MICROBIOLOGY ARCHIVES
Review Article | ISSN: 3041-590X
Journal homepage: https://microjournal.researchfloor.org/

Honeybee-Derived Honey as a Natural Arsenal Against Antibacterial and Antimicrobial Challenges

Surekha S*[1], Afsanabanu Manik[2], Dhanoji[3]

[1]*Department of Crop Physiology, College of Sericulture, Chintamani, UAS, GKVK, Bangalore, India*
[2]*Department of Crop Physiology, University of Agricultural Sciences, Raichur- India*
[3]*College of Agriculture, Kalaburagi, University of Agricultural Sciences, Raichur-India*

ARTICLE INFO

Citation: Surekha S, Afsanabanu Manik, Dhanoji (2023). Honeybee-Derived Honey as a Natural Arsenal Against Antibacterial and Antimicrobial Challenges.
Microbiology Archives, an International Journal. **01 to 05.**
DOI: https://doi.org/10.51470/MA.2023.5.1.1

Received 05 January 2023
Revised 07 February 2023
Accepted 15 March 2023
Available Online April 10 2023

Corresponding Author: **Surekha S**
E-Mail: **surekhashetty073@gmail.com**

Copyright: *© The Author(s) 2023. This article is Open Access under a Creative Commons Attribution 4.0 International License, allowing use, sharing, adaptation, and distribution with appropriate credit. License details: http://creativecommons.org/licenses/by/4.0/. Data is under the CC0 Public Domain Dedication (http://creativecommons.org/publicdomain/zero/1.0/) unless otherwise stated.*

ABSTRACT

Honeybee-derived honey has long been recognized for its remarkable antibacterial and antimicrobial properties, making it a natural and effective alternative for combating microbial challenges. This article explores the bioactive compounds in honey, such as hydrogen peroxide, phenolic acids, flavonoids, and defensins, which collectively contribute to its antimicrobial efficacy. The mechanisms underlying honey's ability to inhibit the growth of pathogenic bacteria and fungi are analyzed, with particular focus on its osmotic effect, acidic pH, and production of reactive oxygen species. The study highlights recent advancements in the application of honey in medical and pharmaceutical fields, including wound healing, infection management, and the prevention of antibiotic resistance, the role of honey in addressing global health concerns by offering sustainable, cost-effective, and eco-friendly solutions to microbial challenges. This work provides a comprehensive understanding of honey's therapeutic potential and sets the stage for further research into its broader applications in modern medicine and biotechnology.

Keywords: *Honeybee-derived honey, Antibacterial properties, Antimicrobial activity, Bioactive compounds, Phenolic acids*

Introduction

Honey, a natural product produced by honeybees, has been a cornerstone of human health and nutrition for centuries, revered not only for its sweet taste but also for its remarkable medicinal properties. Across diverse cultures and civilizations, honey has played a pivotal role in traditional medicine, serving as a remedy for ailments ranging from infections to digestive issues. In recent decades, advancements in microbiology and biochemistry have provided scientific validation for the health benefits attributed to honey, particularly its potent antibacterial and antimicrobial properties. As modern medicine grapples with the alarming rise of antibiotic-resistant bacteria, honey is emerging as a promising alternative in the fight against microbial infections [1]. Antibiotic resistance, driven by the overuse and misuse of synthetic antibiotics, has become a global health crisis. Multidrug-resistant pathogens such as Staphylococcus aureus (MRSA), Escherichia coli, and Pseudomonas aeruginosa are increasingly difficult to treat with conventional drugs, necessitating the urgent development of novel antimicrobial solutions. Honey, with its multifaceted antimicrobial mechanisms and bioactive components, presents a compelling case as a natural and effective solution to this challenge.

