Pro Index | Journal of Science in Medicine and Life
Volume: 3 Issue: 1 Year: 2025
ISSN: 2992-9202 | http://journals.proindex.uz

Staphylococcus Hominis Improving the Efficiency of Cephalexin in Treating of Resistant Staphylococcus Hominies

Othaim Razzaq Faliyh Al-asadi, Oras Saleh Hassan Al Shamry, Alaa Alaa Abdul Hussein Karim Al daami

Abstract: **Objective:** The current study aimed to manufacture a hybrid nano-antibiotic from the antibiotic Cephalexin to enhance its efficacy against the antibiotic-resistant bacteria Staphylococcus hominis. **Methods:** Direct ion exchange between the zinc oxide (ZnO) and cephalexin (CEPH) layers was used to create a hybrid antibiotic known as Cephalexin-ZnO. Atomic force microscopy (AFM), scanning electron microscopy (SEM), FT-IR spectroscopy, X-ray diffraction (XRD), and CHNS elemental analysis were used to identify the novel nanobiotic. The study examined the hybrid nanocellulose cephalexin's antibacterial activity against Staphylococcus hominis bacteria that were isolated from the blood of a patient who had been diagnosed with sepsis using the Vitek 2 device. **Results:** The sensitivity test results in the Vitek 2 device for the bacteria Staphylococcus hominis showed that it is resistant to the antibiotic Cephalexin. FTIR infrared spectroscopy, XRD X-ray diffraction, AFM atomic force microscopy, and SEM scanning electron microscopy indicated the successful loading of this antibiotic into ZnO layers, with a loading percentage reaching 36.88% according to CHNS elemental analysis results. Additionally, With inhibition zone diameters of 0, 0, 2.63, 12.1, 18.67, and 26.71 mm against the used bacteria at the following concentrations (0, 10, 20, 40, 80, 160) mg/ml, the hybrid nanocomposite demonstrated superior inhibitory activity against the resistant bacteria in comparison to the free antibiotic. For the same concentrations, the inhibition zone diameters for the free antibiotic were 0, 0, 0, 10.3, 15.04, and 21.58 mm. **Conclusion:** It can be concluded from the current study that the antibiotic Cephalexin was successfully loaded into zinc oxide layers and a hybrid nanocomposite was fabricated, which has been shown to improve its antibacterial efficacy against resistant bacteria.

Key points: Staphylococcus hominis, Cephalexin, resistant bacteria, hybrid nanobiotic.

Introduction

The strictest definition of bacteremia is the presence of live bacteria in the blood. Asymptomatic bacteremia can happen after minor medical procedures and during regular dental hygiene. These benign infections are clinically temporary and do not cause long-term harm to a healthy individual.Bacteremia, on the other hand, is a bloodstream infection that can progress into several clinical spectra and is differentiated from sepsis when immune response systems malfunction or are overloaded [1]. If left untreated, clinically significant bacteremia progresses to sepsis, multiple organ dysfunction syndrome (MODS), sepsis, and systemic inflammatory response syndrome (SIRS) [2,3].

Since antibiotics are among the most widely used medications worldwide to treat diseases brought on by harmful bacteria, their significance to global health cannot be overstated. The long-term efficacy of antibiotics is threatened by resistance. The overuse and overuse of antibiotics is the primary source of antibiotic resistance [4.[More than 700,000 instances are thought to be killed by antimicrobial resistance (AMR) each year globally [5], and this issue is becoming more and more of a global concern. All resistance to antimicrobial agents is collectively referred to as "antimicrobial resistance." Traditional therapies are less successful and take longer to finish because of antibiotic

resistance, which raises the risk of disease transmission One of the primary causes of antibiotic resistance is human misuse of antibiotics [6,7].

A first-generation cephalosporin antibiotic, cephalexin has been chosen as a prototype medicine candidate due to its enhanced stability, palatability, and attractiveness for youngsters. It is also affordable and simple to use. Cephalosporins are commonly used to treat skin infections due to their wide range of action and safety against both gram-positive and gram-negative bacteria. Cephalexin is also a reasonable first-line treatment for joint infections and cellulitis. It is believed to be an excellent alternative to penicillin hypersensitivity and safe for those with penicillin allergies. but care should always be taken because cephalexin and other first-generation cephalosporins are known to have a slight cross-reactivity in patients with penicillin hypersensitivity. Furthermore, beta-hemolytic streptococci-induced throat infections can be effectively treated with cephalexin. Cephalexin functions by preventing the bacterial cell wall from forming, which causes it to burst and kill the bacteria. Cephalexin is a zwitterion, meaning it has both an acidic and a basic group. Its isoelectric point in water is between 4.5 and 5. Eighty percent of cephalexin is eliminated unaltered in the urine after six hours of intake due to its favorable pharmacokinetics, which enable it to be effectively absorbed.

The kidneys eliminate cephalexin, which has a half-life of 0.5–1.2 hours. Otitis media, cellulitis, pneumonia, bone and joint infections, streptococcal pharyngitis, and urinary tract infections are among the illnesses that it is used to treat [8].

Gram-positive cocci in clusters make up the non-pathogenic human staphylococci, which belong to the Staphylococcus genus. It is known to produce thiol alcohol molecules that contribute to body odor and is frequently found on human and animal skin as a harmless commensal. Similar to several other coagulase-negative staphylococci, S. hominis can sporadically infect people with weakened immune systems, such as those resulting from chemotherapy or disease [9].

Human coagulase-negative staphylococci (S. hominis) are commonly recognized as contaminants in blood cultures as part of the natural skin flora, but in rare cases, they may also cause native valve endocarditis (NVE) with septic phenomena. Its predominance as a contaminant, along with its less virulent characteristics compared to the more common infectious agents of endocarditis, makes S. hominis infections difficult to diagnose [10].

