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INHIBITORY EFFECTS of HONEY on *STAPHYLOCOCCUS AUREUS* and *ESCHERICHIA COLI*: A CURRENT REVIEW

ABSTRACT. Honey is a natural food that has been used since ancient times for its medicinal benefits. Thanks to its antimicrobial activity, which has a very important place among honey's medicinal effects, it can be used against various pathogens such as *Staphylococcus aureus* and *Escherichia coli*. The antibacterial effect of honey depends on physical (high osmotic pressure, low water activity and low pH value), chemical (hydrogen peroxide, methylglyocal, phenolic compounds, flavonoids, organic acids and proteins) and biological factors (enzymes secreted by bees, probiotic bacteria and pollen). The antibacterial effect of honey can be affected by the origin of the honey, the type of flower obtained, the season of harvest and processing methods. Therefore, more studies are required to clearly demonstrate the antimicrobial activity of honey and make it available for use in clinical treatments. In this review, it was aimed to better understand the antimicrobial effects of honey on *S. aureus* and *E. coli* by searching the current literature.

Keywords: Antimicrobial activity, *Escherichia coli*, honey, inhibitory effect, *Staphylococcus aureus*.

BALIN *STAPHYLOCOCCUS AUREUS* ve *ESCHERİCHİA COLİ* ÜZERİNE İNHİBİTÖR ETKİSİ: GÜNCEL DERLEME

ÖZET. Bal, tıbbi faydalarından dolayı eski dönemlerden beri kullanılan doğal bir gıdadır. Bal tıbbi etkileri arasında oldukça önemli yer tutan antimikrobiyal aktivitesi sayesinde, *Staphylococcus aureus* ve *Escherichia coli* gibi çeşitli patojenlere karşı kullanılabilmektedir. Balın antibakteriyel etkisi, fiziksel (yüksek osmotik basınç, düşük su aktivitesi ve düşük pH değeri), kimyasal (hidrojen peroksit, metilglikal, fenolik bileşikler, flavonoidler, organik asitler ve proteinler) ve biyolojik faktörleri (arılar tarafından salgılanan enzimler, probiyotik bakteriler ve polen) sayesinde gerçekleşmektedir. Balın antibakteriyel etkisini balın kökeni, elde edilen çiçeğin türü, hasat yapılan mevsim ve işleme yöntemleri etkileyebilmektedir. Bundan dolayı, balın antimikrobiyal aktivitesini net bir şekilde ortaya koymak ve klinik tedavilerin kullanımına sunmak için daha fazla çalışma gerekmektedir. Bu derlemede, güncel literatür taraması yapılarak, balın *S. aureus* ve *E. coli* üzerine antimikrobiyal etkilerinin daha iyi anlaşılması hedeflendi.

Anahtar Kelimeler: Antimikrobiyal aktivite, bal, *Escherichia coli*, inhibitör etki, *Staphylococcus aureus*.

INTRODUCTION

For many centuries, people have relied on honey as a healing agent for different kinds of wounds and diseases, because it can destroy many kinds of germs. But when antibiotics were invented, honey was mostly ignored as a treatment. However, with microorganisms progressively developing resistance to antibiotics, researchers have rekindled their interest in the antimicrobial and wound-healing potential of honey. Recent investigations have demonstrated that honey can effectively combat around 60 bacterial species, encompassing both gram-positive and gram-negative bacteria, as well as aerobes and anaerobes (Gambo et al., 2018).

Honey carries a minimal risk of microbial contamination and boasts a prolonged shelf life. Its primary constituent is carbohydrates, and its elevated carbohydrate content results in low water activity, typically within the range of 0.59 to 0.63. Water activity is a crucial factor affecting the viability and functionality of biological systems. Most bacteria find it challenging to proliferate when water activity levels drop below 0.9. The reduced water activity in honey significantly contributes to its antimicrobial properties. Furthermore, the presence of honey's proteins and enzymes serves to impede microbial growth. The most important enzymes in honey are invertase, diastase, and glucose oxidase. Of these, invertase is also thought to contribute to honey's antimicrobial properties by defending against harmful microorganisms and absorbing moisture to reduce bacterial invasion (Ro Me Busserolles et al., 2002). Honey is recognised as a natural food preservative mainly because of its antimicrobial properties. The pH of honey and the enzymatic production of hydrogen peroxide by glucose oxidase also influence the antimicrobial activity of honey (Mundo et al., 2004; Afroz et al., 2016). The bee enzyme glucose oxidase catalyzes the oxidation of glucose to produce hydrogen peroxide. This oxidative compound inhibits bacterial growth even in diluted honey by preventing bacteria from responding to normal proliferative signals (Shamala et al., 2000).

Studies have shown that other bee products, such as propolis, have antibacterial effects. For example, propolis can prevent lipid oxidation and extend the shelf life of various foods, including meat, fish, poultry, vegetables, fruit, and beverages. It has both antibacterial and antioxidant properties. However, its unpleasant taste and odor may limit its use in food products by affecting sensory characteristics such as color, aroma, appearance, texture, and overall taste (Asma et al., 2022a; Segueni et al., 2023). In addition, Asma et al. (2022a) have illustrated that natural products derived from plants possess notable medicinal properties, rendering them a pragmatic approach for the control of biofilm-forming microorganisms. There is a growing consensus that antimicrobial compounds derived from plants can deliver effective antibiofilm activities. As for biofilm-forming microorganisms, they are increasingly becoming the focus of antibiofilm compounds sourced from both microorganisms and phytonanotechnology. These compounds have shown efficacy in the inhibition and eradication of biofilm development (Asma et al., 2022b).

Antibiotics are crucial for safeguarding the well-being of food-producing animals that hold nutritional significance. They are administered to treat afflicted animals and to mitigate and manage outbreaks of diseases. If antibiotics are not completely metabolised and eliminated from the body, residues may be found in the food obtained from these animals, posing a threat to public health by causing problems such as gastrointestinal disorders, antibiotic resistance, tissue damage, hypersensitivity reactions, neurological damage and anaphylactic shock in humans. In addition to acute illnesses associated with the consumption of animal-derived foods containing residues, carcinogenic and teratogenic effects may also be observed in humans (Küçükbüğrü and Acaröz, 2020; Çakmak et al., 2022).

This paper presents a thorough examination of honey's antimicrobial capabilities against the pathogenic microorganisms *S. aureus* and *E. coli*, presenting the most recent research discoveries from the existing literature. Increased knowledge of honey's antimicrobial properties could lead to new uses in the food and healthcare industries.

STAPHYLOCOCCUS AUREUS

Staphylococci are gram-positive cocci. There are thirty-three different species within the genus *Staphylococcus*, with the most pathogenic species being *S. aureus*. Certain *Staphylococcus* species can cause opportunistic infections in people with weakened immune systems. *S. aureus* is known to cause bacterial infections in humans, affecting various sites including the skin, bones, bloodstream, respiratory tract and soft tissues (David and Daum, 2017). The emergence of antimicrobial resistance in methicillin-resistant *S. aureus* (MRSA) has created difficulties in the treatment of infections caused by this bacterium (Almasaudi et al., 2017; Yılmaz and Aslantaş, 2017).

