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Study of the inhibitory ability of honey against some types of gram-positive and gram-negative bacteria

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Abstract: The objective of this research was to examine the antimicrobial properties of a honey sample against specific microbial isolates. Various concentrations (50% and 100%) of the honey sample were evaluated for their antimicrobial effects on several medically significant microorganisms, including Escherichia coli and Staphylococcus aureus. The minimum inhibitory concentrations (MIC) of the honey sample were established for the selected microorganisms through the diffusion method. The honey sample exhibited an inhibitory effect in vitro at both 50% and 100% concentrations on the different microorganisms studied. The findings indicate that honey possesses antimicrobial properties similar to those of antibiotics, demonstrating sensitivity in certain organisms and offering a potential alternative treatment against specific bacterial infections. Additionally, it has been shown to exert antimicrobial activity against a wide range of bacteria, encompassing both gram-positive and gram-negative strains.

Keywords: E. coli, Staphylococcus aureus, Honey, antibacterial activity of honey, Tobruk university.

دراسة القدرة التثبيطية للعسل تجاه بعض أنواع البكتيريا موجبة الجرام وسالبة الجرام

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المستخلص: هدفت هذه الدراسة إلى دراسة النشاط المضاد للميكروبات لعينة العسل ضد بعض العزلات الميكروبية. تم فحص تركيزات مختلفة (50 و 100٪) من عينة العسل بحثًا عن أنشطتها المضادة للميكروبات، باستخدام بعض الكائنات الحية الدقيقة المهمة طبيًا بما في ذلك الإشريكية القولونية والمكورات العنقودية الذهبية. تم تحديد الحد الأدنى من التركيزات المثبطة (MIC) لعينة العسل على الكائنات الحية الدقيقة المختارة باستخدام تقنية الانتشار. أظهرت عينة العسل تأثيرًا مثبطًا في المختبر عند تركيز 50 و 100٪ على الكائنات الحية الدقيقة المختلفة التي تم التحقيق فيها. تُظهر الدراسة أن العسل، مثل المضادات الحيوية، يحتوي على كائنات حية معينة حساسة له، ويوفر علاجًا بديلاً ضد بعض البكتيريا، كما ثبت أن له تأثيرًا مضادًا للميكروبات ضد مجموعة واسعة من البكتيريا (سواء كانت موجبة أو سالبة الجرام).

الكلمات المفتاحية: الإشريكية القولونية، المكورات العنقودية الذهبية، العسل، النشاط المضاد للبكتيريا في العسل، جامعة طبرق.

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Introduction:

Gram-negative Escherichia coli is capable of surviving on a broad range of substrates. The habitat of E. coli is determined by the nutrients that are available in the host species' intestine. E. coli's primary niche is the gastrointestinal (GI) tract of humans and many other warm-blooded animals. Warm-blooded animal intestines and the environment (soil, sediment, and water) are its two main habitats, and they differ greatly in terms of physical conditions, nutrient availability, and range. E. Coli and its host develop a reciprocal interaction.

Paraphrased Text: E. coli in the colon produces K and B complex vitamins and defends the gastrointestinal tract against colonization by harmful microorganisms, while the host provides an ecological habitat and nutrients. E. coli is the most prevalent type of facultative anaerobes in the intestine, making up approximately 0.1% of the gut microbiome (Eckburg PB, Bik EM., et al. 2005). Escherichia coli bacteria are a part of the normal flora in the intestine, but certain strains can lead to various illnesses in humans if they emerge in diverse environments of the human body, and some strains of Escherichia coli can exist. Within the gastrointestinal tract, particularly the intestine, the pathogen, which exists external to the intestine, is known as the group of Escherichia coli, the pathogen external to the intestine (Korzeniewska E, Korzeniwska A., et al, 2013). One of its variations may exist in the gastrointestinal tract, yet it does not result in any disease in the intestinal area (Nielsen, K.L., Dynesen, P., et al 2014). Escherichia coli is among the most significant agents of infections (Bexiga, R. Koskinen, M.T., et al 2011), and the leading cause of loose stools in children globally. Various distinct medical syndromes accompany infections with diarrhea-inducing Escherichia coli strains, such as traveler's diarrhea (Escherichia coli enteritis), bloody colitis, hemolytic uremic syndrome (Escherichia coli hemorrhagic enteritis), chronic diarrhea (Escherichia coli enteritis), and watery diarrhea in infants (Escherichia coli enteritis) (Drasar B S, Hill M J,1974). The clinical significance has grown due to the severe harm it inflicts in healthcare settings (Bexiga, R; Koskinen, M.T., et al 2011), and because it possesses numerous pathogenic factors that qualify it in injury incidents (Pena, I; Picazo, J.J., et al 2014).

