The Research of Medical Science Review
ISSN: 3007-1208 & 3007-1216 Volume 4, Issue 4, 2026

A STUDY OF COMBINED EFFECTS OF ANTIBIOTIC AND PLANT EXTRACTS AGAINST *CORYNEBACTERIUM DIPHTHERIAE* ISOLATED FROM UPPER RESPIRATORY TRACT

Mareeha Hayat[1], Nasir Ali[2], Asif Mehmood[*3]

[1,2, *3]*Sarhad Institute of Allied Health Sciences, Sarhad University of Science and Information Technology, Peshawar, Khyber Pakhtunkhwa*

[1]mareehahayat1998@gmail.com, [2]nasir.siahs@suit.edu.pk, [*3]asif.siahs@suit.edu.pk

DOI: https://doi.org/10.5281/zenodo.19706836

Keywords
Anti-Bacterial Agents, Corynebacterium Diphtheriae, Drug Resistance, Bacterial, Drug Synergism, Microbial Sensitivity Tests, Musa, Plant Extracts, Respiratory Tract Infections

Article History
Received: 25 February 2026
Accepted: 05 April 2026
Published: 23 April 2026

Corresponding Author: *
Asif Mehmood

Abstract
The development of antimicrobial resistance (AMR) in Corynebacterium diphtheriae, including multidrug-resistant and toxigenic strains, requires new therapeutic approaches. Plant-based compounds are a potential source of synergistic agents to boost conventional antibiotics. This paper examined the synergetic effect of antibiotics and Musa acuminata (banana) peel extracts against clinical isolates of C. diphtheriae. A total of 23 confirmed C. diphtheriae isolates from the upper respiratory tract were used in an experimental study. Banana peels were dried, and bioactive compounds were extracted by ethanol and hexane solvents. Antibiotic susceptibility was tested by the disk diffusion method against a panel of antibiotics. The antibacterial activity of individual extracts and the synergistic effect of antibiotics was determined by the agar well diffusion method. There is a high level of antibiotic resistance, especially to sulphonamide (35.8%), clindamycin (46.2%), and ciprofloxacin (29.9%). Tetracycline (86.2%) and erythromycin (88.9%) were the most effective. The ethanolic extract of banana peel had a better antibacterial effect (22.5 mm zone of inhibition) than the hexane extract (18 mm). Synergy testing showed a significant enhancing effect of the ethanolic extract, especially with erythromycin (98.9% improvement) and tetracycline (91.1% improvement). In comparison, there were very low synergistic effects with penicillin (17.5%) and ciprofloxacin (32%). Ethanolic extract of banana peel has good antibacterial activity against C. diphtheriae and shows a good synergistic effect with erythromycin and tetracycline. This combination therapy offers a potential solution to the fight against antibiotic-resistant diphtheria infection, which valorizes agricultural waste for pharmaceutical use.

INTRODUCTION
Over the past centuries, plants were used to treat several diseases, and plant-derived products have become a crucial element in the development of the pharmaceutical industry because of their exclusive pharmacological characteristics [1]. It is estimated that 80 percent of the world population, especially in developing countries, continues to use plants as a major source of treating diseases, which demonstrates the relevance and increasing popularity of traditional medicine [2]. This has prompted increased efforts to discover bioactive compounds of botanical origin, particularly with the world on the grip of a serious threat posed by