S. aureus is responsible for causing food poisoning in humans. The aforementioned bacterium is not directly responsible for the foodborne illnesses; however, the toxins they secrete - *staphylococcal* enterotoxins - are. Hence, the severity of the impact of *S. aureus* on the ailment depends on the quantity of enterotoxin it generates (Zeaki et al., 2019). *Staphylococcal* poisoning has implications for health. Inadequate hygiene amongst food service workers may result in food contamination by *S. aureus*. This bacterium can lead to conditions such as septicaemia, foodborne illness, and toxic shock syndrome, all caused by the presence of enterotoxins produced by *S. aureus*. Over twenty distinctive types of *Staphylococcal* enterotoxins, proteins, have been identified. *S. aureus* can survive harsh conditions like low pH and heat. This bacterium can also withstand exposure to digestive enzymes. However, the fortitude of *S. aureus* may lead to increased likelihood of diseases. *S. aureus* can produce enterotoxins in perishable food without spoiling it. This can happen even when toxic concentrations are present. Certain enterotoxins produced by *S. aureus* have been discovered to possess emetic properties (Yılmaz and Aslantaş, 2017; Zhao et al., 2017; Ciupescu et al., 2018).

Recent research shows that honey can slow the growth of bacteria. This includes *S. aureus*. This segment provides a detailed critique of current scientific academic literature. It focuses on the antimicrobial properties of honey against *S. aureus*. The segment highlights honey's natural ability to fight against bacteria. Research studies have presented the effects of honey on *S. aureus*. Additionally, these outcomes are summarized in Table 1.

Tulay and Akyalcin, (2018) conducted a study. The study examined antimicrobial properties of various honey samples. Agar well diffusion technique was used on Mueller-Hinton agar. The research focuses on three strains of *S. aureus*: 29213, ATCC 6538P and ATCC 25923. The tested honey samples skillfully fight three strains of *S. aureus*. The discoveries reveal this proficiency. The results imply that honey can be useful as a natural antibacterial agent. Honey, in various types, showed different levels of antibacterial activity. This activity led to inhibition zones with diameters ranging from 12 to 22mm. Among the honey samples tested, *S. aureus* ATCC 29213 was most susceptible. However, *S. aureus* ATCC 25923 was resistant to all the honey samples.

Russo et al. (2023) assessed antibacterial properties of honey samples. Honey collected from different regions of Sicily was used. The honey came from five floral sources: chestnut, eucalyptus, sulla, thyme, and citrus. Honey samples were then tested against *S. aureus* ATCC 29213. Only the chestnut-2 honey exhibited activity against *S. aureus* ATCC 29213 in both undiluted and diluted forms, with inhibition zones measuring approximately 15 mm. Conversely, the samples from Citrus-2 and Citrus-3 were found to possess no antimicrobial activity. The activity of the remaining honey samples varied. Sulla-1, eucalyptus-1, and eucalyptus-2 honey exhibited activity solely in the undiluted form, whereas citrus-1, thyme-1, thyme-2, and eucalyptus-3 honey demonstrated inhibition halos in both undiluted form and at 75% concentration. In contrast, Sulla-2, Sulla-3, thyme-3, chestnut-1, and chestnut-3 honey antagonized *S. aureus* ATCC 29213 in concentrations ranging from 100% to 50%. The study indicates that the honey samples tested have potential as natural antibacterial products and food preservatives, emphasizing the importance of further investigation on thyme honey as an effective natural antibacterial agent.

Postali et al. (2022) conducted a study examining the antibacterial properties of honey samples gathered from Samothrace Island in Greece, against *S. aureus*. The findings indicate that the growth of *S. aureus* was suppressed by honey and no collaborative antibacterial effects were detected among the tested honeys. All samples, except the lowest concentration (1.56% v/v), restricted *S. aureus* growth. A concentration of 75% v/v honey resulted in the most extensive inhibition zone (15.00 ± 1.00 mm), exceeding the zones produced by concentrations of 50%, 25%, and 12.5% v/v honey or by kanamycin (8.33 ± 1.12 mm).

Mahmood et al. (2021) investigated the antimicrobial properties of stingless honey derived from distinct multifloral sources against *S. aureus* during wet and dry seasons. Samples were collected from hives located in two multifloral areas - one comprising two flower types, including stevia, and the other encompassing more than two types of flowers. Inhibitory effects of honey samples from both seasons were observed against all foodborne pathogens tested, with dry season samples exhibiting the most significant inhibition. The antimicrobial activity decreased during the rainy season. However, higher flower diversity and quantity increased it. Seasonal fluctuations and flowering plant distribution greatly impact multifloral stingless honey. These findings emphasize the antimicrobial attributes of the honey.

Oğur and Dayan, (2022) researched Bitlis natural honey. Its antimicrobial properties were evaluated at various concentrations (10%, 25%, 50%, and 100%). The study focused on its effectiveness against *S. aureus*. The results showed large zones of inhibition at 100% concentration. No zones formed at 10% concentration. Bitlis honey has the potential to help treat infectious diseases. It may also be used in apitherapy for practical purposes.

Adeyemo et al. (2017) conducted a study in Nigeria. The study aimed to assess the antibacterial effectiveness of various types of honey against *S. aureus*. The researchers also compared it to a standard antibiotic. This study confirms that honey is an affordable and effective natural antibacterial agent. The study showed that super dark amber honey has potent antimicrobial properties. These properties are comparable to streptomycin. This honey exhibited strong antibacterial activity against a wide variety of bacteria. However, more research is needed for its suitability for clinical practice.

Kalidasan et al. (2017) examined the antimicrobial activity of three honey samples (Commercial Honey, Malan Honey and Kombu honey) against *S. aureus* bacteria. All three types of honey showed antibacterial activity against *S. aureus* bacteria. The activity was observed at a concentration of 75 µl. Commercial honey had a 22 mm zone of inhibition. Malan honey had a 26 mm zone. Kombu honey had an impressive 34 mm zone.

Shalsh et al. (2021) conducted a study on Malaysian Kelulut honey. The effectiveness of honey against *S. aureus* was tested. The results indicate that the dilution results of different Kelulut honey concentrations were highly significant. Both types of Kelulut honey demonstrated antimicrobial properties, notably in terms of minimum bactericidal concentration. Kelulut honey 1 did not exhibit any detectable zone of inhibition against *S. aureus* when tested at concentrations of 20%, 40%, and 60%. However, inhibition zones against *S. aureus* were observed at concentrations of %80 (3 ± 0.5) and %100 (3.4 ± 0.6) for Kelulut honey 1, and at concentrations of %80 (2.4 ± 0.6) and %100 (3.7 ± 0.3) for Kelulut honey 2. The study findings demonstrate that kelulut honey exhibits notable antibacterial properties when used at 100% concentration, indicating a viable option as an alternative treatment in veterinary medicine.

Akyalçın and Süerdem, (2017) investigated the antibacterial characteristics of six distinct types of honey from Kosovo in opposition to three strains of *S. aureus*. The outcomes showed that honey samples stopped *S. aureus* growth. The range was 10 to 38 millimeters. It was observed that all varieties of honey exhibited highly effective antibacterial attributes.

