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Effectiveness of the Antibiotics Ciprofloxacin and Erythromycin on Staphylococcus aureus Bacteria Isolated from Various Infection Sources

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Abstract: This study aimed to test the Effectiveness of the Antibiotics Ciprofloxacin and Erythromycin on Staphylococcus aureus Bacteria Isolated from Various Infection Sources such as wounds, burns, and urine, using these antibiotics to treat infections caused by these bacteria, mitigate their negative effects on patients, and prevent the occurrence of chronic infections. S. aureus bacteria are characterized by their gram-positive spherical cells and absence of spores or capsules. When grown on blood agar medium, colonies appear circular, slightly convex, with a smooth surface and a halo of β -hemolysis. The optimal temperature for their growth is 37°C. When grown on mannitol salt agar, the medium turns golden yellow due to mannitol fermentation. Twenty-four samples of S. aureus bacteria were obtained, constituting 24% of the total samples, including 5 samples from wounds, 15 from burns, and 4 from urine from Baqubah General Hospital and Muqdadiyah General Hospital. The results showed that 37.5% of the isolates were resistant to ciprofloxacin, 33.33% were sensitive, and 29.16% showed intermediate resistance. Regarding erythromycin, 33.33% of the isolates were resistant, 50% were sensitive, and 16.66% showed intermediate resistance. The study results indicated that some bacterial isolates were resistant to antibiotics, necessitating the use of antibiotic sensitivity tests prior to prescription and the development of new antibiotics. Based on the results, the researchers recommended the development of a rapid and accurate diagnostic technique for S. aureus using nanotechnology or artificial intelligence, and exploring the use of alternative therapies such as beneficial bacteria therapy or immunotherapy to treat antibiotic-resistant S. aureus infections. The research provides recent data on S. aureus antibiotic resistance in the region and contributes to improving treatment protocols and reducing the risk of chronic infection.

Keywords: Staphylococcus aureus bacteria, antibiotic sensitivity, ciprofloxacin, erythromycin.

فعالية المضادين الحيويين سيبروفلوكساسين وإريثروميسين على بكتيريا المكورات العنقودية الذهبية المعزولة من مصادر إصابة مختلفة [(1)]

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المستخلص: هدفت هذه الدراسة إلى اختبار فعالية المضادين الحيويين سيبروفلوكساسين (Ciprofloxacin) وإريثرومايسين (Erythromycin) على بكتيريا المكورات العنقودية الذهبية (Staphylococcus aureus) المعزولة من مصادر إصابة مختلفة، مثل الجروح والحروق والأدرار، باستخدام هذين المضادين لعلاج الالتهابات التي تسببها هذه البكتيريا والحد من آثارها السلبية على المرضى ومنع حدوث الالتهابات المزمنة، تمتاز بكتيريا S. aureus بخلاياها الكروية موجبة لصبغة جرام، وعدم احتوائها على أسواط أو أبواغ. عند نموها على وسط أكار الدم، تظهر مستعمرات دائرية، محدبة قليلاً، وذات سطح أملس مع هالة تحلل من نوع β -hemolysis . درجة الحرارة المثلى لنموها هي 37°م. عندما تُنمّى على وسط أكار المانيتول الملحي، يتحول الوسط إلى اللون الأصفر الذهبي نتيجة لتخمر سكر المانيتول، تم الحصول على 24 عينة من بكتيريا S. aureus بنسبة 24% من مجموع العينات، تضمنت 5 عينات من الجروح، 15 من الحروق، و4 من الأدرار من مستشفى بعقوبة العام ومستشفى المقدادية العام. أظهرت النتائج أن 37.5% من العزلات كانت مقاومة لسيبروفلوكساسين، و33.33% كانت حساسة، و29.16% كانت متوسطة المقاومة. بالنسبة لإريثروميسين، كانت 33.33% من العزلات مقاومة، و50% حساسة، و16.66% متوسطة المقاومة، أظهرت نتائج الدراسة أن بعض العزلات البكتيرية مقاومة للمضادات الحيوية، مما يستدعي استخدام اختبارات حساسية المضادات قبل وصفها وتطوير مضادات حيوية جديدة، بناء على النتائج أوصت الباحثات بتطوير تقنية تشخيصية سريعة ودقيقة لـ S. aureus باستخدام تقنيات النانو أو الذكاء الاصطناعي، واستكشاف استخدام العلاجات البديلة مثل العلاج بالبكتيريا المُفيدة أو العلاج المناعي لعلاج عدوى S. aureus المقاومة للمضادات الحيوية. يُقدم البحث بيانات حديثة حول مقاومة S. aureus للمضادات الحيوية في المنطقة، كما يُساهم البحث في تحسين بروتوكولات العلاج وتقليل خطر العدوى المزمنة.