antimicrobial resistance (AMR) [3]. The success of antibiotics, which have transformed modern medicine, is being quickly undermined by the emergence of multidrug-resistant (MDR) bacteria, making infections more challenging to treat and necessitating the development of new treatment approaches [4].
A major pathogen of concern is Corynebacterium diphtheriae, the Gram-positive bacterium that causes diphtheria. This organism secretes a powerful exotoxin, which may result in a serious systemic infection, manifested by the development of a pseudo-membrane in the upper respiratory tract that may cause suffocation and cardiac and nervous complications that are fatal [5, 6]. Diphtheria, once under control in many countries due to vaccination, has recently re-emerged, and making treatment even more difficult is the development of antimicrobial resistance in this species. Recent surveys have identified alarming patterns, such as isolates that are resistant to first-line penicillin, and about 10.4 percent of clinical isolates are multidrug-resistant [7-9]. Concerningly, there have been incidences of toxigenic, penicillin-resistant C. diphtheriae, including a fatal respiratory infection caused by a strain that was resistant to all β-lactam antibiotics due to a novel acquired resistance mechanism [10, 11]. Moreover, the detection of non-toxigenic toxin-gene bearing (NTTB) strains poses further diagnostic and public health problems.
A promising approach to the fight against AMR is combination therapy, in which conventional antibiotics are combined with natural products to increase their effectiveness and possibly restore sensitivity [12]. Agro-industrial waste products are a rich, sustainable, and economically feasible source of such bioactive compounds. A notable example is banana (Musa spp.) peel, a lignocellulosic waste that is disposed of in huge amounts- about 36 million tons per annum, which is a challenge to the environment [13]. This waste is, however, known to have a broad spectrum of biological activities, such as strong antibacterial, antioxidant, and anti-inflammatory effects [14]. Banana peel contains a high number of phenolic compounds and various phytochemicals, including flavonoids, tannins, alkaloids, and glycosides, which explain its enormous medicinal value [15]. Its traditional use in traditional medicine to treat a variety of ailments and its protective effects that have been demonstrated in pharmacological studies make it valuable [16].
The rising threat of antimicrobial resistance in Corynebacterium diphtheriae, including emerging multidrug-resistant and toxigenic strains, necessitates the exploration of novel therapeutic strategies. This study is therefore rationalized by the potential of plant-derived compounds to act synergistically with conventional antibiotics to enhance efficacy and combat resistance. The aim of this research was to investigate the efficacy of combined therapy using antibiotics and plant extracts against C. diphtheriae isolates, with specific objectives to determine the individual antimicrobial activity of both antibiotics and plant extracts, and to evaluate and compare the synergistic inhibitory effects of their combinations.

Methodology

The research methodology used was an experimental study design to determine the impact of antibiotics, plant extracts, and combinations of antibiotics and plant extracts on isolates of Corynebacterium diphtheriae. The research was carried out in October 2023-August 2024. Musa acuminata fresh bananas were bought in a local market in Peshawar and taken to the microbiology laboratory. The peels were washed, cut into small pieces, disinfected, and dried in the air at room temperature, and then ground into a fine powder and kept in airtight containers. The extraction was carried out by soaking 25 mg of powdered peel in 75 mL of either ethanol or hexane solvent in a conical flask, which was then sealed and left at room temperature and allowed to stand 72 hours. The extracts were then filtered, partly solidified using a rotary evaporator, and lastly dried in an oven to give the final product. The isolation of bacteria was done using 23 cotton swab samples taken from patients with respiratory infections; the samples were serially diluted to the McFarland standards, spread on nutrient agar

plates, and incubated at 37 o C for 24 hours. Pure isolates were obtained by subculture of distinct colonies [17].
Morphological identification was done by Gram stain, with purple-colored Gram-positive isolates being chosen to be analyzed further. Biochemical identification was done through catalase, oxidase, carbohydrate fermentation, and urease tests as recommended by Bergey's Manual [18]. Molecular identification was later done by 16S rRNA gene sequencing; DNA was extracted and amplified by PCR using universal primers, and the resulting sequences were compared to the GenBank database using BLAST [19]. Antibiotic susceptibility test was done by disk diffusion method on Mueller-Hinton Agar (MHA) plates against a panel of antibiotics: penicillin, erythromycin, and ciprofloxacin, and results were interpreted by the diameter of inhibition zones [20]. The antibacterial activity of the extracts was evaluated by the agar well diffusion method, where wells were made in inoculated MHA plates, filled with extract, and incubated, after which zones of inhibition were measured [21].
Lastly, the synergistic action of antibiotics and extracts was tested using the same well diffusion assay with both agents added to wells at concentrations of 100 µg/mL and 150 µg/mL, and any synergistic effects were noted after incubation [22]. The inclusion criteria were fresh, validated plant material and confirmed C. diphtheriae isolates of upper respiratory tract samples with known antibiotic sensitivity patterns, whereas the exclusion criteria were contaminated samples and antibiotics that are not relevant to clinical practice against this pathogen.