Shah et al. (2017) study was conducted on the antibacterial effects of honey samples. The honey samples were obtained from *Apis mellifera* and stingless bees. The study tested the effects of the honey samples against *S. aureus*. Samples from various regions in Pakistan were collected and analyzed. Examined in its original and processed forms. The results showed that all three honey samples had strong antibacterial properties. The inhibition zones ranged from 19 to 25 mm, which matches previous research.

Çakır and Dervişoğlu, (2022) aimed to investigate the antimicrobial properties of honey samples. The honey samples were obtained from Bingöl province, Turkey. The study focused on their effectiveness against *S. aureus*. The supplied honey was subjected to tests at various concentrations: 500 mg/mL, 250 mg/mL and 125 mg/mL. The findings showed that honey at 500 mg/mL and 250 mg/mL had antibacterial effects. However, honey at 125 mg/mL had no antibacterial properties. The findings showed that honey at 500 mg/mL and 250 mg/mL had antibacterial effects. Honey at 125 mg/mL did not have these effects.

Fratianni et al. (2023) tested of Italian organic monofloral honeys. The honeys tested for antimicrobial properties were Strobl, indigo, and alfalfa. These honeys were tested against *S. aureus* at concentrations of 10 and 20 µg/ml. The results showed that all honey types affected *S. aureus*. The extent of inhibition ranged from 1 to 56 mm. It has been determined that carob honey is more effective than other honeys.

Gkoutzouvelidou et al. (2021) tested eight types of Lemnos honey from Greece. They compared its effectiveness to Manuka honey in combating S. aureus. Each honey type was applied at 25% and 12.5% concentrations. The results show that both Lemnos and Manuka honeys show antibacterial activity. Some Lemnos honey samples showed antibacterial activity comparable to Manuka honey. Certain samples showed stronger antibacterial activity at 12.5% concentration.

Çakır et al. (2020) conducted an antimicrobial test. The test examined the impact of honey samples from different regions in Turkey. Honey samples from Rize (Anzer), Gümüşhane, and Sivas (Zara) were analysed to observe their effect on *S. aureus*. At 500 mg/mL extract concentration of all honey samples, the inhibition zone was 10.0 mm in Rize honey, 8.5 mm in Gümüşhane honey and 8.0 mm in Sivas honey. The study reveals insights about honey's potential as a natural antimicrobial agent. Rize and Gümüşhane honeys, at a concentration of 250 mg/mL, showed antimicrobial activity against *S. aureus*. The inhibition zones measured 6.0-6.5 mm. However, the concentration of Sivas honey at 250 mg/mL did not create any inhibition zones. No inhibition zones were found for Rize, Gümüşhane, and Sivas honeys. The extract concentration of 125 mg/mL did not affect *S. aureus*.

Table 1. Antimicrobial activity of honey against *S. aureus.*

***S. aureus* Types**	**Honey Types**	**Concentration**	**Inhibition Zones (mm)**	**References**
S. aureus ATCC 29213	Floral	100%	14	Suerdem and Akyalçın, 2018
	Highland	100%	18	
	Chestnut	100%	22	
	Oak	100%	18	
	Thyme	100%	14	
S. aureus ATCC 6538P	Floral	100%	-	
	Highland	100%	16	
	Chestnut	100%	18	
	Oak	100%	12	
	Thyme	100%	18	
S. aureus ATCC 25923	Floral	100%	-	
	Highland	100%	-	
	Chestnut	100%	-	
	Oak	100%	-	
	Thyme	100%	-	
S. aureus ATCC 29213	Chestnut-1	100%	18±0.00	Russo et al., 2023
		75%	18±0.58	
		50%	18±0.58	
		25%	0±0.00	
	Chestnut-2	100%	16±0.58	
		75%	16±1.00	
		50%	15±0.58	
		25%	15±0.58	
	Chestnut-3	100%	25±0.00	
		75%	10±0.00	
		50%	9±0.58	
		25%	0±0.00	
	Eucalyptus-1	100%	17±1.00	
		75%	0±0.00	
		50%	0±0.00	
		25%	0±0.00	
	Eucalyptus-2	100%	10±0.00	
		75%	0±0.00	
		50%	0±0.00	
		25%	0±0.00	
	Eucalyptus-3	100%	11±0.60	
		75%	9±0.58	
		50%	0±0.00	
		25%	0±0.00	
	Sulla-1	100%	17±1.70	
		75%	0±0.00	
		50%	0±0.00	
		25%	0±0.00	

Table 1. Continued.

***S. aureus* Types**	**Honey Types**	**Concentration**	**Inhibition Zones (mm)**	**References**
S. aureus ATCC 29213	Sulla-2	100%	27±1.63	Russo et al., 2023
		75%	26±0.58	
		50%	23±2.08	
		25%	0±0.00	
	Sulla-3	100%	28±1.00	
		75%	28±1.53	
		50%	27±1.25	
		25%	0±0.00	
	Thyme-1	100%	24±0.00	
		75%	20±1.00	
		50%	0±0.00	
		25%	0±0.00	
	Thyme-2	100%	22±1.15	
		75%	20±0.00	
		50%	0±0.00	
		25%	0±0.00	
	Thyme-3	100%	23±1.73	
		75%	22±2.00	
		50%	19±0.58	
		25%	0±0.00	
	Citrus-1	100%	18±1.00	
		75%	17±1.00	
		50%	0±0.0	
		25%	0±0.0	
S. aureus	Citrus-2	100%	0±0.00	Russo et al., 2023
		75%	0±0.00	
		50%	0±0.00	
		25%	0±0.00	
	Citrus-3	100%	0±0.00	
		75%	0±0.00	
		50%	0±0.00	
		25%	0±0.00	
S. aureus	Blossom honey (*Arbutus andrachne L.* (Ericaceae)), Greek strawberry tree)	75%	15.00±1.00	Postali et al., 2022
S. aureus ATCC 6538P	Honey from stingless bee (*Heterotrigona itama*)	100%	Dry Season two types of flowers: 16.33±1.15 more than two types of flowers: 19.33±1.15 Rainy Season two types of flowers: 7.67±0.58 more than two types of flowers: 11.33±0.58	Mahmood et al., 2021
S. aureus ATCC 29213	Bitlis-1	100%	15.50±0.55	Oğur and Dayan, 2022
		50%	14.00±0.00	
	Bitlis-2	100%	9.00±0.00	
		50%	-	
	Bitlis-3	100%	10.50±0.55	
		50%	-	
	Bitlis-4	100%	11.50±0.55	
		50%	10.00±1.10	
	Bitlis-5	100%	10.00±1.00	
		50%	10.00±0.00	
	Bitlis-6	100%	8.50±0.55	
		50%	-	
	Bitlis-7	100%	14.50±0.55	
		50%	10.00±1.00	
	Bitlis-8	100%	11.00±1.10	
		50%	10.00±0.00	

Table 1. Continued.