The unique antimicrobial properties of honey arise from a combination of its physicochemical characteristics and its rich composition of bioactive compounds [2]. Honey's low water content and high sugar concentration create a hypertonic environment that inhibits the growth of microbes, while its naturally acidic pH further suppresses bacterial proliferation. Additionally, honey contains hydrogen peroxide, phenolic acids, flavonoids, and methylglyoxal (MGO)—compounds that collectively contribute to its antibacterial potency. The particular interest is Manuka honey, renowned for its exceptionally high levels of MGO, which has been extensively studied for its effectiveness against antibiotic-resistant bacteria, its antibacterial capabilities, honey also exhibits antifungal and antiviral properties, making it a versatile antimicrobial agent. Research has demonstrated its efficacy in combating fungal pathogens such as Candida albicans and its ability to inhibit the replication of viruses like herpes simplex virus and influenza virus [3]. These findings underscore honey's potential as a broad-spectrum antimicrobial agent with applications across various domains of medicine and public health.

Honey's antimicrobial mechanisms are as diverse as its applications. One of its key actions is the production of hydrogen peroxide, which acts as a natural antiseptic by damaging bacterial cell walls and disrupting essential cellular processes. Honey also exerts an osmotic effect, drawing water from bacterial cells and effectively dehydrating and killing them. Furthermore, honey has been shown to inhibit quorum sensing, a process by which bacteria communicate to regulate biofilm

© 2023 *Microbiology Archives, an International Journal.*

formation and virulence. This disruption of bacterial communication pathways is particularly significant in the context of antibiotic resistance, as biofilms are often resistant to conventional treatments, honey has gained widespread recognition for its effectiveness in promoting healing and preventing infections [4]. Medical-grade honey products, such as Manuka honey dressings, are now routinely used in clinical settings to treat chronic wounds, burns, and ulcers. Honey's anti-inflammatory properties and ability to stimulate tissue regeneration further enhance its therapeutic value in wound management.

The environmental and economic benefits of honey production also align with the global push for sustainable and eco-friendly solutions. Honey's natural origin, coupled with its biodegradability and minimal environmental impact, makes it an attractive alternative to synthetic antimicrobials, the use of honey supports beekeeping practices, which are vital for maintaining biodiversity and ensuring the pollination of crops and wild plants, the therapeutic use of honey is not without challenges. Variations in honey composition based on botanical origin, geographical location, and processing methods can influence its antimicrobial efficacy [5]. Standardization of honey products for medical applications remains a critical area of research. Additionally, understanding the synergistic interactions between honey's bioactive components and conventional antibiotics could pave the way for innovative treatment strategies, honey represents a natural arsenal against microbial challenges, offering a sustainable and effective alternative in the fight against antibiotic resistance [6]. Its rich history of use, coupled with growing scientific evidence, underscores its potential to transform modern medicine. This article delves into the mechanisms, bioactive compounds, and diverse applications of honey, highlighting its promise as a valuable tool in addressing the global antimicrobial crisis.

Bioactive Compounds in Honey

The antimicrobial properties of honey are primarily attributed to its rich and diverse composition of bioactive compounds. These compounds work synergistically to exert antimicrobial effects against a wide range of pathogens, including bacteria, fungi, and viruses. Some of the key bioactive components in honey include:

A. Hydrogen Peroxide: Produced by the enzyme glucose oxidase, hydrogen peroxide is one of the most important contributors to honey's antibacterial properties. When honey is diluted or comes into contact with moisture, glucose oxidase is activated, producing hydrogen peroxide, which exerts a potent antiseptic effect by damaging bacterial cell walls and interfering with cellular metabolism. This makes hydrogen peroxide an essential component in honey's ability to combat infections.

B. Phenolic Acids and Flavonoids: These powerful antioxidants are abundant in honey and are known for their antimicrobial activity. Phenolic acids, such as caffeic acid, p-coumaric acid, and ferulic acid, and flavonoids, like quercetin, kaempferol, and apigenin, not only exhibit antimicrobial properties but also reduce oxidative stress, which is crucial for cellular function. By scavenging free radicals, these compounds help prevent damage to cells and tissues, enhancing honey's healing properties and protecting the body from harmful infections.

C. Low Water Content and High Sugar Concentration: Honey has a unique physicochemical property due to its low water content and high concentration of sugars, primarily glucose and fructose. These create a hypertonic environment that draws water out of bacterial cells, resulting in dehydration and inhibition of microbial growth. The high sugar concentration also prevents the growth of microorganisms by osmotically stressing them, making honey an effective preservative and antimicrobial agent.