Results

A total of 400 samples from the upper respiratory tract were collected using cotton swabs from different departments of tertiary care hospitals, including LRH, HMC, and KTH. The samples were cultured on blood agar plates for bacterial isolation, as shown in Figure 1A. Corynebacterium diphtheriae colonies were observed on the blood agar. The bacteria formed small, white colonies, which were distinct in appearance and easily identifiable due to their characteristic morphology. 23 species were isolated and confirmed as Corynebacterium diphtheria. Gram staining of C. diphtheriae reveals purple, gram-positive, rod-shaped bacteria arranged in characteristic club-shaped or palisade formations, often exhibiting a "Chinese letter" pattern border as shown in Figure 1 B. The antibiotic activity of the selected antibiotics against C. diphtheriae among 23 isolates was evaluated based on CLSI 2024 standards. The results indicate resistance to chloramphenicol (30.8%), clindamycin (46.2%), sulphonamide (35.8%), Ciprofloxacin 29.9% and penicillin (10.8%), as reflected by very small zones of Inhibition. Intermediate susceptibility is observed for linezolid (63.3%), demonstrating that Tetracycline (86.2%) and erythromycin (88.9%) show the highest efficacy, with a greater zone of inhibition, showcasing their superior effectiveness as shown in Figures 1 C and 1 F.

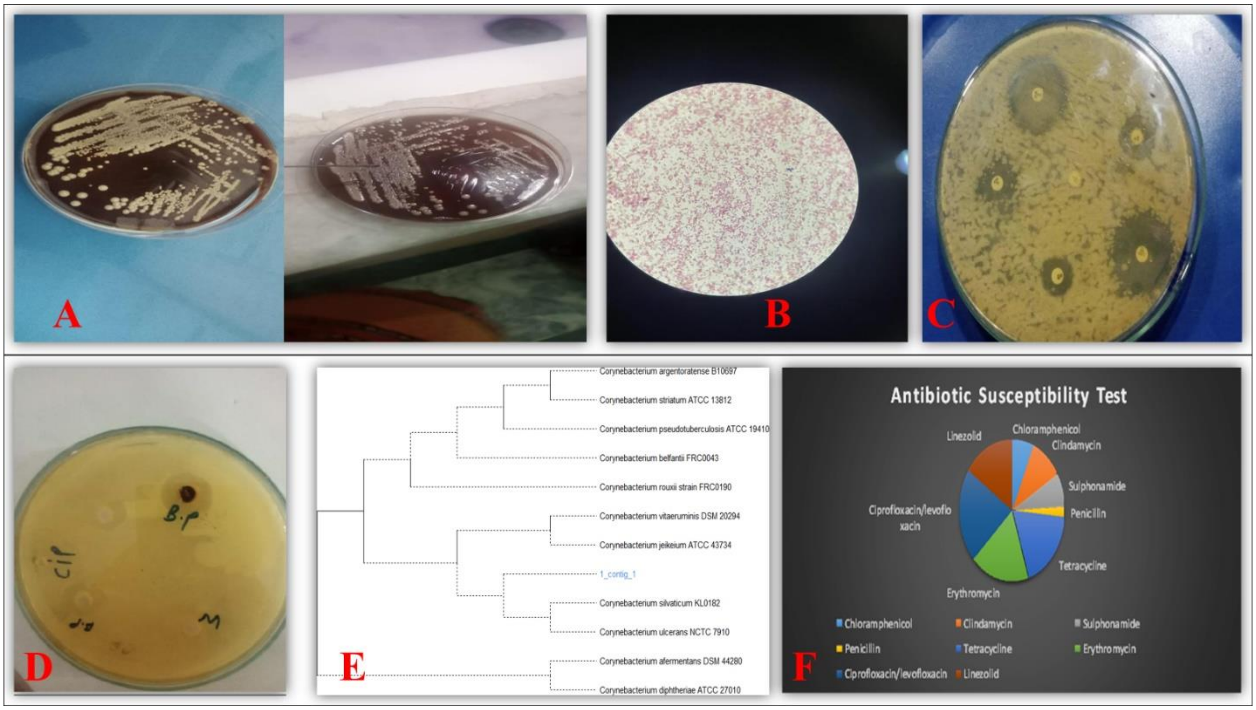

Figure 1:

A: Corynebacterium Diphtheria Isolates on Blood Agar Plate,
B: Microscopic Observation of Corynebacterium Diphtheria,
C: Antibiotic Susceptibility of Corynebacterium Diphtheriae,
D: Antibacterial Activity Against C. Diphtheriae,
E: Phylogenetic Tree Shows the Evolutionary Relationships among Different Corynebacterium Species Based on Genetic Similarity, with 99% Similarity to Corynebacterium Diphtheriae,
F: Shows Percentage of Antibiotic Susceptibility against C. Diphtheria

The result of the Agar Well Diffusion method indicates that banana peel extracts can inhibit the growth of Corynebacterium diphtheriae substantially. An 18 mm zone of inhibition showed that the hexane extract had antibacterial activity. The ethanolic extract showed a much greater zone of inhibition, which was 22.5 mm was indicating that it has higher effectiveness against C. diphtheriae as shown in Table 1 and Figure 1D. The 16S rRNA sequence analysis demonstrated 99% similarity to C. diphtheriae, as given in Figure 1E.