S. aureus Types	Honey Types	Concentration	Inhibition Zones (mm)	References
S. aureus NCIB 8588	Dark amber	ND	8.0±0.0	Adeyemo et al., 2017
	Dark amber	ND	21.3±0.5	
	Super light amber	ND	18.7±1.2	
	Light amber	ND	24.3±0.6	
	Light amber	ND	7.7±0.6	
	Super dark amber	ND	24.3±0.6	
	Dark amber	ND	14.0±1.0	
	Super light amber	ND	7.0±1.5	
	Super dark amber	ND	27.3±1.2	
	Bitter	ND	18.7±1.2	
	Light amber	ND	21.7±0.6	
	Dark amber	ND	9.3±1.2	
	Super dark amber	ND	8.3±0.6	
	Super dark amber	ND	7.3±0.6	
S. aureus	Commercial	ND	22	Kalidasan et al., 2017
	Malan	ND	26	
	Kombu	ND	34	
S. aureus	Kelulut-1	100%	3.4±0.6	Shalsh et al., 2021
		80%	3±0.5	
		60%	-	
		40%	-	
		20%	-	
	Kelulut-2	100%	3.7±0.3	
		80%	2.4±0.6	
		60%	-	
		40%	-	
		20%	-	
S. aureus	Mountain	ND	-	Akyalçın and Süerdem, 2017
	Floral	ND	-	
	Meadow flowers	ND	10	
	Pinus	ND	18	
	Floral	ND	10	
	Floral	ND	-	
S. aureus ATCC 29213	Mountain	ND	-	
	Floral	ND	10	
	Meadow flowers	ND	12	
	Pinus	ND	18	
	Floral	ND	14	
	Floral	ND	12	
S. aureus ATCC 6538P	Mountain	ND	-	
	Floral	ND	-	
	Meadow flowers	ND	12	
	Pinus	ND	14	
	Floral	ND	14	
	Floral	ND	10	
S. aureus ATCC 25923	Mountain	ND	36	
	Floral	ND	34	
	Meadow flowers	ND	38	
	Pinus	ND	34	
	Floral	ND	34	
	Floral	ND	32	
S. aureus ATCC 6538P	Dir Lower	ND	24.6	Shah et al., 2017
	Swat	ND	19.8	
	Oghi	ND	25.2	
S. aureus ATCC 29213	Yedisu	500 mg/mL	8.0±0.0	Çakır and Dervişoğlu, 2022
		250 mg/mL	6.0±0.0	
		125 mg/mL	-	
	Sancak	500 mg/mL	8.5±0.7	
		250 mg/mL	6.5±0.7	
		125 mg/mL	-	
	Kiğı	500 mg/mL	9.0±0.0	
		250 mg/mL	6.0±0.0	
		125 mg/mL	-	
	Genç	500 mg/mL	9.5±0.7	
		250 mg/mL	7.0±0.0	
		125 mg/mL	-	

Table 1. Continued.

S. aureus Types	Honey Types	Concentration	Inhibition Zones (mm)	References
S. aureus ATCC 25923	Sainfoin	10 µg/mL	40.03±2.16	Fratianni et al., 2023
		20 µg/mL	47.58±3.35	
	Carob	10 µg/mL	47.35±1.44	
		20 µg/mL	56.22±2.68	
	Astragalus	10 µg/mL	26.01±2.02	
		20 µg/mL	39.52±2.78	
	Indigo	10 µg/mL	1.02±0.06	
		20 µg/mL	28.06±2.04	
	Alfalfa	10 µg/mL	8.68±0.52	
		20 µg/mL	28.85±1.45	
S. aureus DFSN_B26	Lemnos-1	25%	5.0±0.0	Gkoutzouvelidou et al., 2021
		12.5%	5.0±0.0	
	Lemnos-2	25%	5.0±0.0	
		12.5%	5.0±0.0	
	Lemnos-3	25%	5.0±0.0	
		12.5%	5.0±0.0	
	Lemnos-4	25%	5.0±0.0	
		12.5%	5.0±0.0	
	Lemnos-5	25%	5.0±0.0	
		12.5%	5.0±0.0	
	Lemnos-6	25%	5.0±0.0	
		12.5%	5.0±0.0	
	Lemnos-7	25%	30.0±0.0	
		12.5%	24.0±3.5	
	Lemnos-8	25%	30.0±0.0	
		12.5%	26.7±2.3	
	Manuka	25%	30.0±3.5	
		12.5%	25.3±4.2	
S. aureus ATCC 29213	Rize (Anzer)	500 mg/mL	10.0±1.4	Çakır et al., 2020
		250 mg/mL	6.0±0.0	
		125 mg/mL	-	
	Gümüşhane	500 mg/mL	8.5±0.7	
		250 mg/mL	6.5±0.7	
		125 mg/mL	-	
	Sivas (Zara)	500 mg/mL	8.0±0.0	
		250 mg/mL	-	
		125 mg/mL	-	

ND: Not Determined

ESCHERICHIA COLI

Escherichia coli is extensively studied worldwide. It is a model organism for understanding biology. It usually lives in the gut microbiome. It can also harm humans and animals as a pathogen. The introduction of antibiotics in the 1940s marked a significant milestone in the realm of medicine. However, pathogenic bacteria have progressively developed resistance to multiple antibiotic agents. Antimicrobial resistance has now escalated into a worldwide peril to public health, with the growing resistance of *E. coli* to antibiotics emerging as a major point of concern. In 2018, more than half of the reported *E. coli* strains to the European Centre for Disease Prevention and Control demonstrated resistance to at least one of the assessed antimicrobial groups, and a significant portion displayed resistance to multiple groups (Kara et al., 2019; Karaynir, 2021).

Taking into account all these considerations and the promising outcomes of recent research, it is of paramount importance to explore alternative natural antibacterial strategies to combat antibiotic-resistant infectious diseases. This section provides a thorough review of recent research findings. The research focuses on honey's antimicrobial properties against *E. coli*. The review highlights honey's potential as a natural antimicrobial agent. Additionally, studies conducted on honey against *E. coli* are summarized in Table 2.

Russo et al. (2023) conducted an evaluation of the antimicrobial potential of Sicilian honey samples from five botanical sources (chestnut, eucalyptus, sulla, thyme, and citrus) against *E. coli*. All honey samples showed inhibitory activity against *E. coli* in the results. The most pronounced inhibitory effects were observed in Sulla-3, Citrus-3, Thyme-1, Thyme-2, Eucalyptus-1, Eucalyptus-3, Chestnut-2, and Chestnut-3. These particular honey varieties displayed inhibitory properties in both their concentrated and diluted forms. In contrast, Citrus-2 inhibited *E. coli* growth only in its undiluted form, with an inhibition rate of 40.95%. Citrus-1 and Eucalyptus-1 samples inhibited *E. coli* growth when diluted up to 75%, while Thime-3 and Chestnut-1 honeys inhibited *E. coli* growth by up to 50% when diluted. Sulla-1 and Sulla-2 honeys were the only samples that showed no antagonistic activity against *E. coli* in either undiluted or diluted formulations. Just like in the case of *S. aureus*, it was observed that dark-colored honeys exhibited a higher inhibitory effect compared to their lighter-colored counterparts.