الكلمات المفتاحية: بكتيريا المكورات العنقودية الذهبية، حساسية المضادات الحيوية، سيبروفلوكساسين، إريثروميسين

Introduction.

S.aureus bacteria are characterized by having spherical cells that are Gram positive, non-flagellated, and non-motile. In addition, they do not produce spores and are positive for the enzyme catalase and the clotting factor Coagulast. It is found mainly on the skin and nasal mucosa of most healthy individuals (Myles and Datta., 2012). It is also found in wounds, burns, and blood. Disease-causing agents inhabit healthy people as a natural habitat without causing symptoms or illness (Al-Rasheed and Al-Hussein, 2021). When S.aureus bacteria grow on blood culture media, the colonies appear circular, slightly raised, and convex, and have smooth surfaces. They are also distinguished by their shiny pigment surrounded by a halo of decay. Of the β-heamolysis type, the optimal temperature for its growth is when grown on mannitol salt agar medium. We notice the color of the medium changing from pink to golden yellow due to the presence of the red phenol reagent. This indicates the ability of these bacteria to ferment mannitol sugar (Al-Saadi et al., 2014).

Staphylococcus aureus is a frequent cause of clinically significant infections ranging in severity from mild infection to severe invasive disease (Deng et al., 2014). S. aureus causes wound infections and bloodstream infections, and is considered an opportunistic pathogen that infects humans and naturally colonizes various areas of the body, such as the nose, ears, respiratory tract, and skin, direct contact with an infected person, or an object contaminated with bacteria, or inhaling cough or sneeze droplets containing bacteria.. It also infects animals, and is considered one of those infections that come from hospitals, (Jassem and Al-Zubaidi, 2021) indicated that infection with this type of bacteria occurs as a result of its entry through wounds and burns into the body's tissues or through its contact with the surface of the host's skin tissue, as it causes disorder and imbalance in these tissues due to its secretion of many enzymes such as the lipase enzyme, which works On the breakdown of fats. The enzyme hyaluronidase, which helps bacteria spread and destroy the basic substance of connective tissue. Protease enzyme, which breaks down peptides. Skin infections or infections are the most common form of Staphylococcus aureus infection. This bacterium has the ability to produce many virulence factors that help it escape the host's defenses and thus enable it to invade and infect. These factors include staphylokinase, protease, in addition to sometimes possessing certain mechanisms such as a capsule. and the ability to produce biofilms that facilitate their adhesion to host epithelial cells (Ana et al., 2020). And also the enzyme hemolysin, which works to attack cells, damage platelets, destroy lysosomes, and necrosis (Imanishi et al., 2019). The pathogenicity of S. aureus bacteria reaches approximately 80% of the purulent diseases recorded in medical health centers located all over the world, especially patients in hospitals who suffer from weakness in the body's defense mechanisms (Zhu et al., 2014). These bacteria have the ability to produce a biofilm, in addition to the sticky layer, which contributes to providing them with protection from the body's defenses. It also helps them to adhere to various living and non-living surfaces, where they work to form colonies that enable them to penetrate wounds and burns and thus enter the damaged tissues and work. It causes serious infections that often lead to death (Prasad et al., 2012).

Staphylococcus aureus (S. aureus) infections are among the most common and widespread bacterial infections worldwide, causing a wide range of diseases, including skin and soft tissue infections, pneumonia, bloodstream infections, and healthcare-associated infections. Antibiotic resistance poses a growing threat to public health, as antibiotics lose their effectiveness against these bacteria, making infections more difficult to treat.