As a Gram-positive bacterium with a diameter of 1 μm, Staphylococcus aureus is the most virulent and harmful staphylococci for humans. It belongs to the genus Staphylococcus. Since S. aureus is one of the most prevalent bacteria that cause nosocomial infections, it is very important in human pathology because of its aggressiveness and resistance to conventional medications (Ouidri, 2018). According to Onyeagwara et al. (2014), S. aureus is a major contributor to deep-seated infections like osteomyelitis and endocarditis, as well as superficial skin lesions like boils and furunculosis and acute infections like pneumonia and UTIs.

Bloodstream infections are frequently caused by S. aureus, which can have a 20% mortality rate (Salas et al., 2017). According to David and Daum (2010), S. aureus is also a major contributor to both hospital-associated (HA) and community-associated (CA) bacterial infections in humans. It is linked to a variety of mild skin and soft tissue infections, as well as potentially fatal conditions like sepsis, pneumonia, bacteremia, osteomyelitis, endocarditis, and toxic shock syndrome. Because of its capacity to spread from patient to patient, methicillin-resistant S. aureus (MRSA) is regarded as one of the most nosocomial pathogens of major worldwide importance infections. It is also a growing source of

community-acquired infections that result in significant morbidity and mortality (Behzad et al., 2015).

phylococcus aureus can inhabit the human body as a component of the normal microbiota. Approximately 30% of individuals carry S. aureus, predominantly in the anterior nares (Akmatov et al., 2010). The anterior nares serve as a primary site for the colonization of this bacterium, and the prevalence of skin carriage is influenced by nasal colonization (Ouidri, 2018). The association between nasal carriage of S. aureus and the occurrence of Staphylococcal diseases was initially documented by Danbolt in 1931, who investigated cases of furunculosis. The presence of methicillin-resistant Staphylococcus aureus (MRSA) in the nasal passages has been recognized as a significant risk factor for surgical site infections. When left untreated, MRSA can lead to mucopurulent crusting and discharge in patients, adversely impacting postoperative recovery in those undergoing Otorhinolaryngology procedures (Onyeagwara et al., 2014). Fleming uncovered penicillin in the 1940s and initiated the period of antibiotics for treating infections (Klevens et al., 2007; Klein et al., 2017). During that time, the infectious diseases caused by S. aureus were effectively managed, but with the extensive use of penicillin in the 1950s, penicillin-resistant S. aureus emerged in clinical settings (Rayner and Munckhof, 2005; Pichereau and Rose, 2010). Penicillin-resistant S. aureus can generate penicillinase, which has the ability to break down the penicillin b-lactam ring, resulting in resistance to penicillin. Subsequently, researchers created a new penicillinase-resistant semisynthetic penicillin called methicillin, which is immune to the hydrolysis of b-lactamase (Rayner and Munckhof, 2005; Khoshnood et al., 2019). After its introduction to clinical use in 1959, methicillin successfully managed the infection of penicillin-resistant S. aureus (Chambers and Deleo, 2009; Jokinen et al., 2017).

However, a British scientist named Jevons reported isolating an MRSA strain in 1961, just a few years after methicillin was used. This resistance was caused by a gene that encoded the penicillin-binding protein 2a or 2′ (PBP2a or PBP2′) (mecA), which was incorporated into the methicillin-sensitive S. aureus chromosomal element (SCCmec) (Schulte and Munson, 2019). Furthermore, in many regions of the world, including Europe, the US, North Africa, the Middle East, and East Asia, MRSA has quickly emerged as the most common resistant infection found (Mediavilla et al., 2012; Lakhundi and Zhang, 2018). MRSA is divided into two categories based on its initial source: community-acquired MRSA (CAMRSA) and hospital-acquired MRSA (HA-MRSA) (Lindsay, 2013; Otto, 2013). Hospital-acquired MRSA has increased to 50.4% in China (Shang et al., 2016). Furthermore, according to the US Centers for Disease Control (CDC), the fatality rate from MRSA infection has surpassed that of AIDS, Parkinson's disease, and homicide (Lessa et al., 2012). Therefore, the study of S. aureus's molecular traits, which are now the subject of international public health concerns, can aid in understanding the bacteria's prevalence, tracking its evolution, identifying new molecular traits, and providing data for the development of innovative anti-S. aureus medications.