Table 1: Extracts Efficacy against Corynebacterium Diphtheriae

Extracts	Bacteria	Zone of Inhibition ± Standard deviation (mm)
Hexane Solvent	C. diphtheria	18 ± 0.5
Ethanol Solvent	C. diphtheria	22 ± 0.7

The synergistic effect of antibiotics combined with banana peel ethanol extracts against C. diphtheriae shows enhanced antibacterial activity. Demonstrates the highest improvement (98.4%), followed by erythromycin (98.9%) and tetracycline (91.1%), while moderate effects are seen with linezolid (68.8%) and clindamycin (50%). Limited enhancement is observed with chloramphenicol

(42.3%), sulphonamide (38.8%), ciprofloxacin (32%), and penicillin (17.5%), showing resistance as shown in Table 2.

Table 2: Synergistic Effect of Antibiotics Combined with Extracts against C. Diphtheria

Antibiotics + Ethanol Extract	Zone of Inhibition	Effect
Erythromycin + Extract	98.90%	Strong synergistic effect
Tetracycline + Extract	91.10%	Strong synergistic effect
Linezolid + Extract	72.30%	Intermediate effect
Clindamycin + Extract	50.70%	Moderate effect
Sulphonamide + Extract	48.80%	Minimal effect
Chloramphenicol + Extract	33.60%	Limited enhancement
Ciprofloxacin + Extract	32.10%	Limited enhancement
Penicillin+ Extract	17.50%	Limited enhancement

Table 3 shows the zones of inhibition (in mm) formed by different antibiotics (Tetracycline, Erythromycin, Streptomycin, Gentamicin) alone and in combination with banana peel extract (BPE) against C. diphtheriae. All antibiotics showed antibacterial activity against the tested strain, indicated by clear zones of inhibition. Combining antibiotics with banana peel extract (BPE) increased their efficacy, resulting in larger zones of inhibition. The increase in zones of inhibition when BPE is added suggests that banana peel extract may contain bioactive compounds (such as phenolics or alkaloids) that boost the antimicrobial potential of conventional antibiotics.

Table 3: Effect Of Antibiotics Alone and in Combination with Banana Peels Extracts

Bacteria	Antibiotic	Zone of Inhibition	Antibiotics + Ethanol Extract	Zone of Inhibition	Percent Change
C. Diphtheria	Penicillin	-10.80%	Penicillin + Extract	17.50%	6.70%
	Clindamycin	-46.20%	Clindamycin + Extract	50%	3.80%
	Linezolid	-72.30%	Linezolid + Extract	68.80%	-3.50%
	Sulfonamide	-35.80%	Sulfonamide+ Extract	38%	2.20%
	Tetracycline	-80.20%	Tetracycline+ Extract	94.10%	13.90%
	Ciprofloxacin	-29.90%	Ciprofloxacin + Extract	32.90%	3.00%
	Erythromycin	-79.60%	Erythromycin+ Extract	98.40%	18.80%
	chloramphenicol	-30.80%	chloramphenicol + Extract	31.30%	0.50%

Discussion

C. diphtheriae causes the production of a potent exotoxin that causes a pseudo-membrane to form over the throat and tonsils, which causes airway obstruction and difficulty breathing. Diphtheria is mostly transmitted by respiratory droplets, and it has worse effects in unvaccinated populations or those areas with poor access to healthcare. The combination of antitoxins (extracts) and antibiotics, as well as preventive measures, including vaccination, is important in the effective management of C. diphtheriae infections, which underlines the importance of the need to understanding its antimicrobial susceptibility patterns and resistance mechanisms.