Research Problem:

The research problem lies in the need to evaluate the effectiveness of the antibiotics Ciprofloxacin and Erythromycin against S. aureus strains isolated from different infection sources.

Research Questions:

1- What is the effectiveness of Ciprofloxacin and Erythromycin against S. aureus strains isolated from different infection sources؟
2- Does the effectiveness of Ciprofloxacin and Erythromycin differ against antibiotic-resistant S. aureus strains؟
3- What are the potential side effects of Ciprofloxacin and Erythromycin when used to treat S. aureus infections؟
4- What factors influence the effectiveness of Ciprofloxacin and Erythromycin against S. aureus؟

Research Objectives:

1- To evaluate the effectiveness of Ciprofloxacin and Erythromycin against S. aureus strains isolated from different infection sources.
2- To compare the effectiveness of Ciprofloxacin and Erythromycin against antibiotic-resistant S. aureus strains.
3- To determine the potential side effects of Ciprofloxacin and Erythromycin when used to treat S. aureus infections.
4- To investigate the factors that influence the effectiveness of Ciprofloxacin and Erythromycin against S. aureus.

Significance of the Research:

- **Scientific Aspects:**
  - The research will contribute to a better understanding of the mechanisms of S. aureus antibiotic resistance.
  - It will help identify the most effective antibiotics for treating S. aureus infections, especially in the face of worsening antibiotic resistance.
  - It will contribute to the development of new treatment strategies for S. aureus infections.
- **Practical Aspects:**
  - The research findings will provide valuable information to physicians, nurses, and other healthcare providers when selecting appropriate antibiotics for treating S. aureus infections.
  - It will help improve the treatment outcomes for patients with S. aureus infections.

- It will contribute to reducing the spread of S. aureus infections, especially in healthcare settings.

- Application Aspects:
  - The research findings can be used to develop new treatment protocols for S. aureus infections.
  - The research findings can be used to develop prevention programs for S. aureus infections.
  - The research findings can be used to develop new diagnostic tools for S. aureus infections.

2-Materials and methods:

(24%) samples were collected out of a total of (100) samples, at a rate of (24%) from various sources of injuries and from both sexesby using special isolation media (Swap Media or transport media) to transport the bacteria to the laboratory until they are cultured. It is a sterile cotton transport media containing a substance that prevents it from being destroyed until it is cultured, but for a period not exceeding 18 hours after which it was transferred to the laboratory and cultured on a saline-mannitol medium for confirmation. From the presence of bacterial growth, the samples were examined microscopically under an electron microscope and by examining the coagulase enzyme. Samples were collected from patients with wounds, burns, and urinary tract infections from patients hospitalized in Baquba General Hospital and Al-Muqdadiya General Hospital after official approvals had been obtained and under the supervision of a specialist doctor. Swabs were taken from patients of both sexes using special isolation media (Swap Media or transport media) for transfer. Bacteria are transported to the laboratory to be grown on special culture media. It is a sterile transport medium containing a substance that prevents the destruction of bacteria until they are cultivated, but for a period not exceeding 18 hours, after which the samples were transferred to the laboratory and cultured on a saline mannitol medium to confirm the presence of bacterial growth. The samples were examined microscopically under an electron microscope and the coagulation enzyme for diagnosing bacteria was examined.. Samples were taken from wounds, burns, and urine injuries, and were transferred in a special transport medium, then cultured on mannitol saline medium, and then incubated upside down. After the end of the incubation period, the medium was observed to turn from pink to yellow. After that, microscopic examination and Coagulase test were performed to confirm the diagnosis. (24%) samples were obtained out of a total of (100) samples (24%) from various sources of infections, as the results appear in Table (1).