Nanotechnology is the science and technology that focuses on the precise adaptation of the structure of matter at the molecular level, meaning the adaptation of materials to reach a very small scale, which is the nanoscale. This results in a change in the size of the material, causing the behavior of the atoms and molecules of the material to change and exhibit different properties compared to larger materials, leading to new uses and applications for these materials [11]. Since the nanoscale scale is the most precise metric unit of measurement, it is given the name "nanotechnology" [12], and the word "nano" is the Greek word for "dwarf," often referring to materials with diameters between 1 and 100 nanometers [11].Applying nanotechnology to create and find ways to transport drugs and medicinal materials, as well as to reduce their sizes to the nanoscale, in order to improve their pharmacological properties—particularly in the treatment of diseases—is known as nanopharmaceutics [13].Thus, the purpose of this work was to try to construct the antibiotic Cephalexin, which has demonstrated resistance by Staphylococcus hominis bacteria, using nanotechnology. The hybrid nano-antibiotic was prepared, and its antimicrobial efficiency was tested to ascertain its effectiveness.

Materials and Methods

The bacterial sample: This study was conducted from January to April 2024, during which the bacterial isolate Staphylococcus hominis was obtained from the laboratories of Al-Husseini Hospital in Karbala after being diagnosed using the Vitek 2 system.

Preparation of the hybrid nano cephalexin (Cephalexin Nano hybrid):

The hybrid antibiotic was prepared using the method of Kolekar et al. (2011) [14] as follows:

Solution of cephalexin: 0.5 g of cephalexin was dissolved in 50% ethanol to create this solution, and once the dissolution process was finished, more ethanol was added to get the volume up to 50 ml. Solution of zinc oxide (ZnO):This solution was made by dissolving one gram of zinc oxide in fifty percent ethanol. Once the dissolution process was finished, ethanol was also used to modify the volume to fifty milliliters. Creating the hybrid nanocomposite using cephalexin and zinc oxide layers Gel Sol, an ion exchange technique: In accordance with the previously employed methods credited to Kolekar [14].

Solution of zinc oxide ZnO: To make this solution, 1 gram of zinc oxide was dissolved in 50% ethanol. Once the dissolution process was finished, ethanol was also used to increase the volume to 50 ml. Using the cephalexin ion exchange technique to manufacture the hybrid nanocomposite from zinc oxide layers Gel Sol: Using methods that were previously employed and credited to Kolekar [14].

Nutrient agar preparation

1. In an appropriately sized glass beaker with 1000 milliliters of deionized water (DDW), 28 grams of the medium powder are added in accordance with the manufacturer's instructions.
2. To fully dissolve the medium, the mixture is then brought to a boil.
3. After that, the dissolved medium is autoclaved for 15 minutes at a pressure of 15 pounds (121 degrees Celsius) to sterilize it.
4. The flask is taken out and allowed to cool to around 40 degrees when the sterilizing procedure is finished.

45°C.

5. Next, in sterile circumstances, the sterile medium is transferred onto sterile Petri plates.
6. The cast plates can be put in a low-temperature hot air oven once they have solidified. for a few minutes to remove any moisture present on the plates before use.

Preparation of the required concentrations and Petri dishes

1. We prepare 36 plates, 18 of which are for testing the hybrid nanocloxacillin antibiotic, and 18 of which are for free cephalexin.
2. Label each plate for the free antibiotic and the hybrid nano-antibiotic according to the following concentrations: (0, 10, 20, 40, 80, 160) mg/ml, with three replicates for each concentration.
3. Make holes in the center of all Petri dishes using a cork borer with a diameter of 5 mm.
4. We prepare 12 test tubes to prepare the required concentrations of the antibodies mentioned in point 2, including 6 for the free antibody and 6 for the hybrid nanobody, as shown in Table 1.

Stock solution preparation: 1.6 grams of each antibiotic were weighed separately and put in different test tubes to create the stock solutions for free cephalexin and hybrid nano cephalexin. The stock solution, which will be utilized in the next procedures to generate the concentrations employed in this investigation, had a concentration of 160 mg/ml after 10 ml of distilled water was added.

Preparation of free and hybrid nano cefalexin concentrations: In accordance with the methodology, the concentrations utilized in this investigation for free cephalexin and cephalexin nano hybrid were made independently.according to Table 1.

Table 1: Preparation of the antibiotic Cephalexin's free and hybrid nano concentrations

No. of tube	Distal Water (? l)	Stock Solution (? l)	Final Volume (? l)	Final Concentration (mg/ml)
1	1000	0	1000	0
2	937.5	62.5	1000	10
3	875	125	1000	20
4	750	250	1000	40
5	500	500	1000	80
6	0	1000	1000	160

Description of the hybrid nanobiotic:

Several techniques, such as Fourier-transform infrared spectroscopy (FT-IR), X-ray diffraction (XRD), atomic force microscopy (AFM), accurate measurement of C, H, N, and S elements, and scanning electron microscopy (SEM), were used to describe the hybrid nanobiotic under investigation.

1. FT-IR: By creating a disc of the compound under investigation using potassium bromide (KBr) and finely grinding it, the infrared spectrum of both the hybrid nanocloxacillin and free cloxacillin, as well as zinc oxide (ZnO), was assessed. The infrared spectrum was measured within the wave range of 400–4000 cm^-1.
2. X-ray diffraction (XRD): The hybrid nanocelphalosporin was described using the diffraction spectrum.

Using Bragg's rule ($n\lambda = 2d\sin\theta$), the XRD illustrates the variation in layer thickness before and after the antibiotic cephalexin impregnation procedure.

3. Atomic Force Microscope (AFM): AFM was used to analyze hybrid nanocloxacillin samples in order to assess the diameters, sizes, and aggregation of nanoparticles.
4. Analysis of CHNS Elements: The proportions of C, H, N, and S in free and hybrid nanocapsule cephalexin were examined.
5. The exterior surface of cefalexin nanoparticles and free ZnO layers are also examined using a scanning electron microscope (SEM).

Measuring the antibacterial efficacy of free and hybrid nano Cephalexin:

The effectiveness of the free and hybrid nano cefalexin antibiotics was examined using the methodology outlined by El-Rabi [15], as explained below:

Healthy broth Broth with nutrients: Following the manufacturer's recommendations, 13 grams of the medium were weighed, dissolved in one liter of distilled water, and sterilized for fifteen minutes to create the nutritional broth. The bacteria were activated using this media.

In the center of Muller Hinton Steel is Muller Hinton Agar.