Because it contains nutrients that are beneficial to the body, like carbohydrates, of which fructose, glucose, and sucrose constitute 85% to 95% of the total, honey is a vital food item for humans (White, 1993). Aside from trace amounts of other acids, proteins, vitamins, enzymes, minerals, pollen, fungus remnants, algae, yeasts, and other solid components like

wax, honey also contains water and a small percentage of formic acid (Alamanni et al., 1992).

Van Ketel was the first to identify honey's antibacterial properties in 1892 (Dustmann, 1979). Honey comes from a variety of sources, and depending on where it comes from and how it is processed, its antibacterial action varies significantly (Molan, 1992). Many cultures have historically utilized honey as a medication (Quinn et al., 1994). The medical community has rediscovered it, and it is becoming more widely accepted as an antibacterial treatment for topical infections brought on by burns and wounds (Abuharfeil et al., 1999). Honey has been shown in numerous investigations to have antibacterial properties (Dustmann, 1979; Molan, 1992). According to recent reports, honey has the ability to limit the growth of some harmful vegetative microorganisms (Chick and Shin, 2001) and kill about 60 different types of bacteria, including gram-positive and gram-negative aerobes and anaerobes (Molan, 1992). All of the common dermatophytes (Brady et al., 1997) and certain yeasts and species of Aspergillus and Penicillium have also been shown to have an antifungal effect (Quinn et al., 1994). A combination of low water activity and high osmotic pressure gives honey its intrinsic antibacterial qualities. The low water activity of honey inhibits the growth of most bacteria, as well as many yeasts and molds. When administered topically to wounds, osmosis should suck water from the wound into the honey, reducing bacterial development and drying the affected tissue.

Honeys are expected to maintain a water activity low enough to prevent the growth of the majority of bacteria, even when diluted with water absorbed from wounds. With a pH of 3.2 to 4.5, honey has a mildly acidic pH. The oxidation of glucose to gluconic acid is catalyzed by the enzyme glucose oxidase, which bees secrete. The low pH of honey alone inhibits many pathogenic bacteria and may be enough to have an inhibitory effect, at least in topical applications (Molan, 1995). The aim of this study was to investigate the antimicrobial activity of honey sample against certain microbial isolate.

Materials and Methods:

Materials

1.1. Glassware:

1. Beakers
2. cylinder
3. Bunsen burner
4. flask
5. petri dishes
6. plastic loop

1.2. Equipment

1.Autoclave
2.Hot air oven
3.Incubator
4.Magnetic stirrer
5.Sensitive balance
6.micropiptte

1.3. Materials used:

1. Bees honey

2. distilled water

1.4. culture media

1.nutrient agar

1.5. tested bacterial samples

Gram-positive bacteria (Staphylococcus aureus), and gram- negative bacteria (Escherichia coli) were used as the tested organisms which included .(Source: Tobruk medical centre)

Test

First, sterilization: Aldalel Laboratory provided ready-to-use, sterile culture media. The glassware, on the other hand, was cleaned with distilled water and then sterilized in a hot oven set at 180 C. The work surface was sterilized with alcohol, and the job was done close to the flame.

Second: natural honey (spring honey) was obtained from one of the bee farms in the city of Tobruk. The research was conducted using two concentration of honey 50% and 100%

***100% concentration:** uses undiluted honey.

***50% concentration:** add 50ml of honey to a sterilized beaker and add 50ml of distilled water to it mix until water and honey mix.

Thirdly, the zone of inhibition was determined by pipetting 0.5 ml of honey at 100% and 50% concentration into each 6-mm-diameter well of the bacterial culture media. For 18 to 24 hours, the plates were incubated at 37 °C. By measuring the diameters of zone inhibition surrounding the crude extracts, the antibacterial activity was assessed. Millimeters were used to measure th**e inhibition zones.**

The assay was carried out using the broth microdilution method and the agar well diffusion method to determine the inhibition zone.

Statistical analysis

MINITAB (Version 14) was used to analyze all of the data. To determine whether the data were normal, the Anderson-Darling test was used. The findings were deemed significant at α=0.05. T. The test was performed to identify which bacteria were most resistant to honey and to find out how varying quantities of honey affected each bacterium.