Table (1) Common variance by source

N	Source of isolates	Number	Percentage
1	Wounds	5	20.83%
2	Burns	15	62.5%
3	Urine	4	16.66%

The results the highest rate of infection with Staphylococcus aureus bacteria was found among burn patients.where the infection rate was (62.5%) and Number of patients (15) patients (sample) out of the total samples (24) isolates. The lowest rate of infection with this bacteria was from sources of urine, with a rate of (16.66%) and the number of isolates. (4) isolates. The percentage of infection from wounds was (20.83%), with a number of isolates (5).

Statistical Analysis:

Data are analyzed through the use of SPSS (Statistical Process for Social Sciences) version 10.0 application Statistical analysis system and Excel (Statistical package).

Diagnosis of Staphylococcus aureus bacteria:

Colonies of Staphylococcus aureus bacteria were identified as Gram-positive, catalase-positive (Soares *et al.*, 2017). This bacteria is characterized by changing the medium from pink (pink) to yellow (gold) when it grows on mannitol salt medium as a result of its ability to ferment mannitol sugar (Khan *et al.*, 2011). As for the test for plasma coagulase production, it gives a positive result. The Coagulase test for all samples showed a positive test, as all samples showed the ability to secrete the Coagulase enzyme at a rate of (100%). (Namvar *et al.*, 2014), as it was found that all S.aureus produced the coagulase enzyme at a rate of 100%. As shown in Figure (1), (2).