To produce this medium, 38 grams of the medium were weighed, dissolved in one liter of distilled water, and then sterilized for 15 minutes. The antibacterial activity of free and hybrid nanocellulose cephalexin against the Staphylococcus hominis bacterium was examined using these medium.

Bacterial activation:

Staphylococcus hominis was activated in nutrient broth for one hour before

Using it to pollinate agricultural crops.

Measuring antimicrobial efficacy:

After activating the bacteria, three wells (5 mm in diameter) were made in each plate (Muller Hinton agar), and 80 microliters of antibiotic concentration were added to each well. Then, 50 microliters of the activated bacterial suspension were spread on each plate, and the plates were incubated at 37 degrees Celsius for one day. The diameter of the inhibition zone around the wells was then observed and measured using a ruler.

Statistical analysis:

The results were statistically analyzed using the t-test for comparing two means and the one-way ANOVA test at a significance level of 0.05, using the SPSS program. Version 22.

Results and Discussion

Characterization of the hybrid nanobiotic

FTIR infrared spectrum:

The FT-IR spectrum of zinc oxide (ZnO) showed distinctive frequencies at 4000-400 cm-1, which are attributed to the vibration of the Zn-O metal bond, as zinc oxide is an inorganic oxide, as shown in Figure 1 [16]

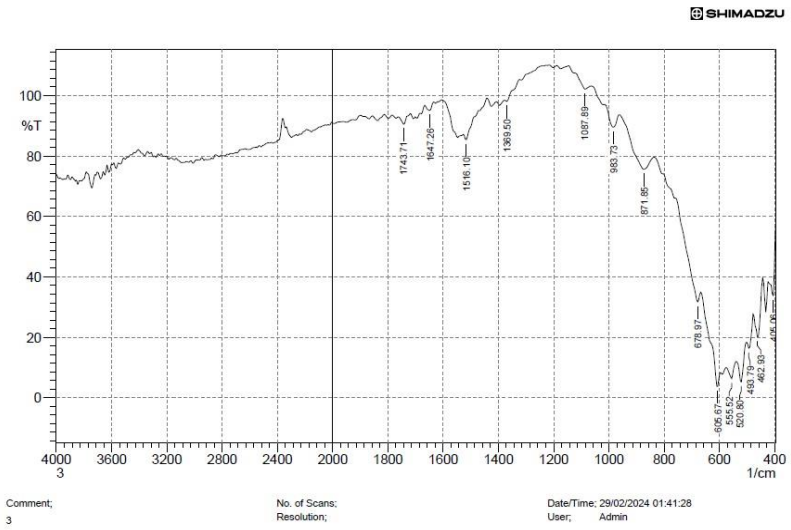

Figure 1: FTIR analysis of zinc oxide ZnO

The structure of cephalexin can be confirmed from the FTIR spectrum in Figure 2 and as shown below:

1. The appearance of bands at frequencies 3498 and 3271 cm-1 indicates the presence of NH2, NH, OH (very broad band due to hydrogen bonding).
2. The appearance of the band at the frequency of 3051 cm-1 indicates the presence of the aromatic CH double bond.(CH=aromatic), as well as the appearance of bands at frequencies 1454 and 1593 cm-1 due to the double bond between carbon atoms (C=C) in the benzene ring.
3. The appearance of a band at the frequency of 2929 cm-1 (which is a stretching band) indicates the presence of (Methyl group CH3).
4. The sharp strong bands at frequencies 1693 and 1759 cm-1 indicate the presence of two carbonyl groups (C = O), one belonging to the β-lactam ring and the other to the ring [17] (Thiazolidine ring)

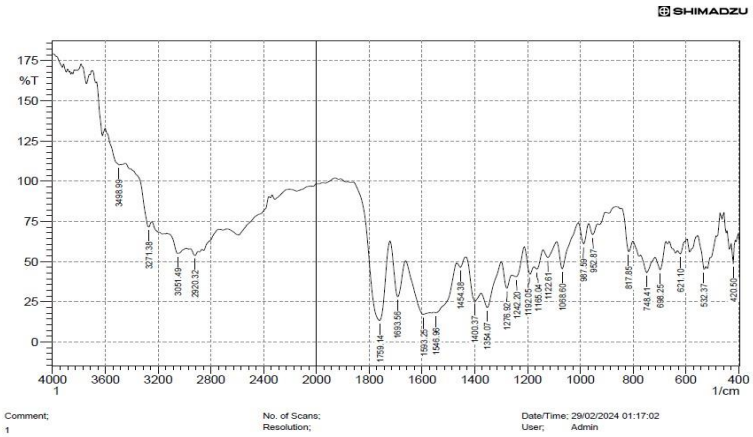

Figure 2: FTIR analysis of free cephalexin

It is evident from Figure 3 of the hybrid nanoantibody that the formation of the hybrid nanoantibody was successful.Cephalexin-zinc oxide) and it seems that all the characteristic peaks of cephalexin were retained, in addition to the appearance of a spectral difference in the fingerprint region that appears at the peaks.For frequencies from 1500 – 400 cm-1, which are considered a distinctive region for both the free compound and the hybrid nanocomposite, this confirms the formation of a new compound that differs from free cephalexin. [17].

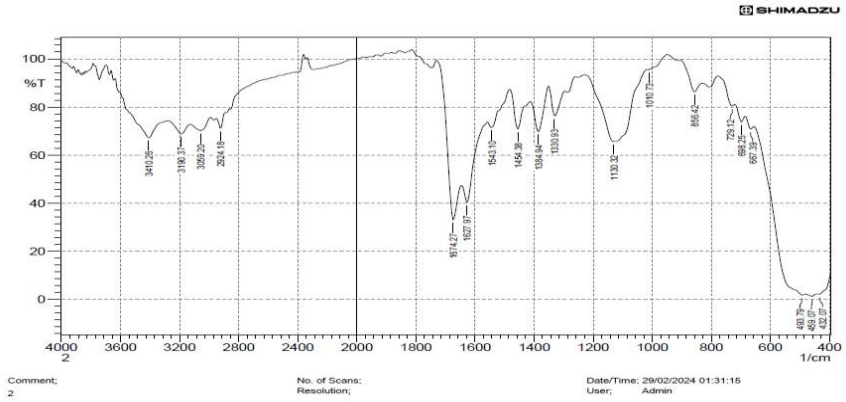

Figure 3: FTIR analysis of the hybrid nanocaphalexin antibiotic Cephalexin Nanohybrid

