enabling the medical standardization of honey application. This line of research will help to determine how to safely and effectively utilize honey in healthcare, hopefully serving as a potential lifeline for humanity as we continue battling the ever-evolving AMR calamity.

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