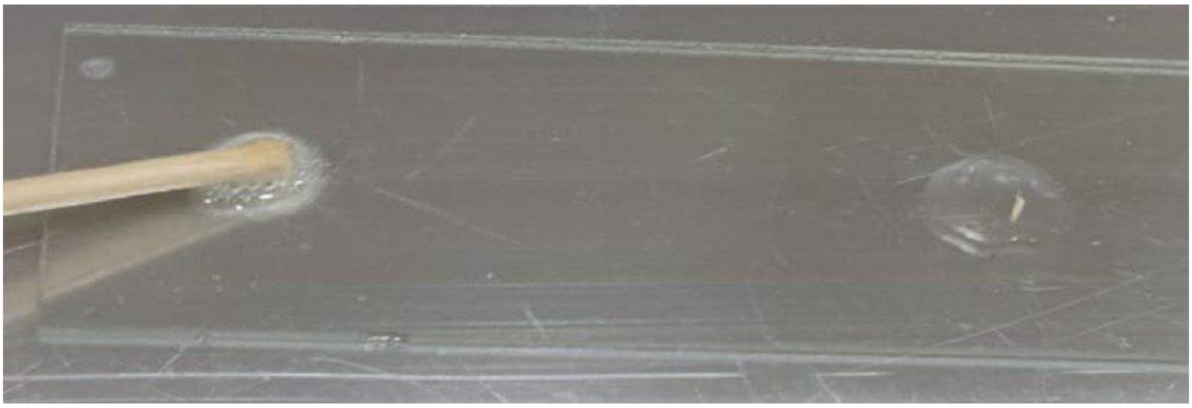

Figure (1) shows the appearance of bacteria on Mannitol Salt Agar medium

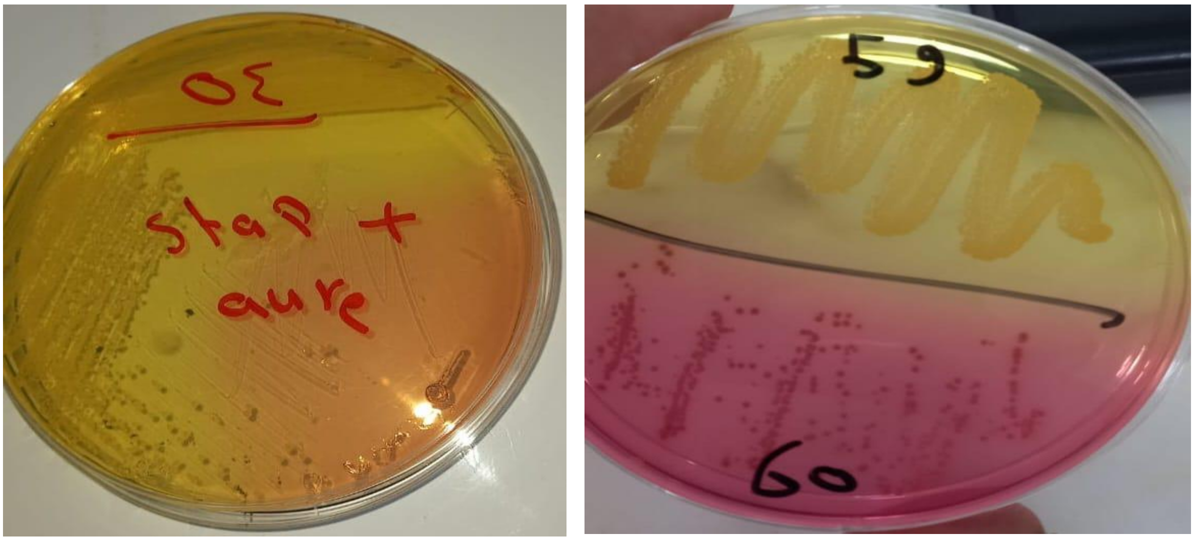

Figure (2) reveals. the Coagulase test for S.aurcue bacteria

3-Results.

Antibiotic Susceptibility Test for S.aurcue:

When the pathogenic microorganism is already known or identified, treatment with a specific type of antibiotic can be started. This usually involves the use of a narrow-spectrum antibiotic. The choice of antibiotic also depends on its cost. Identifying the type of bacteria causing the disease is crucial because it can reduce the cost and toxicity of antibiotic treatment and also reduce the likelihood of antibiotic resistance *emerging (*Flowers et al., 2013). Antibiotics can also be used as prophylaxis before surgical procedures to prevent infection of the wound. It has an important role in preventing endocarditis, as it is taken before tooth extraction or when performing any oral surgery that would transfer bacteria through the blood to the heart. Antibiotics are also used to prevent infection in cases of neutropenia, especially those associated with cancer(Bollenbach, 2015).

An experiment was conducted to test the sensitivity of S.aurcue bacteria to the commonly used antibiotics Ciprofloxacin and Erythromycin in Mueller-Hinton culture media to demonstrate the effectiveness of the antibiotic in inhibiting the bacteria and preventing it from growing on the culture medium. The culture medium was poured into Petri dishes, and the patient samples were then cultured by spreading them on Mueller-Hinton medium and leaving them for 5 minutes afterward. The antibiotic tablets were taken, the tablet was placed on the plate in regular places, the plate was placed moderately to prevent the antibiotic tablets from falling, and it was left for a whole day.. The dishes were then left for a whole day, and after incubation, the results were read and the diameters of inhibition were measured, The effect of antibiotics in inhibiting bacterial growth has a fundamental role in preventing the spread of bacteria, and this has a major role in reducing infections with this type of bacterial infection, which prevents the aggravation of wounds and burns, as the sensitivity of bacteria to these antibiotics is evidence of the effectiveness of these antibiotics, especially since most types have become Resistance to antibiotics due to their widespread use. It is currently preferable to use other, more effective substances in addition to antibiotics, so that their effect becomes more efficient in treatment, such as nanocomposites and plant extracts to increase the efficiency of antibiotics. as shown in the table (2).