The X-ray diffraction spectrum (XRD) of zinc oxide (ZnO) is displayed in Figure 4 along with the crystalline levels (003), (006), and (009). With a crystal distance of 0.4150 nanometers, the (003) level appears at an angle of 31.6º, while the (006) level appears at an angle of 34.36º with a crystal distance of 0.4226 nanometers. At a crystal distance of 0.4265 nanometers at an angle of 36.12º, the (009) level is visible. The hybrid nanocapsule of the Cephalexin nanoparticles' X-ray diffraction spectrum, shown in Figure 5, shows the diffraction of the (003) plane at an angle of 31.46º and a crystalline distance of 0.3542 nanometers. With a crystalline distance of 2453.0 nanometers and an angle of 34.132º, the (006) plane is visible, while the (009) plane is visible at an angle of 35.9213º and a crystalline distance of 0.4133 nanometers.

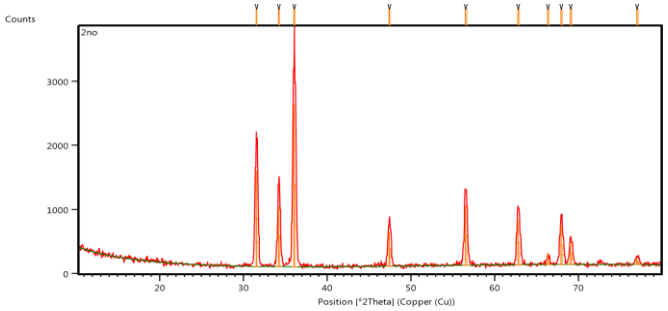

Figure 4: X-ray diffraction (XRD) pattern of zinc oxide (ZnO)

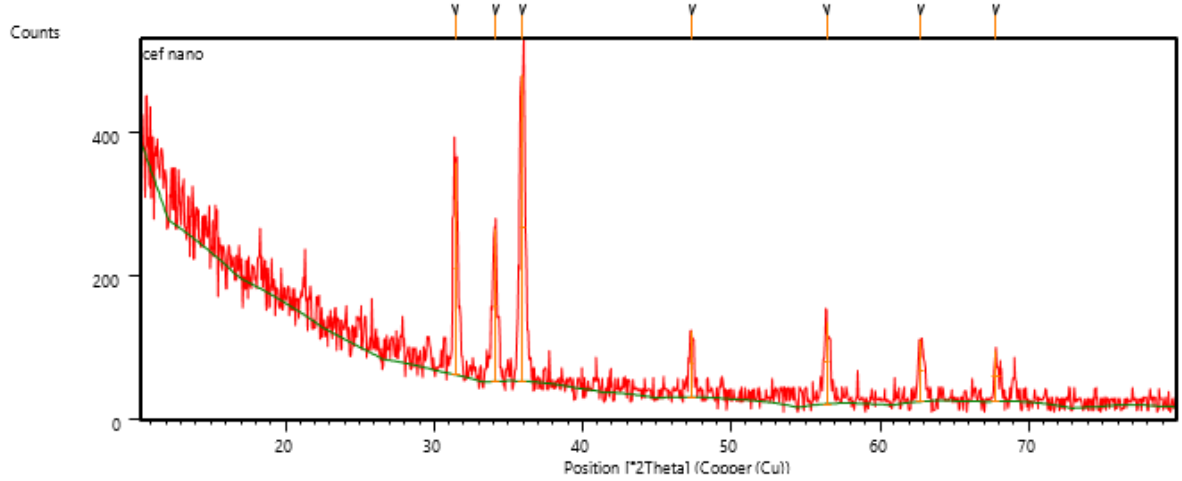

Figure 5: X-ray diffraction (XRD) spectrum of the hybrid nanocaphalexin Cephalexin Nanohybrid

Scanning Electron Microscope (SEM): Figure 6 shows a scanning electron microscope image of ZnO oxide layers, with plate-like structures having few pores and irregular shapes and sizes of 262.21 nanometers [16]. As for figures 7, they show a scanning electron microscope image of the hybrid nanocapsule Cephalexin, where rough and irregular surfaces appeared in the hybrid nanocapsule powder with diameters of approximately 80.82 nanometers [17].

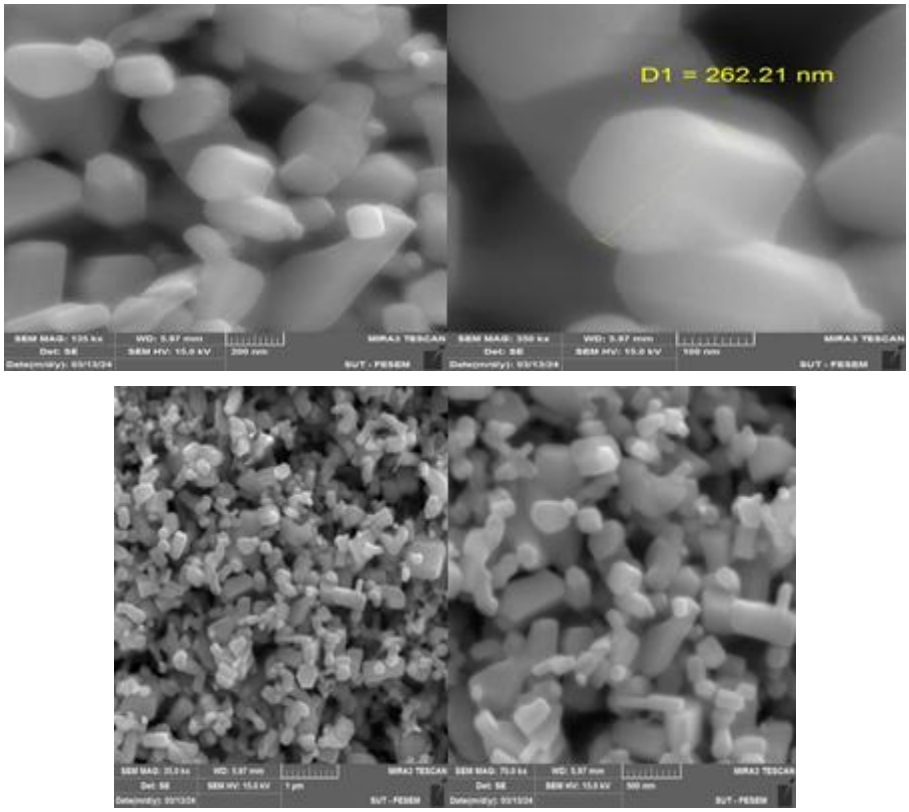

Figure 6: SEM analysis of ZnO oxide layers at 100, 200, 500 nanometers, and 1 micrometer