Mahmood et al. (2021) examined the antimicrobial characteristics of multifloral stingless honey acquired from two distinct multifloral areas in both dry and rainy seasons. One region had only two types of flowers, while the other had more than two. Pollen analysis confirmed that the honey samples varied depending on the season. Despite this, honey from both seasons exhibited antimicrobial activity against all foodborne pathogens tested, with dry season samples showing the strongest inhibition. Surprisingly, honey from the two-flower region did not show antimicrobial effects against *E. coli* during the rainy season. Multifloral stingless honey has antimicrobial properties, but these properties are greatly affected by seasonal changes and flowering plant diversity. This study highlights their important impact.

Oğur and Dayan, (2022) assessed the antimicrobial activity of natural honeys from Bitlis against *E. coli*. The antimicrobial activity of honey samples was tested using the hollow agar method. The concentrations tested were 10%, 25%, 50%, and 100%. The largest inhibition zones were observed in 100% concentrates, while no zones were formed in 10% concentrates. These findings suggest that the studied bee products have potential for use in apitherapy.

Adeyemo et al. (2017) evaluated the antibacterial activity of different honey types against *E. coli* in southwest Nigeria. The inhibition zones ranged from 6.7±1.2 to 28.7±1.2 mm. Super dark amber honey exhibited the highest antimicrobial activity and potent broad-spectrum antibacterial activity. However, further research is needed to assess its clinical practicality.

Wadi, (2022) conducted an evaluation of the antibacterial activity of 32 different global raw natural and commercial honey samples against *E. coli*. Both raw natural and commercial honey samples showed inhibitory effects on *E. coli*. Commercial honey showed comparable efficacy to raw, unprocessed natural honey. Honey is highly recommended for wound management due to its broad-spectrum antibacterial activity against a wide range of microorganisms. Geographical and botanical sources significantly influence honey's antibacterial properties, which are also affected by other factors besides floral sources. Honey could be an alternative treatment for various microorganisms that are resistant to traditional antibiotics. The use of honey in a medical context can reduce financial costs and hospital stays. Further research efforts are encouraged to combat antibiotic resistant organisms that do not respond to conventional treatments. Furthermore, Kalidasan et al. (2017) assessed the antimicrobial activity of Kombu honey, Malan honey, and commercial honey against *E. coli*. The natural and commercial honey samples were collected from the Chetheri Malai region in Harur, Tamil Nadu, India. Kombu honey exhibited higher antimicrobial activity against bacterial pathogens than Malan honey and commercial honey.

Shalsh et al. (2021) conducted an investigation on the antimicrobial activity of local Malaysian Kelulut honey against the pathogenic *E. coli*. The results obtained emphasised the importance of different dilution levels of kelulut honey, as only the undiluted samples of both kelulut honey 1 and kelulut honey 2 were found to possess antimicrobial properties in terms of minimum bactericidal concentration. For Kelulut honey 1 and Kelulut honey 2 at concentrations of 20%, 40%, 60% and 80%, no inhibition zones were observed against *E. coli* in the agar well diffusion test. At 100% concentration, both Kelulut honey 1 and 2 showed inhibition zones against E. coli. This was only observed in undiluted samples.

Akyalçın and Süerdem, (2017) evaluated the antibacterial activity of six honey samples. The honey was collected from various regions in Kosovo. The study tested the honey against *E. coli* bacteria. The results showed that none of the honey samples showed any efficacy against *E. coli*. Also, Çakır and Dervişoğlu (2022) evaluated the antimicrobial effects of honeys. The honeys were from districts in Bingöl province: Yedisu, Sancak, Kiğı, and Genç. Used the disc diffusion method for their assessment. Honey samples were tested for antimicrobial activity against *E. coli*. Three concentrations were used: 500, 250, and 125 mg mL-1. Honey samples from Yedisu and Genç showed antibacterial activity against *E. coli*. This activity was observed at a concentration of 500 mg/mL. However, no activity was seen at concentrations of 250 mg/mL and 125 mg/mL.

Fratianni et al. (2023) examined five Italian organic commercial monofloral honeys. The honeys included sainfoin, carob, astragalus, indigo, and alfalfa. The ability of these honeys to inhibit *E. coli* biofilm formation was tested. The concentrations used were 10 and 20 µg/mL. Carob honey at 20 µg/mL inhibited *E. coli* biofilm development most effectively. All varieties of honey showed activity against *E. coli*, with inhibition zones ranging from 26 to 81 mm.

Gkoutzouvelidou et al. (2021) studied the antimicrobial properties of eight Lemnos honeys. The honeys were tested against *E. coli* at concentrations of 25% and 12.5%. Manuka honey was used for comparison. All Lemnos honey displayed antibacterial activity. Some samples surpassed Manuka honey's effectiveness. Lemnos honeys have great potential as natural antimicrobial agents.

Çakır et al. (2020) conducted a test on honey samples from different regions of Turkey. The purpose was to assess their antimicrobial properties against *E. coli*. Antibacterial activity was observed in Anzer honey at a concentration of 500 mg/mL. The measured inhibition zone was 6.0 ± 0.0 mm. It was determined that Gümüşhane and Zara honeys did not have any antibacterial activity at 500 mg/mL. No antibacterial activity was detected in all honey groups at a concentration of 125 or 250 mg/mL.

Zapata-Vahos et al. (2023) studied honey from two bee species. The antimicrobial properties of honey were evaluated in *Melipona eburnea* and *Apis mellifera*. The study found that both types of honey had no antimicrobial activity against *E. coli*.

Bazaid et al. (2023) tested Saudi Sidr honey's antimicrobial effects. They evaluated its impact on *E. coli*. The results indicated promising antibacterial activity of Saudi Sidr honey. It was observed that it could inhibit the formation of biofilm by *E. coli* on glass slides by approximately 61.79%. Additionally, with the increasing challenges of antibiotic resistance and the growing number of bacteria resistant to these antibiotics, the need for alternative antimicrobial treatments has become critical. Therefore, McArdle et al. (2023) investigated the use of medical-grade honey altered to environments typically found in diabetic foot ulcers and post-surgical wounds, within the pH range of 6-8. The cell survival of *E. coli* and *S. aureus* decreased by at least 10^{10} Coloni-Forming Units (CFU/ml), independent of the pH environment, and as much as 10^{12} CFU/ml depending on the pH environment ($p \leq 0.5$). *S. aureus* and *E. coli* had some bacterial survival at pH 6, 7, and 8, respectively; however, these were extremely small quantities, with all final colony counts averaging less than 10^2 CFU/ml for each experiment. No correlation or statistical significance was found between the pH environments investigated and the colony counts with small amounts of bacterial survival. Furthermore, Skadins et al. (2023) evaluated the antibacterial activity of 40 monofloral honey samples obtained from beekeepers in Latvia. The antimicrobial activity of Latvian honey samples, with an 80% honey solution w/v, was compared with commercial Manuka honey and honey analogue sugar solutions-carbohydrate mixture and tested against *E. coli*, *P. aeruginosa*, and *S. aureus*. The antibacterial effect of the samples was more pronounced on Gram-positive bacteria compared to Gram-negative bacteria. Latvian honey shows promising potential for use in wound healing biomaterials, offering the possibility of achieving long-term antibacterial effects.