Table (2) shows the sensitivity of Staphylococcus aureas bacteria to antibiotics

Sequence	Isolation number	The agricultural medium	The name of isolation	Ciprofloxacin (Cip) 5 mg	Erythromycin (E) 15 mg
1	14	Manitol	Staphylococcus aureas	(I)	(S)
2	15	Manitol	Staphylococcus aureas	R	R
3	16	Manitol	Staphylococcus aureas	(S)	(S)
4	18	Manitol	Staphylococcus aureas	(R)	(R)
5	40	Manitol	Staphylococcus aureas	(S)	(R)
6	50	Manitol	Staphylococcus aureas	(I)	(S)
7	54	Manitol	Staphylococcus aureas	(I)	(R)
8	56	Manitol	Staphylococcus aureas	(S)	(S)
9	59	Manitol	Staphylococcus aureas	(I)	(S)
10	63	Manitol	Staphylococcus aureas	R	(S)
11	67	Manitol	Staphylococcus aureas	(R)	(S)
12	68	Manitol	Staphylococcus aureas	(I)	(I)
13	71	Manitol	Staphylococcus aureas	(I)	(S)
14	72	Manitol	Staphylococcus aureas	(R)	(S)
15	75	Manitol	Staphylococcus aureas	(S)	(S)
16	76	Manitol	Staphylococcus aureas	(R)	(R)
17	78	Manitol	Staphylococcus aureas	(S)	(R)
18	79	Manitol	Staphylococcus aureas	(I)	(I)
19	80	Manitol	Staphylococcus aureas	(R)	(S)
20	81	Manitol	Staphylococcus aureas	(R)	(I)
21	83	Manitol	Staphylococcus aureas	(S)	(S)
22	94	Manitol	Staphylococcus aureas	(R)	(R)
23	97	Manitol	Staphylococcus aureas	(S)	(I)
24	100	Manitol	Staphylococcus aureas	(S)	(R)
the total				9 = R 7 =I	8 = R 4 =I

				8= S	12 = S

The results of our current study showed that Staphylococcus aureas bacteria It is not inhibited by antibiotic (Ciprofloxacin) a total (9) isolates out of (24) isolates, at a rate of (37.5%), and they were sensitive to this antibiotic with a number of (8) isolates, at a rate of (33.33%). As for the number of isolates that It was moderately resistant, and there were (7) isolates, with a percentage of (29.16%).

As for the antibiotic (Erythromycin), the Samples of S. aureas The bacteria were resistant to antisense inhibition (8 isolates) at a rate of (33.33%), sensitive to the antibiotic (12 isolates) at a rate of (50%), and moderately resistant to the antibiotic (4 isolates) at a rate of (16.66%) As shown in Figure (3).

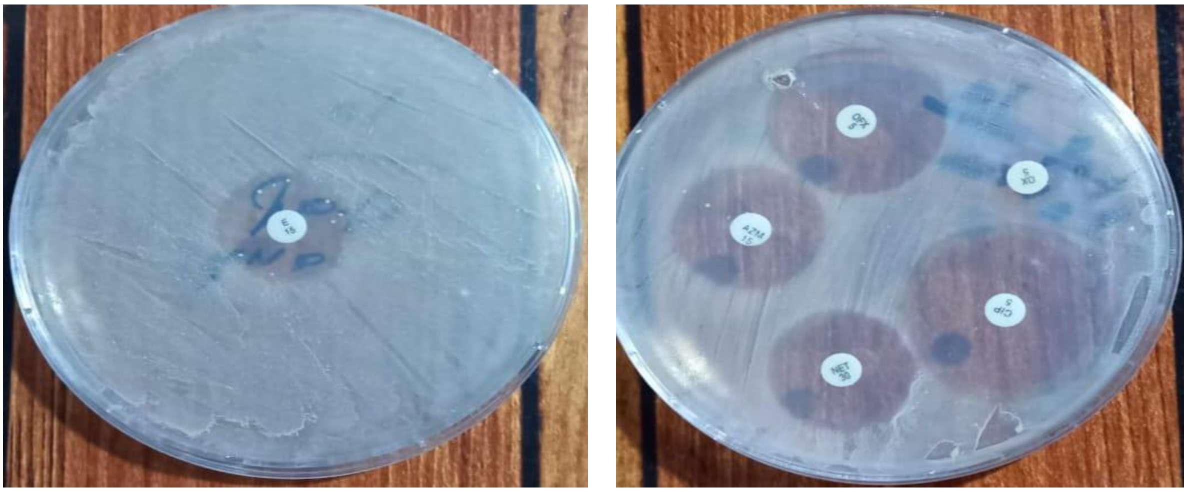

Figure (3) shows the effect of the antibiotic Erythromycin and Ciprofloxacin on bacteria

Discussion.