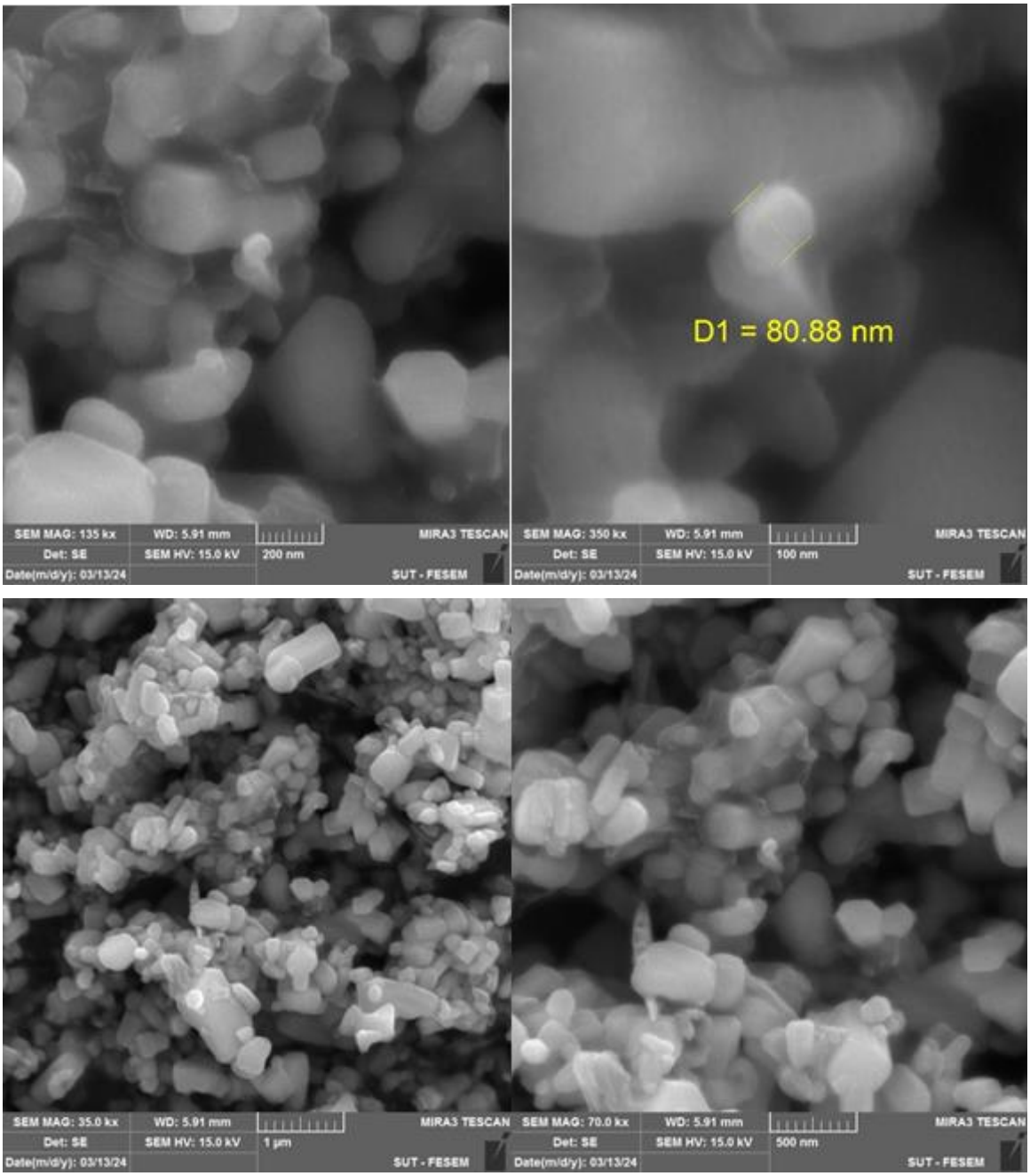

Figure 7: Scanning Electron Microscopy (SEM) analysis of the hybrid nanocapsule Cephalexin at 100, 200, and 500 nanometers. and 1 micrometer

Atomic Force Microscope (AFM):

AFM was used to examine the Nanohybrid-Cephalexin's exterior. The hybrid nanocapsule Cephalexin's quasi-spherical forms are shown in two dimensions in Figure 8. With a molecular aggregate height of 8.78 nanometers, the figure also shows a three-dimensional picture of the hybrid nanobiotic's surface section, demonstrating the effectiveness of the preparation process.