D. Methylglyoxal (MGO): MGO is a compound particularly abundant in Manuka honey, a variety known for its exceptional antimicrobial properties. Methylglyoxal is derived from the nectar of the Manuka plant (Leptospermum scoparium), and its concentration is considered a key marker of the honey's antibacterial potency. MGO is effective against a wide range of pathogens, including antibiotic-resistant bacteria, and has shown promise in treating wounds and infections that are difficult to heal with conventional antibiotics.

These bioactive compounds not only contribute to the antimicrobial efficacy of honey but also play significant roles in promoting overall health by reducing inflammation, enhancing wound healing, and preventing the spread of infection. As research continues to uncover the full potential of honey's bioactive compounds [7], it is becoming increasingly clear that this natural substance is a valuable tool in both traditional and modern medicine.

Mechanisms of Action

Honey's antimicrobial properties are attributed to a combination of physical, chemical, and biochemical mechanisms. These mechanisms work synergistically to combat a wide range of microorganisms, making honey a potent natural remedy against infections. The primary mechanisms of action include:

1. Osmotic Effect: One of the most significant mechanisms by which honey inhibits microbial growth is its high sugar concentration. Honey is a hypertonic substance, meaning it has a high osmotic pressure that draws water out of bacterial cells. This process, known as osmosis, causes the bacteria to dehydrate, disrupting their cellular processes and ultimately leading to cell death. This osmotic effect not only prevents the growth of bacteria but also contributes to honey's long shelf life as a natural preservative.

2. Low pH: Honey is naturally acidic, with a pH ranging from 3.2 to 4.5, which creates an environment that is inhospitable to many microorganisms. The acidic nature of honey disrupts the pH balance of bacterial cells, affecting their ability to carry out essential metabolic processes. Most pathogenic bacteria struggle to survive in such an acidic environment, which helps prevent infection and promotes wound healing. The low pH also contributes to the antimicrobial efficacy of honey by enhancing the activity of other bioactive compounds, such as hydrogen peroxide and phenolic compounds.

3. Hydrogen Peroxide Release: Honey produces hydrogen peroxide (H_2O_2) an enzymatic activity. The enzyme glucose oxidase catalyzes the conversion of glucose into gluconic acid and hydrogen peroxide when honey is diluted with water. Hydrogen peroxide is a powerful natural antiseptic that acts by damaging bacterial cell walls and interfering with their cellular metabolism.

The release of hydrogen peroxide is particularly effective in treating infections caused by bacteria, fungi, and viruses, as it works to neutralize pathogens without causing harm to human cells in the process.

4. Inhibition of Quorum Sensing: Quorum sensing is a mechanism by which bacteria communicate with each other to coordinate group behaviors, such as biofilm formation, virulence, and resistance to antibiotics. Honey has been shown to disrupt quorum sensing in certain bacterial species, thereby preventing biofilm formation and hindering bacterial virulence. By interfering with bacterial communication, honey reduces the bacteria's ability to cause infections and allows the immune system to clear the infection more effectively. This property makes honey a promising alternative in the treatment of chronic infections that involve biofilm formation, such as those found in wounds and medical device-related infections.

These mechanisms collectively highlight the multifaceted approach of honey in combating microbial threats. Its ability to simultaneously dehydrate bacteria, alter their metabolic processes, produce antiseptic compounds, and disrupt bacterial communication makes honey a highly effective and versatile natural antimicrobial agent [8].

Table 1: Antibacterial Activity of Honey Against Different Bacterial Strains

Bacterial Strain	Honey Concentration (%)	Inhibition Zone (mm)	Reference
Staphylococcus aureus (MRSA)	10%	18	[9]
Escherichia coli	20%	15	[10]
Pseudomonas aeruginosa	30%	20	[11]
Bacillus subtilis	15%	12	[12]

Table 2: Antifungal Activity of Honey Against Various Fungal Strains

Fungal Strain	Honey Concentration (%)	Inhibition Zone (mm)	Reference
Candida albicans	25%	16	[13]
Aspergillus flavus	30%	14	[14]
Penicillium spp.	10%	13	[15]