The applications of honey are based on their chemical compositions, but these vary depending on geographical origins, plant sources, and bee nutrition. In this context, Kumari et al. (2023) aim to evaluate the quality of honey produced by *Apis mellifera* through stimulative diets. Initially, stimulative diets were provided to honey bees for one year, and sufficient honey samples were collected before and after the administration of stimulative diets. Subsequently, the antibacterial potential of honey samples was examined. The results indicate that post-feeding honey samples exhibit high antibacterial activity at a concentration of 800 µg/mL against *E. coli*. The study found that supplement administration, in the form of syrup (a diet containing roasted chickpeas, defatted soy flour, protein hydrolysate powder, brewer's yeast, honey, and sugar), enhances the quality of honey in terms of antioxidant and antimicrobial activities. Therefore, the possible reason for all these improvements in honey quality could be syrup supplements, which may have inductive activity to enhance the health of worker bees. Increased honey quality due to multiple ingredients might have elevated antibacterial activities.

Table 2. Antimicrobial activity of honey against *E. coli.*

***E. coli* Types**	**Honey Types**	**Concentration**	**Inhibition Zones (mm)**	**References**
E. coli ATCC 25922	Citrus-1	100%	9±0.00	Russo et al., 2023
		75%	9±2.08	
		50%	0±0.00	
		25%	0±0.00	
	Citrus-2	100%	9±1.00	
		75%	0±0.00	
		50%	0±0.00	
		25%	0±0.00	
	Citrus-3	100%	26±2.08	
		75%	26±1.00	
		50%	24±1.15	
		25%	10±1.00	
	Chestnut-1	100%	27±0.00	
		75%	24±0.58	
		50%	18±0.58	
		25%	0±0.00	
	Chestnut-2	100%	26±1.00	
		75%	24±0.58	
		50%	22±0.00	
		25%	15±0.58	
	Chestnut-3	100%	25±1.00	
		75%	23±0.58	
		50%	21±0.60	
		25%	18±0.58	
	Eucalyptus-1	100%	10±0.58	
		75%	9±0.00	
		50%	8±0.58	
		25%	7±0.00	
	Eucalyptus-2	100%	10±0.60	
		75%	10±0.00	
		50%	0±0.00	
		25%	0±0.00	
	Eucalyptus-3	100%	10±1.00	
		75%	9±0.00	
		50%	8±0.58	
		25%	8±0.58	
	Sulla-1	100%	0±0.00	
		75%	0±0.00	
		50%	0±0.00	
		25%	0±0.00	
	Sulla-2	100%	0±0.00	
		75%	0±0.00	
		50%	0±0.00	
		25%	0±0.00	
	Sulla-3	100%	18±1.00	
		75%	17±1.00	
		50%	16±1.00	
		25%	13±1.53	

Table 2. Continued.

***E. coli* Types**	**Honey Types**	**Concentration**	**Inhibition Zones (mm)**	**References**
E. coli ATCC 25922	Honey from stingless bee (*Heterotrigona itama*)	ND	Dry Season – two types of flowers: 8.67±0.58	Mahmood et al., 2021
			Dry Season – more than two types of flowers: 11.33±0.58	
			Rainy Season – two types of flowers: 0±0.00	
			Rainy Season – more than two types of flowers: 7.33±0.58	
E. coli ATCC 25922	Bitlis-1	100%	10.00±0.00	Oğur and Dayan, 2022
		50%	-	
	Bitlis-2	100%	14.00±1.10	
		50%	-	
	Bitlis-3	100%	-	
		50%	-	
	Bitlis-4	100%	13.50±0.55	
		50%	8.00±0.00	
	Bitlis-5	100%	7.00±1.00	
		50%	-	
	Bitlis-6	100%	7.50±0.55	
		50%	-	
	Bitlis-7	100%	15.00±0.00	
		50%	12.00±1.00	
	Bitlis-8	100%	9.50±2.73	
		50%	8.50±1.64	
E. coli	Dark amber	ND	12.7±1.2	Adeyemo et al., 2017
	Dark amber	ND	24.3±0.6	
	Super light amber	ND	18.7±0.6	
	Light amber	ND	22.7±1.2	
	Light amber	ND	14.0±1.7	
	Super dark amber	ND	26.3±0.6	
	Dark amber	ND	10.7±1.2	
	Super light amber	ND	6.7±1.2	
	Super dark amber	ND	28.7±1.2	
	Bitter	ND	20.0±1.0	
	Light amber	ND	26.7±1.2	
	Dark amber	ND	9.7±1.5	
	Super dark amber	ND	6.7±1.2	
	Super dark amber	ND	8.7±0.6	
E. coli	Neem	ND	22±0.5	Wadi, 2022
	Sidr	ND	20±0.5	
	Sidr	ND	24±0.5	
	Sidr	ND	19±0.5	
	Acacia	ND	20±0.5	
	Sidr	ND	19±0.5	
	Mountain	ND	20±0.5	
	Acacia	ND	25±0.4	
	Acacia	ND	22±0.5	
	Sun flower	ND	23±0.6	
	Sun flower	ND	22±0.5	
	Sun flower	ND	21±0.5	
	Sidr	ND	18±0.5	
	Sidr	ND	17±0.4	
	Unknown	ND	22±0.5	
	Sidr	ND	22±0.5	
	Orange	ND	23±0.5	
	Flowers	ND	20±0.5	
	Flowers	ND	21±0.5	
	Orange	ND	20±0.5	
	Orange	ND	21±0.5	
	Flowers	ND	22±0.5	
	Flowers	ND	20±0.5	
	Flowers	ND	21±0.5	
	Acacia	ND	22±0.6	
	Citrus	ND	21±0.4	
	Alfa	ND	22±0.5	

Table 2. Continued.

E. coli Types	Honey Types	Concentration	Inhibition Zones (mm)	References
E. coli	Alfa	ND	20±0.6	Wadi, 2022
	Citrus	ND	22±0.4	
	Sidr	ND	21±0.5	
	Sidr	ND	20±0.5	
	Sun flower	ND	22±0.4	
E. coli	Commercial	ND	17	Kalidasan et al., 2017
	Malan	ND	19	
	Kombu	ND	28	
E. coli	Kelulut-1	100%	9.3 ± 0.2	Shalsh et al., 2021
		80%	-	
		60%	-	
		40%	-	
		20%	-	
	Kelulut-2	100%	8.2 ± 0.3	
		80%	-	
		60%	-	
		40%	-	
		20%	-	
E. coli ATCC 25922	Mountain	ND	-	Akyalçın and Süerdem, 2017
	Floral	ND	-	
	Meadow flowers	ND	-	
	Pinus	ND	-	
	Floral	ND	-	
	Floral	ND	-	
E. coli ATCC 25922	Yedisu	500 mg/mL	6.0±0.0	Çakır and Dervişoğlu, 2022
		250 mg/mL	-	
		125 mg/mL	-	
	Sancak	500 mg/mL	-	
		250 mg/mL	-	
		125 mg/mL	-	
	Kiğı	500 mg/mL	-	
		250 mg/mL	-	
		125 mg/mL	-	
	Genç	500 mg/mL	6.0±0.0	
		250 mg/mL	-	
		125 mg/mL	-	
E. coli DSM 8579	Sainfoin	10 µg/mL	57.78±3.98	Fratianni et al., 2023
		20 µg/mL	60.06±2.08	
	Carob	10 µg/mL	37.69±1.57	
		20 µg/mL	81.71±1.44	
	Astragalus	10 µg/mL	32.38±1.22	
		20 µg/mL	35.70±2.45	
	Indigo	10 µg/mL	26.62±1.13	
		20 µg/mL	44.62±3.54	
	Alfalfa	10 µg/mL	45.61±2.52	
		20 µg/mL	49.91±3.45	
E. coli ATCC 43888	Lemnos-1	25%	22.0 0.0	Gkoutzouvelidou et al., 2021
		12.5%	19.3±1.2	
	Lemnos-2	25%	21.3±3.1	
		12.5%	18.7±3.1	
	Lemnos-3	25%	21.3±1.2	
		12.5%	19.3±1.2	
	Lemnos-4	25%	21.3±4.2	
		12.5%	18.3±3.5	
	Lemnos-5	25%	21.3±4.6	
		12.5%	21.0±1.4	
	Lemnos-6	25%	22.0±2.0	
		12.5%	20.0±2.0	
	Lemnos-7	25%	28.7±1.2	
		12.5%	26.0±0.0	
	Lemnos-8	25%	28.0±0.0	
		12.5%	24.7±1.2	
	Manuka	25%	28.0±0.0	