Result and Discussion

The effect of the 100%,50% concentration of honey:

The results of the study demonstrated that honey may prevent the growth of both of the study's bacterial species. Additionally, it demonstrated that the impact of honey on the two concentrations of E. coli bacteria (100%, 50%) did not differ significantly (T. test, t5 =1.12, P=0.312). Moreover, average concentrations of 50% and 100% (18.75 and 14.50) are shown in Figure1.

The results indicated that, similar to Staphylococcus aureus, there was no significant difference in the impact of honey on the average concentrations of 50% and 100% (11.00, 16.25) and both concentrations (100%, 50%) (T. test, t5 = -1.62, P=0.167) (Fig 2). Additionally, the findings indicate that the effects of the two bacterial species utilized in the study were not significantly different at 50% honey concentration (T. test, t5 = 1.89, P=0.117) and 100% honey concentration (T. test, t5 = -0.61, P=0.567).(Figures 3 and 4).

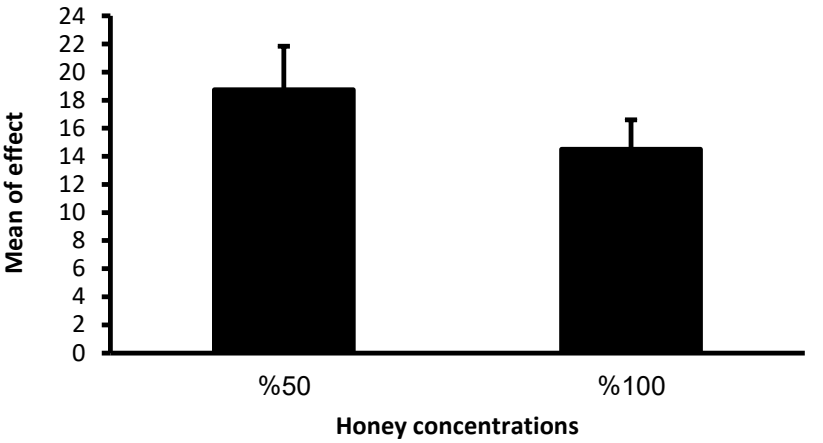


Figure 1. Mean (±SE) the ability to discourage honey in 50 % and 100 % concentrations to prevent the growth of *E.coli* bacteria.

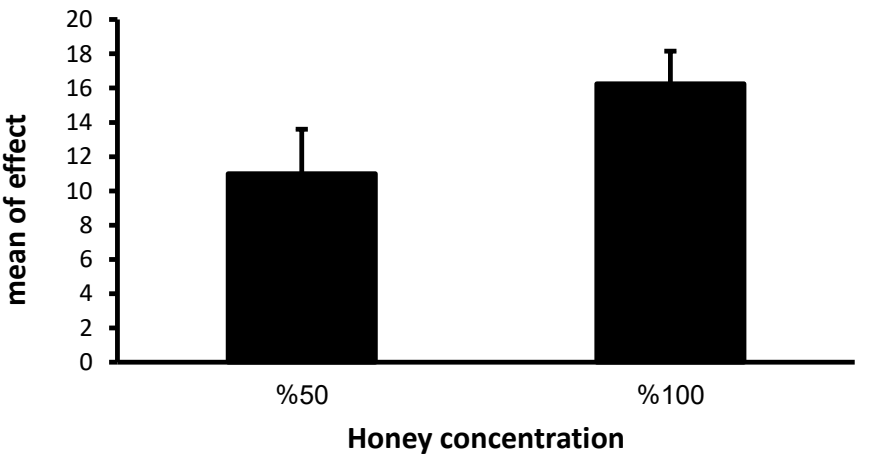
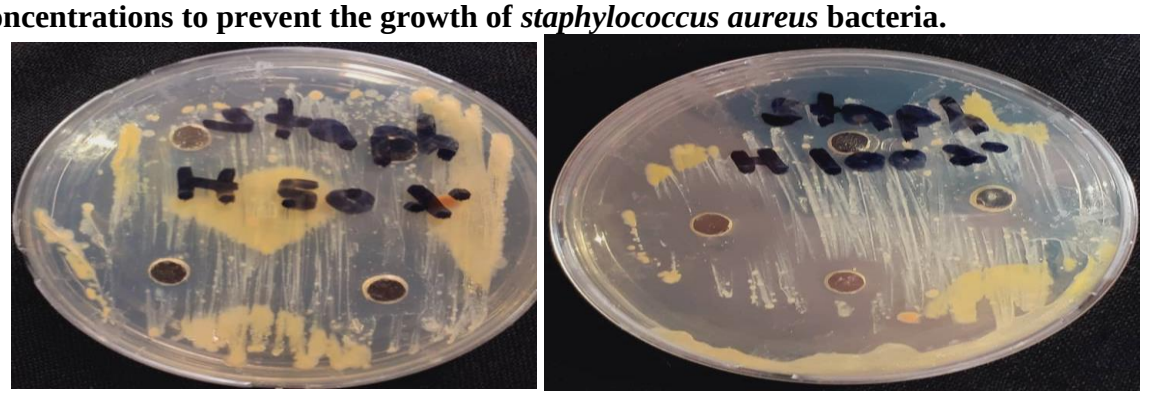