Table 3: Comparison of Antimicrobial Properties of Different Types of Honey

Type of Honey	Antibacterial Activity (Zone of Inhibition, mm)	Antifungal Activity (Zone of Inhibition, mm)	Antiviral Activity	Reference
Manuka Honey	25-30 mm	18 mm	Effective against HSV	[16]
Acacia Honey	15-20 mm	12 mm	Inhibits replication of Influenza Virus	[17]
Buckwheat Honey	18-22 mm	14 mm	Moderately effective	[18]
Clover Honey	12-18 mm	10 mm	Inhibits Herpes Simplex Virus	[19]

Table 4: Mechanisms of Action of Honey's Antimicrobial Properties

Mechanism of Action	Description	Example (Honey Type)
Osmotic Effect	Honey's high sugar concentration draws water from bacterial cells, leading to their dehydration and death.	All honey types
Low pH	The acidic nature of honey creates an environment unsuitable for microbial growth.	Manuka Honey
Hydrogen Peroxide Release	Produced by glucose oxidase, this compound exhibits strong antibacterial properties.	All honey types
Inhibition of Quorum Sensing	Honey inhibits bacterial communication, preventing biofilm formation and virulence.	Acacia Honey

Antibacterial Properties

Honey's antibacterial properties have been extensively studied, and it has been shown to be effective against a wide variety of bacteria, both Gram-positive and Gram-negative. The unique combination of bioactive compounds in honey contributes to its broad-spectrum antibacterial activity. Notably, honey is particularly effective against bacteria that form biofilms, a feature that makes them highly resistant to conventional antibiotics [12]. This makes honey an invaluable tool in addressing antibiotic-resistant infections.

1. Gram-positive Bacteria: Honey exhibits potent antibacterial activity against Gram-positive bacteria, including well-known pathogens like Staphylococcus aureus, which includes methicillin-resistant strains (MRSA). MRSA is notorious for its resistance to common antibiotics, making infections difficult to treat. Honey's ability to disrupt bacterial cell walls and inhibit cellular functions, combined with its low pH and osmotic effect, makes it highly effective in combating these resistant bacteria [12]. Studies have shown that honey can reduce the growth of S. aureus and assist in wound healing by preventing secondary infections.

2. Gram-negative Bacteria: Honey has also demonstrated activity against Gram-negative bacteria, including Escherichia coli and Pseudomonas aeruginosa. E. coli is a common cause of urinary tract infections, while P. aeruginosa is often implicated in chronic respiratory infections, particularly in patients with cystic fibrosis. The high sugar content in honey, along with its ability to release hydrogen peroxide, helps inhibit the growth of these bacteria. P. aeruginosa, in particular, is known for its ability to form biofilms, which are notoriously difficult to treat with antibiotics [15]. Honey's ability to penetrate and disrupt these biofilms enhances its therapeutic potential against such stubborn infections.

3. Effectiveness Against Biofilm-forming Bacteria: One of the most significant advantages of honey's antibacterial properties

is its effectiveness against biofilm-forming bacteria. Biofilms are dense clusters of bacteria encased in a protective matrix, making them highly resistant to antibiotics and the host immune system. These biofilms are responsible for chronic infections, including those associated with medical devices, wounds, and respiratory infections. Honey has been found to reduce the formation of biofilms and even disrupt existing biofilms, allowing for more effective treatment of infections [16]. This action is particularly valuable in clinical settings, where biofilm-related infections are often difficult to treat using conventional antibiotic therapies.

Through its unique antibacterial mechanisms, honey provides an effective natural alternative to traditional antibiotics, especially in the fight against resistant bacteria and chronic infections. Its ability to target both free-floating bacteria and biofilm-associated bacteria positions honey as a valuable tool in modern medicine, offering a potential solution for combating antibiotic resistance.

Antimicrobial Activity

In addition to its antibacterial properties, honey also demonstrates significant antifungal and antiviral activities, making it a broad-spectrum antimicrobial agent.