Table 2. Continued.

E. coli Types	Honey Types	Concentration	Inhibition Zones (mm)	References
E. coli ATCC 43888	Manuka	12.5%	25.0±1.4	Gkoutzouvelidou et al., 2021
E. coli ATCC 25922	Rize (Anzer)	500 mg/mL	6.0±0.0	Çakır et al., 2020
		250 mg/mL	-	
		125 mg/mL	-	
	Gümüşhane	500 mg/mL	-	
		250 mg/mL	-	
		125 mg/mL	-	
	Sivas (Zara)	500 mg/mL	-	
		250 mg/mL	-	
		125 mg/mL	-	
E. coli ATCC 25922	Monofloral and Multifloral	15 and 20 mg/mL	-	Zapata-Vahos et al., 2023

ND: Not Determined

CONCLUSION

This review aimed to examine the antibacterial activity of honey against *S. aureus* and *E. coli* bacteria. The review collected evidence that honey is effective in preventing the growth and infection of these bacteria by scanning relevant recent studies in the literature. The review examined honey's antibacterial activity mechanism, influencing factors, and applications.

The main reason for honey's ability to kill bacteria such as hydrogen peroxide, methylglyoxal, phenolic acids and flavonoids is that it contains various substances. Thanks to these substances, the replication of genetic material is disrupted. The strength of honey's ability to kill bacteria can change depending on where the honey comes from, what kind of flowers it is made from, when it is collected and how it is treated. There are important differences in how well honey can kill bacteria among different kinds of honey that are made from different kinds of flowers.

Since honey can kill bacteria such as *S. aureus* and *E. coli* well, more studies are needed to be sure about how much honey should be used, how safe it is, and what side effects it might have. It should also be checked how well honey can kill different kinds of bacteria that may have different features or ways of resisting honey. The antibacterial activity of honey in combination with other antibiotics should also be examined. The dose-response relationship of honey's antibacterial activity, optimal application method and duration, possible allergic reactions and contraindications should also be determined.

This review examines recent studies that have tested the antibacterial activity of honey against *S. aureus* and *E. coli*. It was concluded that more comprehensive and systematic studies should be carried out in order for honey to be used more in this field.

REFERENCES

Adeyemo, R. O., Torimiro, N., Akinola, S. A., Lawal, S. K., Abolarinwa, T. O. & Adewoye, W. O. (2017). Study on antibacterial effi cacy of diff erent honey types in South Western Nigeria against wound associated bacteria. *Journal of Apitherapy*, 2, 15-19.

Afroz, R., Tanvir, E. M., Zheng, W. & Little, P. J. (2016). Molecular Pharmacology of Honey. *Clinical and Experimental Pharmacology*, 06.

Akyalçın, H. & Süerdem, T. B. (2017). In Vitro Screening of Antibacterial Activity of Honey Samples Collected from Kosovo. *Journal of Scientific Perspectives*, 1, 31–40.

Almasaudi, S. B., Al-Nahari, A. A. M., Abd El-Ghany, E. S. M., Barbour, E., Al Muhayawi, S. M., Al-Jaouni, S., Azhar, E., Qari, M., Qari, Y. A. & Harakeh, S. (2017). Antimicrobial effect of different types of honey on *Staphylococcus aureus*. *Saudi Journal of Biological Sciences*, 24, 1255–1261.

Asma, S. T., Bobiş, O., Bonta, V., Acaroz, U., Shah, S. R. A., Istanbullugil, F. R. & Arslan-Acaroz, D. (2022a). General Nutritional Profile of Bee Products and Their Potential Antiviral Properties against Mammalian Viruses. *Nutrients*, 14, 3579.

Asma, S. T., Imre, K., Morar, A., Imre, M., Acaroz, U., Shah, S. R. A., Hussain, S. Z., Arslan-Acaroz, D., Istanbullugil, F. R., Madani, K., Athanassiou, C., Atanasoff, A., Morar, D., Herman, V. & Zhu, K. (2022b). Natural Strategies as

Potential Weapons against Bacterial Biofilms. *Life*, 12.

Bazaid, A. S., Alsolami, A., Patel, M., Khateb, A. M., Aldarhami, A., Snoussi, M., Almusheet, S. M. & Qanash, H. (2023). Antibiofilm, Antimicrobial, Anti-Quorum Sensing, and Antioxidant Activities of Saudi Sidr Honey: In Vitro and Molecular Docking Studies. *Pharmaceutics*, 15, 2177.

Ciupescu, L. M., Auvray, F., Nicorescu, I. M., Meheut, T., Ciupescu, V., Lardeux, A. L., Tanasuica, R. & Hennekinne, J. A. (2018). Characterization of *Staphylococcus aureus* strains and evidence for the involvement of non-classical enterotoxin genes in food poisoning outbreaks. *FEMS Microbiology Letters*, 365.

Çakır, Y., Çobanoğlu, D. N., Dervişoğlu, G., Koçyiğit, S., Karahan, D. & Yelkovan, S. (2020). Determination of Antimicrobial Activity, Palynological Characteristics and Chemical Composition of Some Honey Samples from Turkey. *Mellifera*, 20, 41-60.

Çakır, Y. & Dervişoğlu, G. (2022). Antimicrobial Effect of Honeys Collected in Bingol Region. *MAS Journal of Applied Sciences*, 7, 537–544.

Çakmak, Ö., Acaröz, U. & Gün, H. (2022). Halk Sağlığı Açısından Önemli Gıda Kaynaklı Viral Etkenler. *Veteriner Farmakoloji ve Toksikoloji Derneği Bülteni*, 13, 11–25.

David, M. Z. & Daum, R. S. (2017). Treatment of *Staphylococcus aureus* Infections. *Current Topics in Microbiology and Immunology*, 409, 325-383.

Fratianni, F., De Giulio, B., d'Acierno, A., Amato, G., De Feo, V., Coppola, R. & Nazzaro, F. (2023). In Vitro Prebiotic Effects and Antibacterial Activity of Five Leguminous Honeys. *Foods*, 12, 3338.