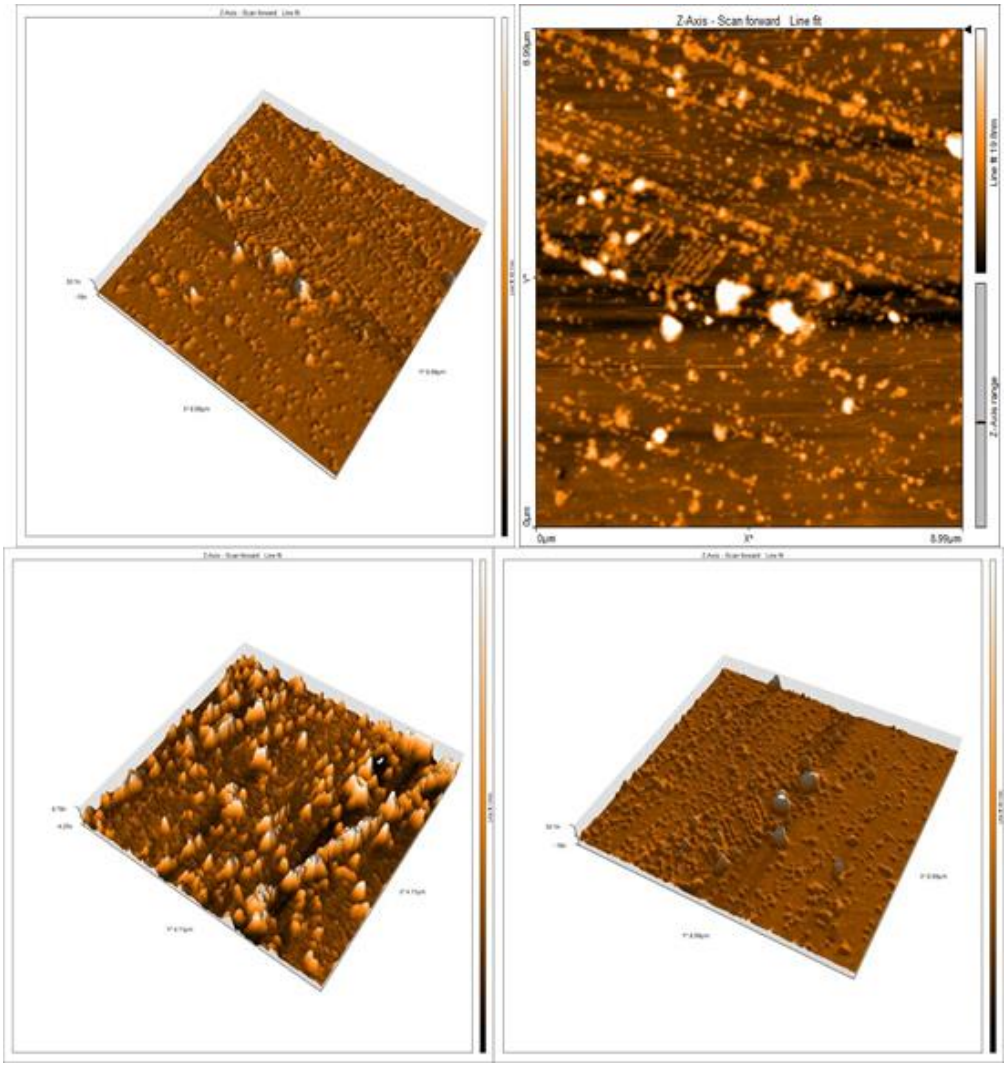

Figure 8: Two-dimensional and three-dimensional dimensions under an AFM atomic force microscope for the hybrid nanocloxacillin.