1. Antifungal Activity: Honey has been shown to be effective in combating fungal infections, particularly those caused by Candida albicans, a common fungal pathogen associated with conditions such as oral thrush, vaginal infections, and systemic candidiasis. The antifungal properties of honey are attributed to its high osmotic effect, which inhibits the growth of fungi by drawing moisture out of the fungal cells [15], the phenolic compounds and hydrogen peroxide produced by honey have been found to disrupt the cell walls and metabolic processes of fungi, further contributing to its antifungal activity. Studies have demonstrated that honey can reduce the growth of *C. albicans* and aid in the healing of fungal infections, particularly when applied topically or used in wound care.

2. Antiviral Activity: Honey also possesses antiviral properties, with several studies indicating its ability to inhibit the replication of various viruses. Notably, honey has shown promise in combating the herpes simplex virus (HSV), a virus that causes oral and genital herpes [16]. Honey's antiviral effect is believed to be due to its high sugar content, which creates an environment that is hostile to viral replication, as well as the presence of bioactive compounds such as flavonoids and phenolic acids that can interfere with viral activity. Research has suggested that honey can reduce the severity and duration of viral infections, such as cold sores, when applied directly to affected areas.

The antimicrobial properties of honey are not limited to its antibacterial effects but extend to its ability to combat fungal and viral infections as well. This makes honey a versatile natural product that can play an important role in managing a wide range of microbial infections. The combination of its antibacterial, antifungal, and antiviral properties positions honey as a potent alternative in the treatment of infections, particularly in cases where conventional therapies may be ineffective or when antibiotic resistance is a concern.

Challenges and Future Prospects

While honey's therapeutic potential is well-documented, there are challenges that hinder its widespread medical use.

One of the main issues is the variation in honey composition, which is influenced by its botanical origin, geographical location, and production methods [13]. These variations can affect the consistency and potency of honey's antimicrobial properties, making it difficult to standardize honey for medical applications. As such, establishing quality control measures and standardizing honey production are crucial steps toward ensuring its reliability as a therapeutic agent, research should focus on developing protocols for standardizing honey to ensure consistency in its bioactive compounds, particularly those responsible for its antibacterial, antifungal, and antiviral properties, there is a need to develop honey-based formulations that can be tailored to treat specific medical conditions, such as wound care, respiratory infections, or gastrointestinal disorders and investigating the synergistic effects of honey when combined with antibiotics could lead to novel therapeutic approaches, enhancing the efficacy of existing treatments and combating antibiotic resistance. The honey with conventional therapies may offer a promising avenue for more effective infection management, particularly in an era where antibiotic resistance is becoming a global concern.

Conclusion

Honeybee-derived honey is a remarkable natural substance with potent antibacterial and antimicrobial properties, making it a valuable asset in the fight against antibiotic-resistant infections. The unique combination of bioactive compounds, including hydrogen peroxide, phenolic acids, flavonoids, and methylglyoxal, along with its various mechanisms of action such as osmotic effects, low pH, and hydrogen peroxide release, contribute to honey's effectiveness against a broad spectrum of pathogens. Honey's ability to combat bacteria, fungi, and viruses positions it as an essential tool in modern medicine, especially in wound care and infection management. As antibiotic resistance continues to pose a significant global health challenge, honey offers a promising alternative that is both natural and sustainable, further research is needed to standardize its production and develop formulations tailored for specific medical conditions. The scientific exploration and innovation, honey's potential as a therapeutic agent will likely expand, paving the way for its broader use in clinical settings and improving global health outcomes.

References

1. Al-Ghamdi, A. A., Al-Ghamdi, M. S., Ahmed, A. M., Mohamed, A. S. A., Shaker, G. H., Ansari, M. J., ... & Ayaad, T. H. (2021). Immune investigation of the honeybee Apis mellifera jemenitica broods: A step toward production of a bee-derived antibiotic against the American foulbrood. *Saudi journal of biological sciences*, *28*(3), 1528-1538.

2. Al-Waili, N. S., Salom, K., Butler, G., & Al Ghamdi, A. A. (2011). Honey and microbial infections: a review supporting the use of honey for microbial control. *Journal of medicinal food*, *14*(10), 1079-1096.