Actual search results agreed with study researcher (El Mammery *et al.,* 2023), who explained that in his study, The bacteria Staphylococcus aureus are resistant to the antibiotic erythromycin, and resistance increases in samples of bacteria that are sensitive to methicillin. (MSSA) from 13.6% to 28.9% and This result almost agreed with me personally. Also, The results were consistent with a study conducted by a researcher on an antibiotic Ciprofloxacin (Qutaiba, 2022), as the bacteria were do not inhibit at a rate of (43.2%).

The result was also close to the result of the researcher (Al-Taey, 2021), who found that the S. aureas bacteria is resistant to the antibiotic Ciprofloxacin by (40%). It is consistent with another study that showed that bacteria are resistant at a rate of (37%) (Saber and Kandala, 2018). Our study did not agree with the study of the researcher (Elzbleta and Jerzy) who explained through his study that all bacterial isolates are resistant to the antibiotic erythromycin (100%). The important factor responsible for resistance is the permeability barrier at the level of the cell wall. This would be an as yet unknown mechanism of erythromycin resistance in S. aureus.

Our study also contradicted the study of the researcher (Zubin *et al.,* 2017) who demonstrated that monotherapy with erythromycin did not inhibit bacterial growth and had no effect on bone infection, although it reduced the pro-inflammatory cytokines tumor necrosis factor (TNF)-α and interleukin (IL)-α. 6.

Conclusion.

Antibiotics were effective against the bacteria used in the study (Staphylococcus aureus).Where antibiotics work to inhibit the growth of bacteria Isolates of bacteria showed resistance to the antibiotics used in the study, erythromycin and Ciprofloxacin.

The results of our current study showed that Staphylococcus aureas bacteria were resistant to the antibiotic (Ciprofloxacin) with a total of (9) isolates out of (24) isolates, at a rate of (37.5%), and were sensitive to the antibiotic Ciprofloxacin, with a total of (8) isolates, at a rate of (33.33%).

As for the antibiotic (Erythromycin), isolates of S. aureas bacteria were resistant to the antibiotic (8 isolates) at a rate of (33.33%) and sensitive to the antibiotic (12 isolates) at a rate of (50%). This is evidence that the antibiotic Erythromycin was more effective in inhibiting the isolates. The antibiotic Ciprofloxacin has the ability to treat bacteria isolated from burns, wounds, and urinary tract infections because of its effect on bacteria. This is important for scientific, practical, and health applications. This achieves the objectives of the study, as the study showed that antibiotics are effective on bacterial isolates by evaluating the effectiveness of the antibiotics. When comparing the two antibodies, it was found that Erythromycin is more effective than Ciprofloxacin, and this is one of the objectives of the study.

Recommendations

1- Utilize CRISPR-Cas9 technology to identify and edit target genes in bacteria to study the effect of antibiotics at the genomic level. This can provide precise understanding of bacterial responses to antibiotics and contribute to the development of new antibiotics.
2- Use Whole Genome Sequencing techniques to identify genetic mutations that restore sensitivity to antibiotics in resistant bacteria. This can help design new therapeutic strategies to overcome resistance.
3- Perform quantitative proteomic analysis to identify and evaluate the proteins responsible for virulence factors in bacteria, which can assist in developing treatments targeting these proteins directly.
4- Develop nanodevices capable of detecting the presence of S. aureus with high accuracy and speed by identifying specific proteins or genes, using artificial intelligence to analyze the resulting data.
5- Conduct clinical trials to evaluate the efficacy and safety of phage therapy and immunotherapy as alternatives to conventional antibiotics in treating resistant infections.
6- Launch awareness campaigns through social media and digital education platforms to increase awareness about antibiotic resistance and the importance of prudent antibiotic use.

Proposals for Future Studies:

1) Design platforms that rely on artificial intelligence to analyze interaction data between bacteria and antibiotics in novel ways, aiding in better understanding of resistance mechanisms and development of new antibiotics.
2) Conduct research to understand how the balance of microbes in the human body affects antibiotic response, which can help in designing personalized treatments based on the patient's microbiome status.
3) Explore the potential of using gene-editing techniques like CRISPR to boost the immune response against antibiotic-resistant S. aureus, opening new avenues for sustainable treatments.

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