Cephalexin Nanhybrid

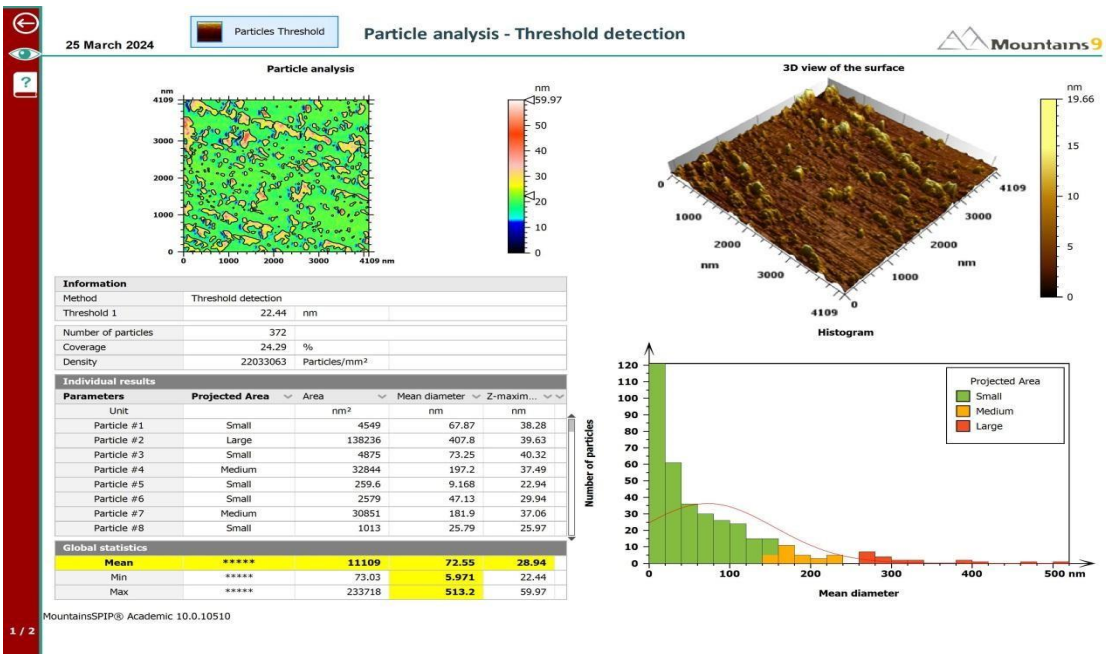

Figure 9: AFM analysis of the threshold detection of Cephalexin Nanohybrid

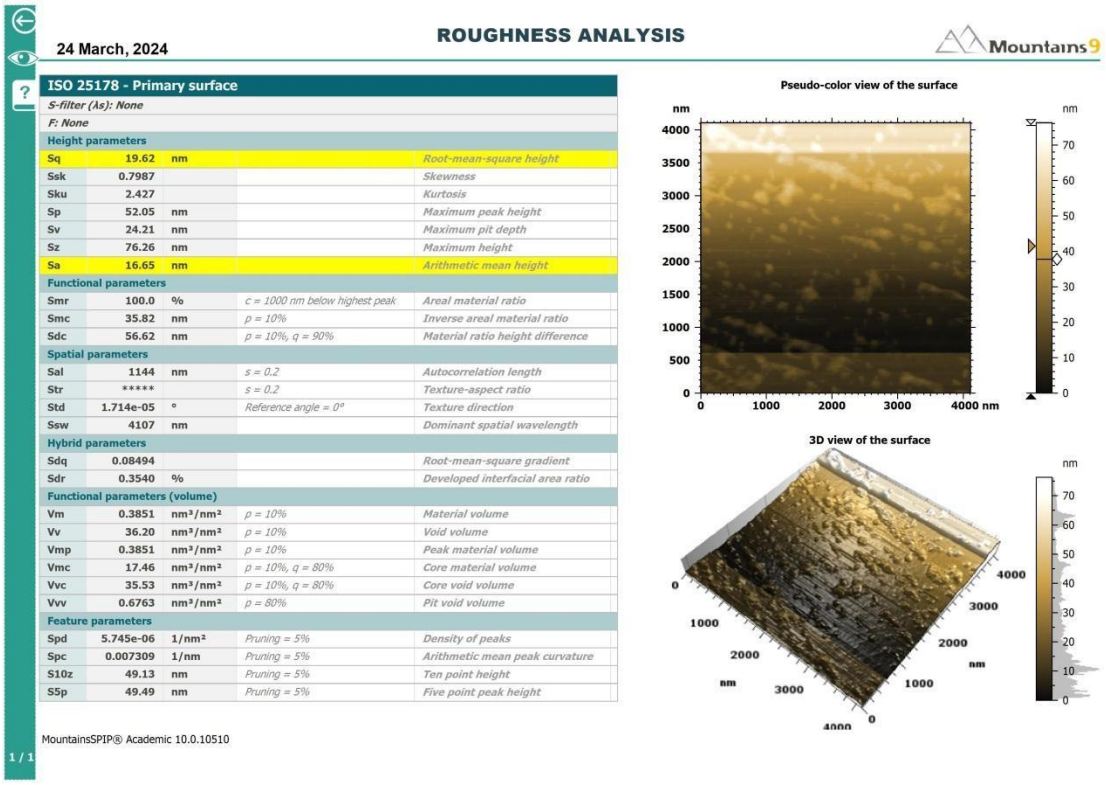

Figure 10: Roughness analysis under an Atomic Force Microscope (AFM) for the hybrid nanocapsule Cephalexin Nanhybrid

Table 2: CHNS elemental analysis of hybrid and free Cephalexin nanoparticles.

Name	Weight (mg)	O_2	C/N Ratio	Content [%]	Peak Area
Nano Cephalexin	6.8010	Index 2	.2518	N: 3.143 C: 6.916 S: 1.772 H: .1013	8561 12725 1324 8344
Free Cephalexin	8.3250	Index 1	2.369	N: 7.914 C: 18.75 S: 5.03 H: 1.211	24122 32793 6434 7345

From the results indicated in Table 2, the percentage of the Cephalexin antibiotic loaded with zinc oxide layers was 36.88%. This result indicates that the use of hybrid nanocapsulated Cephalexin is successful or beneficial as a treatment, which showed from the carbon content that 36.88% of the Cephalexin is present in the hybrid nanocapsule, and despite this percentage, it remains highly active during testing. Bacteria can also cause fewer side effects in this study by increasing the delivery of hybrid nanocapsule Cephalexin inside the cells similarly [18].

The inhibitory efficacy of hybrid and free nano-Cephalexin against Staphylococcus hominis bacteria.The results in Table 3 showed statistically significant differences ($P \leq 0.0071$) in diameters.

Inhibition zone when using free Cephalosporin against Staphylococcus bacteria hominis at concentrations of 40, 80, and 160 mg/ml compared to the control, however, the concentrations of 10 and 20 mg/ml did not show any significant effect. Furthermore, increasing the concentration led to an increase in the inhibition diameter. The diameters of the inhibition zones for the free antibiotic (0, 0, 0, 10.3, 15.04, 21.58) mm for the concentrations (0, 10, 20, 40, 80, 160) mg/ml. When using the hybrid nanomedicine Cephalexin, which was manufactured using the ZnO layer method, there were significant differences in the diameters of the inhibition zones of the hybrid nanomedicine

against the bacteria used, with a significance level of 0.0003 (P≤ 0.01) in all concentrations used compared to the control concentration. Where the diameters of the inhibition zones were (0, 0, 2.63, 12.1, 18.67, 26.71) mm for the following concentrations (0, 10, 20, 40, 80, 160) mg/ml.

Through the statistical comparisons between the inhibition diameters of the hybrid nano-antibiotic and the free antibiotic for each concentration individually, the results of the statistical analysis in Table 3 showed that there are significant differences between the inhibition diameters for the concentrations (20, 40, 80, 160) mg/ml, with significance levels of (0.0000, 0.0421, 0.0375, 0.0304) for the concentrations, respectively. It is worth noting the superiority of the hybrid nanobiotic in its inhibitory efficacy compared to the inhibitory efficacy of the free antibiotic, considering that the loading ratio of the antibiotic in the hybrid nanobiotic was 88.36%, which provided a higher inhibitory effect than the free antibiotic.

Table 3: The inhibitory efficacy of free and hybrid Cephalexin against Staphylococcus hominis bacteria

value P	Inhibition zone diameter/ml		Concentration mg/ml
	Cephalexin nano	Free cephalexin	
1.000	0.000 ± 0	0.000 ± 0	Control(0)
1.000	0.000 ± 0	0.000 ± 0	10 mg/ml
* 0.000	0.42 ± 2.63	0.000 ± 0	20 mg/ml
* 0.0421	1.06 ± 12.1	1.23 ± 10.3	40 mg/ml
* 0.0375	2.59 ± 18.67	1.92 ± 15.04	80 mg/ml
* 0.0304	2.14 ± 26.71	1.88 ± 21.58	160 mg/ml
	* 0.0003	* 0.0071	value P
	3.705	2.481	least significant difference LSD

The mean ± standard deviation is shown by the numbers in the table. * At the 0.01 significance level, the presence of significant differences is shown.

Cephalexin continues to be a very useful and successful antibiotic for treating skin infections brought on by staphylococci and streptococci. Healing rates of 90% or more are still being attained, and twelve years of experience has not lessened its efficacy.