Figure 2. Mean (±SE) the ability to discourage honey in 50 % and 100 % concentrations to prevent the growth of *staphylococcus aureus* bacteria.



(A) (B)

Figure (3). The inhibition area of *staphylococcus aureus* bacteria treated with (A: 50 % concentration of honey , B : 100% concentration of honey).

(A) (B)

Figure (4). The inhibition area of E. *coli* bacteria treated with (A: 50 % concentration of honey, B: 100% concentration of honey).

Since ancient times, people have been aware of honey's sanctity. The Holy Qur'an mentions honey in Surat Al-Nahl (verses 68 and 69), and Allah Almighty describes it as a healing substance for humans. For Muslims, honey is a valuable material that can treat a variety of illnesses. According to our research, honey at 50% and 100% concentrations has a strong inhibitory effect on the growth of the study's bacteria. Our findings agreed with those of Bilal et al. and Wi11ix et al. (1992), who discovered that honey suppressed the growth of S. aureus, E. coli, and Pseudomonas sp.

(1998) discovered that honey had a respectable level of antimicrobial action against both Gram-positive and Gram-negative bacteria, with P. aeruginosa and S. aureus showing particularly strong activity. The study's findings on antimicrobial activity against S. aureus are consistent with those of Molan (1992), who discovered that S. aureus is among the bacterial species most vulnerable to honey's antibacterial properties. These could result from the osmotic effect, the pH effect, and the organisms' susceptibility to hydrogen peroxide, which is an "inhibin" component of honey (Postmes et al., 1993).

The study's findings suggest that one of the primary factors inhibiting the growth of bacteria in high concentrations of honey is the sugar components inside it. The majority of research worldwide has confirmed that the percentage of sugars in alfalfa, alfalfa, and eucalyptus honey is 75%, 77%, and 76%, respectively, as reported in the previously cited study. The other significant factor, which has been supported by numerous research, is that natural honey contains antibacterial compounds that aid in preventing the proliferation of bacteriophages (Kiprianovska et al., 1998).

Apart from the reasons stated above, honey's high acidity could be an additional factor. In addition to the previously mentioned aspects, studies have demonstrated that honey's strong acidity plays a part in preventing bacterial growth (Molane et al., 1988). The action of enzymes secreted by bee workers on the nectar when it is transformed into mature honey, such as Glucosoxidase enzyme, in addition to the action of other enzymes during the ripening process, produces this high acidity in honey, which has a significant impact on inhibiting the growth of bacteria (Ruiz-Argues and Rodriguz-Navarro, 1973).

The fact that honey comes from plants, like in the case of the honey sample, is another reason that might be crucial in paving the way for further research. According to the

findings, this study has a great capacity to stop bacterial growth since it has a number of compounds, including phenols, which have antibacterial properties. Here, honey's high potential to block the growth of bacteria and other pathogens may have come from its plant source. According to (Mandal MD, Mandal S, 2011), the primary cause of the proliferation of E. coli bacteria in honey at low concentrations is the honey's decreased acidity and low sugar content.

Conclusion

The most common cause of diarrhea in children worldwide is Escherichia coli, a serious bacteria linked to infections. Because of its virulence and resistance to common medications, Staphylococcus aureus is a common pathogen that causes hospital-acquired infections, making it a particularly significant bacterium for human health. The antibacterial action of honey varies significantly depending on where it comes from and how it is processed. Numerous cultures have historically utilized honey as a remedy. Both Gram-positive and Gram-negative bacteria were susceptible to honey's reasonably strong antibacterial action, with P. aeruginosa and S. aureus showing particularly strong activity.

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