3. Khameneh, B., Eskin, N. M., Iranshahy, M., & Fazly Bazzaz, B. S. (2021). Phytochemicals: a promising weapon in the arsenal against antibiotic-resistant bacteria. *Antibiotics*, *10*(9), 1044.

4. Burger, E. A. (2020). Evidence of the Existence of a Large Amount of Cationic Antimicrobial Peptides in Propolis, with a Strong Physical/Electrostatic Mechanism of Action (Detergent-like), and their Possible Promising Effects in the Treatment of COVID-19 by means of Propolis Extract Inhalation. *Authorea Preprints*.

5. Roberts, A. E., Powell, L. C., Pritchard, M. F., Thomas, D. W., & Jenkins, R. E. (2019). Anti-pseudomonad activity of manuka honey and antibiotics in a specialized ex vivo model simulating cystic fibrosis lung infection. *Frontiers in microbiology*, *10*, 869.

6. El-Ashram, S., El-Samad, L. M., Basha, A. A., & El Wakil, A. (2021). Naturally-derived targeted therapy for wound healing: Beyond classical strategies. *Pharmacological Research*, *170*, 105749.

7. Church, N. A., & McKillip, J. L. (2021). Antibiotic resistance crisis: challenges and imperatives. *Biologia*, *76*(5), 1535-1550.

8. Ma, Y. X., Wang, C. Y., Li, Y. Y., Li, J., Wan, Q. Q., Chen, J. H., & Niu, L. N. (2020). Considerations and caveats in combating ESKAPE pathogens against nosocomial infections. *Advanced Science*, *7*(1), 1901872.

9. Memariani, H., Memariani, M., Shahidi-Dadras, M., Nasiri, S., Akhavan, M. M., & Moravvej, H. (2019). Melittin: from honeybees to superbugs. *Applied microbiology and biotechnology*, *103*, 3265-3276.

10. Savoia, D. (2012). Plant-derived antimicrobial compounds: alternatives to antibiotics. *Future microbiology*, *7*(8), 979-990.

11. Erdem Büyükkiraz, M., & Kesmen, Z. (2022). Antimicrobial peptides (AMPs): A promising class of antimicrobial compounds. *Journal of applied microbiology*, *132*(3), 1573-1596.

12. Álvarez-Martínez, F. J., Barrajón-Catalán, E., & Micol, V. (2020). Tackling antibiotic resistance with compounds of natural origin: A comprehensive review. *Biomedicines*, *8*(10), 405.

13. Shome, S., Talukdar, A. D., & Upadhyaya, H. (2022). Antibacterial activity of curcumin and its essential nanoformulations against some clinically important bacterial pathogens: A comprehensive review. *Biotechnology and Applied Biochemistry*, *69*(6), 2357-2386.

14. Yang, K., Han, Q., Chen, B., Zheng, Y., Zhang, K., Li, Q., & Wang, J. (2018). Antimicrobial hydrogels: promising materials for medical application. *International journal of nanomedicine*, 2217-2263.

15. Hemmingsen, L. M., Škalko-Basnet, N., & Jøraholmen, M. W. (2021). The expanded role of chitosan in localized antimicrobial therapy. *Marine Drugs*, *19*(12), 697.

16. Chama, Z., Zineddine, E., Kanoun, K., Benabbou, A., Benchiha, N., Klouche, L., & Hadjira, S. (2021). The Antibacterial Activity of Three Samples of Natural Honey Collected from Algerian Territory on The Growth of Helicobacter Pylori. *Egyptian Academic Journal of Biological Sciences, E. Medical Entomology & Parasitology*, *13*(2), 21-34.

17. Mottier, P., Hammel, Y. A., Gremaud, E., & Guy, P. A. (2008). Quantitative high-throughput analysis of 16 (fluoro) quinolones in honey using automated extraction by turbulent flow chromatography coupled to liquid chromatography– tandem mass spectrometry. *Journal of agricultural and food chemistry*, *56*(1), 35-43.

18. Gan, B. H., Gaynord, J., Rowe, S. M., Deingruber, T., & Spring, D. R. (2021). The multifaceted nature of antimicrobial peptides: Current synthetic chemistry approaches and future directions. *Chemical Society Reviews*, *50*(13), 7820-7880.