Its bioavailability is guaranteed by its uniform absorption and resistance to stomach acid destruction, and its effectiveness at a twice-daily dosage improves drug compliance. Young children tolerate the suspension formulation well, and side effects are uncommon and usually moderate. When it comes to treating streptococcal and staphylococcal infections, cephalexin works similarly to erythromycin, clindamycin, dicloxacillin, cloxacillin, and other cephalosporins. Cost considerations may be crucial when selecting one of these antibiotics over another because many of them have comparable effectiveness, palatability, and adverse reaction profiles. The recommended drug for streptococcal skin infections is still penicillin. In the future, cephalexin and other alternative antibiotics could be used more often in the first treatment of mixed streptococcal and staphylococcal lesions if the healing rates of these infections continue to decrease when treated with penicillin [19].

Conclusions: Based on the results of the current study, the following conclusions can be drawn:

1. The successful loading of the antibiotic Cephalexin between layers of zinc oxide ZnO.
2. The loading percentage of the antibiotic in the hybrid nanocomposite was 36.88%.
3. The antimicrobial efficacy of the hybrid nanocapsule Cephalexin against bacteria It was high Staphylococcus hominis.

References

1. Butler-Laporte G, De L'Étoile-Morel S, Cheng MP, McDonald EG, Lee TC. MRSA colonization status as a predictor of clinical infection: A systematic review and metaanalysis. J Infect. 2018 Dec;77(6):489-495. [PubMed].

2. Dagasso G, Conley J, Parfitt E, Pasquill K, Steele L, Laupland K. Risk factors associated with bloodstream infections in end-stage renal disease patients: a population-based study. Infect Dis (Lond). 2018 Nov-Dec;50(11-12):831-836. [PubMed].

3. Arcens M, Stirnemann J, Mayor G, John G. [Epidemiology and strategy to prevent urinary catheters related complications]. Rev Med Suisse. 2018 Aug 29;14(616):1518-1521. [PubMed].

4. van Duijkeren E, Schink AK, Roberts MC, Wang Y, Schwarz S. Mechanisms of Bacterial Resistance to Antimicrobial Agents. Microbiol Spectr. 2018 Jan;6(1). doi: 10.1128/microbiolspec.ARBA-0019-2017. PMID: 29327680.

5. B. T. Tadesse, E. A. Ashley, S. Ongarello, J. Havumaki,M. Wijegoonewardena, I. J. Gonz´alez, and S. Dittrich, Antimicrobial resistance in Africa: a systematic review," BMCInfectious Diseases (2017), vol. 17, p. 616, 2017.

6. World Health Organization, Antimicrobial Resistance, World Health Organization, Geneva, Switzerland, 2014, http://www.who.int/mediacentre/factsheets/fs194/en .

7. E. Melander, K. E. Md, G. J??Nsson, and S. M??Lstad, Frequency of penicillinresistant pneumococci in children is correlated to community utilization of antibiotics," @e Pediatric Infectious Disease Journal, vol. 19, no. 12, pp. 1172–1177, 2000.

8. Rafik Karaman, Chapter 5 - From Conventional Prodrugs to Prodrugs Designed by Molecular Orbital Methods, Editor(s): Zaheer Ul-Haq, Jeffry D. Madura, Frontiers in Computational Chemistry, Bentham Science Publishers, 2015, Pages 187-249, ISBN 9781608059799,

9. Rudden, Michelle; Herman, Reyme; Rose, Matthew; Bawdon, Daniel; Cox, Diana S.; Dodson, Eleanor; Holden, Matthew T.G.; Wilkinson, Anthony J.; James, A. Gordon; Thomas, Gavin H. (2020). "The molecular basis of thioalcohol production in human body odour". Scientific Reports. 10 (1): 12500. Bibcode:2020NatSR..1012500R. doi:10.1038/s41598-020-68860-z. PMC 7385124. PMID 32719469.

10. Society for General Microbiology (30 March 2015). "Bacterial genetic pathway involved in body odor production discovered". ScienceDaily (Press release).

11. Joseph T, and Morrison M. Nanotechnology in Agriculture and food Nanoforum report.org, European nanotechnology gateway. 2006.

12. Ramsden JJ. What is the nanotechnology?. Nanotechnology perceptions. 2005; 1: 3-71

13. Deepak Kumar Dash, Rajni Kant Panik, Anil Kumar Sahu and Vaibhav Tripathi . Role of nanotechnology in pharmaceutical product development. 2020. DOI: 10.5772/intechopen.92796.

14. Kolekar TV, Yadav HM, Bandgar SS. and Deshmukh PY.(2011). Synthesis By Solgel Method And Characterization Of Zno Nanoparticles Indian Streams Research Journal. 2011; 1(1) DOI : 10.9780/22307850.

15. EL-RAB, S. M., HALAWANI, E. M. & HASSAN, A. M. 2018. Formulation of ceftriaxone conjugated gold nanoparticles and their medical applications against extended-spectrum β-lactamase producing bacteria and breast cancer. *Journal of microbiology and biotechnology*, 28**,** 1563-1572.

16. Sorna Prema Rajendran, Kandasamy Sengodan, "Synthesis and Characterization of Zinc Oxide and Iron Oxide Nanoparticles Using Sesbania grandiflora Leaf Extract as Reducing Agent", Journal of Nanoscience, vol. 2017, Article ID 8348507, 7 pages, 2017.

17. Tarun Chaudhary, Manoj Kumar Chaudhary, Bhawani Datt Joshi, Maria Silmara Alves de Santana, Alejandro Pedro Ayala, Spectroscopic (FT-IR, Raman) analysis and computational study on conformational geometry, AIM and biological activity of cephalexin from DFT and molecular docking approach, Journal of Molecular Structure, Volume 1240, 2021, 130594, ISSN 0022-2860,

18. CHO, S.-W., LEE, J. S. & CHOI, S.-H. 2004. Enhanced oral bioavailability of poorly absorbed drugs. I. Screening of absorption carrier for the ceftriaxone complex. Journal of pharmaceutical sciences, 93, 612-.026

19. Derrick CW Jr, Reilly K. The role of cephalexin in the treatment of skin and softtissue infections. Postgrad Med J. 1983;59 Suppl 5:43-6. PMID: 6364089.