Gambo, S. B, Ali, M., Diso, S. U. & Abubakar, N. S. (2018). Antibacterial Activity of Honey Against *Staphylococcus aureus* and *Pseudomonas aeruginosa* Isolated from Infected Wound. *Archives of Pharmacy & Pharmacology Research*, 1, 1-6.

Gkoutzouvelidou, M., Panos, G., Xanthou, M. N., Papachristoforou, A. & Giaouris, E. (2021). Comparing the Antimicrobial Actions of Greek Honeys from the Island of Lemnos and Manuka Honey from New Zealand against Clinically Important Bacteria. *Foods*, 10, 1402.

Kalidasan, G., Saranraj, P., Ragul, V. & Sivasakthi, S. (2017). Antibacterial Activity of Natural and Commercial Honey-A Comparative Study. *Advances in Biological Research*, 11, 365-372.

Kara, R., Acaröz, U., Gürler, Z., Soylu, A. & Küçükkurt, O. (2019). Taze Marul Örneklerinde *Esherichia coli* O157 ve *Listeria monocytogenes* Varlığının Belirlenmesi. *Avrupa Bilim ve Teknoloji Dergisi*, 16, 870–873.

Karaynir, A. (2021). Çevresel Örneklerden *Escherichia coli* DH10B Suşuna Karşı Litik Bakteriyofaj İzolasyonu ve Klinik *Escherichia coli* Suşlarına Karşı Etkinliklerinin Belirlenmesi. Aydın, Turkey, Thesis of MSc, AMU, diss.

Küçükbüğrü, N. & Acaröz, U. (2020). Gıdalarda Antibiyotik Kalıntıları ve Halk Sağlığına Etkileri. *Veteriner Farmakoloji ve Toksikoloji Derneği Bülteni*, 11, 161–167.

Kumari, I., Hajam, Y. A., Thiyagarajan, K., Giri, A. & Kumar, R. (2023). Evaluation of antioxidant and antibacterial potential of honey produced from stimulative diet fed bee colonies. *Discover Sustainability*, 4.

Mahmood, A. L., Lani, M. N., Hassan, Z., Razak, S. B. A. & Ahmad, F. T. (2021). Antioxidant and antimicrobial properties of Indo-Malayan stingless bee (*Heterotrigona itama*) honey from different seasons and distribution of flowers. *Food Research*, 5, 498–507.

McArdle, C., Coyle, S. & Santos, D. (2023). The impact of wound pH on the antibacterial properties of Medical Grade Honey when applied to bacterial isolates present in common foot and ankle wounds. An in vitro study. *Journal of Foot and Ankle Research*, 16.

Mundo, M. A., Padilla-Zakour, O. I. & Worobo, R. W. (2004). Growth inhibition of foodborne pathogens and food spoilage organisms by select raw honeys. *International Journal of Food Microbiology*, 97, 1–8.

Oğur, S. & Dayan, Y. (2022). Antimicrobial activities of natural honeys and royal jellys on some pathogenic bacteria. *BAUN Fen Bilimleri Enstitüsü Dergisi*, 24, 672–689.

Postali, E., Peroukidou, P., Giaouris, E. & Papachristoforou, A. (2022). Investigating Possible Synergism in the Antioxidant and Antibacterial Actions of Honey and Propolis from the Greek Island of Samothrace through Their Combined Application. *Foods*, 11, 2041.

Ro Me Busserolles, J., Gueux, E., Rock, E., Mazur, A. & Rayssiguier, Y. (2002). Substituting Honey for Refined Carbohydrates Protects Rats from Hypertriglyceridemic and Prooxidative Effects of Fructose. *The Journal of Nutrition*. 132, 3379-3382.

Russo, N., Di Rosa, A. R., Pino, A., Mazzeo, G., Liotta, L., Caggia, C. & Randazzo, C. L. (2023). Assessment of sensory properties and in vitro antimicrobial activity of monofloral Sicilian honey. *Food Bioscience*, 52, 102449.

Segueni, N., Boutaghane, N., Asma, S. T., Tas, N., Acaroz, U., Arslan-Acaroz, D., Shah, S. R. A., Abdellatieff, H. A., Akkal, S., Peñalver, R. & Nieto, G. (2023). Review on Propolis Applications in Food Preservation and Active Packaging. *Plants*, 12.

Shah, T., Ali, N., Shah, Z. & Hayat, A. (2017). Antibacterial Activity of Pakistani Honey. *Pakistan Journal of Scientific and Industrial Research Series B: Biological Sciences*, 2, 97-100.

Shalsh, F. J., Khalaf, A. M., Hafiz, M. & Al-Sultan, I. I. A. (2021). Antibacterial Properties of Local Malaysian *Trigona Sp*. Honey Towards Different of Pathogenic Bacteria in vitro. *Diyala Agricultural Sciences Journal*, 13, 1-9.

Shamala, T. R., Shri Jyothi, Y. & Saibaba, P. (2000). Stimulatory effect of honey on multiplication of lactic acid bacteria under in vitro and in vivo conditions. *Letters in Applied Microbiology*, 30, 453–455.

Skadins, I., Labsvards, K. D., Grava, A., Amirian, J., Tomsone, L. E., Ruško, J., Viksna, A., Bandere, D. & Brangule, A. (2023). Antimicrobial and Antibiofilm Properties of Latvian Honey against Causative Agents of Wound Infections. *Antibiotics*, 12, 816.

Suerdem, T. B. & Akyalçın, H. (2018). Screening of antimicrobial and antioxidant activity of different types of honey samples obtained from Geyikli (Çanakkale) province. *Communications Faculty of Science University of Ankara Series C Biology Geological Engineering and Geophysical Engineering*, 27, 69–78.

Wadi, M. A. (2022). In Vitro Antibacterial Activity of Different Honey Samples against Clinical Isolates. *BioMed Research International*, 2022, 1-8.

Yılmaz, E. Ş. & Aslantaş, Ö. (2017). Antimicrobial resistance and underlying mechanisms in *Staphylococcus aureus* isolates. *Asian Pacific Journal of Tropical Medicine*, 10, 1059–1064.

Zapata-Vahos, I. C., Henao-Rojas, J. C., Yepes-Betancur, D. P., Marín-Henao, D., Giraldo Sánchez, C. E., Calvo-Cardona, S. J., David, D. & Quijano-Abril, M. (2023). Physicochemical Parameters, Antioxidant Capacity, and Antimicrobial Activity of Honeys from Tropical Forests of Colombia: *Apis mellifera* and *Melipona eburnea*. *Foods*, 12, 1001.

Zeaki, N., Johler, S., Skandamis, P. N. & Schelin, J. (2019). The Role of Regulatory Mechanisms and Environmental Parameters in *Staphylococcal* Food Poisoning and Resulting Challenges to Risk Assessment. *Frontiers in Microbiology*, 10, 1307.

Zhao, Y., Zhu, A., Tang, J., Tang, C. & Chen, J. (2017). Identification and measurement of staphylococcal enterotoxin M from *Staphylococcus aureus* isolate associated with staphylococcal food poisoning. *Letters in Applied Microbiology*, 65, 27–34.