A recent study found 23 strains of Corynebacterium diphtheriae in clinical samples, and this also highlights its major role in upper respiratory tract infections. This confirms earlier studies, such as Williams et al. (2020), that identified 30 strains of C [23]. In the same study, the medical importance of C. diphtheriae was emphasized, and the need to diagnose and manage it on time was emphasized. In a Spanish study by Hoefer et al. (2021), 39 of the isolates were tested, of which 21 were identified as C. diphtheriae, as 6 of them were toxigenic, and other species included C [24]. C. ulcerans, C. rouxii, and C. bellantii. One of the C. diphtheriae strains was nontoxigenic and Tox gene positive, which is indicative of diversity. These findings indicate the increasing danger of this C. diphtheriae in all locations, and require more surveillance to advance the diagnostic technologies, higher vaccination rates, and quicker therapies to reduce the impact of such infections. Research conducted by Saeed et al. (2023) in Pakistan also indicated that a significant number of patients who are affected by respiratory infection caused by diphtheria develop severe cardiac complications like myocarditis, which has a high mortality rate of 50-75 % [25].

The findings of the current study indicate that there is a great resistance pattern of antibiotics in C. diphtheriae. Chloramphenicol (30.8%), ciprofloxacin (29.9%), sulphonamide (35.8%), and penicillin (10.8%) resistance was observed as there were very small zones of inhibition. These results are comparable to other research studies that have shown similar resistance to these antibiotics, which is a cause of concern regarding the declining efficacy of these antibiotics in the treatment of diphtheria [26, 27]. Moreover, linezolid (73.7%) was found to be intermediate susceptible, and this indicates that although the antibiotics might still be effective to some extent, they might not be effective in severe cases. However, as Hennart et al. (2020) noted, the 2012 outbreak isolates were more resistant to ciprofloxacin than the sporadic isolates [23]. Also, among the isolates of diphtheria, 5.3 percent were resistant to ciprofloxacin and 10.5 percent were resistant to penicillin. Seven isolates (12%) were resistant to more than one drug, including penicillin and vancomycin, and clindamycin and vancomycin and clindamycin [23]. Another study by Zou et al. (2020) showed that tetracycline was the most effective, with a 100% zone of 100%, proving its effectiveness against C. diphtheriae. This is in line with other researchers who have found fluoroquinolones, including ciprofloxacin, to be very effective in the treatment of C. diphtheriae, especially when resistance to other antibiotics is noted [26].

The present study showed that the hexane extract had antibacterial activity against Corynebacterium diphtheriae with an 18 mm zone of inhibition, whereas the ethanolic extract had better efficacy with a 22.5 mm zone of inhibition. This emphasizes the importance of solvent polarity in the extraction of bioactive compounds because ethanol has a higher capability to dissolve both polar and non-polar compounds, which increases its extraction power. Similarly, Crestani et al. (2023) and Sharma et al. (2020) reported that ethanolic extracts contained higher concentrations of phenolic and flavonoid compounds that have potent antimicrobial activity than non-polar solvents such as hexane, which can only extract lipophilic compounds [28, 29]. Santos et al. (2021) also found that ethanolic extracts of medicinal plants showed much larger inhibition zones than hexane extracts, which further confirmed the higher efficacy of ethanol [30]. Narayanan et al. (2023) also showed the high antibacterial effect of ethyl acetate extracts, with a 17.10 mm zone of inhibition against C. diphtheriae, another indication of the effectiveness of polar solvents in increasing antimicrobial activity [31].

The current study showed that there was a synergistic effect of antibiotics with banana peel ethanol extracts against Corynebacterium diphtheriae. Achieved the highest increase (100%), and erythromycin (98.9%) and tetracycline (94.6%) showed the highest synergistic interactions. Moderate improvement was noted with linezolid (73.8%) and clindamycin (50%), whereas chloramphenicol (42.3) was of limited efficacy, and Ciprofloxacin (32.4%) and penicillin (17.5%) were resistant. The literature has shown that extracts of plants containing high amounts of phenolic and flavonoid compounds have high antibacterial properties. As an example, Saquib et al. (2021) found that phenolic-rich extracts augmented the antibacterial activity of erythromycin against gram-positive bacteria, with up to a 96% increase in inhibition zones [32]. Equally, Abo-Shama et al. (2020) found that tetramycin and plant extracts had a synergistic effect on the antibacterial activity of Staphylococcus aureus, which was improved by 95% [32]. Unlike Magryś et al. (2021), the synergistic effect of combining plant extracts with antibiotics, the extract-kanamycin combination showed the highest zones of inhibition (20-25 mm) against all tested bacteria (100%), followed by extract-chloramphenicol (90%), extract-tetracycline (70%), extract-amoxicillin (60%), extract-nalidixic acid (50%), extract-erythromycin (40%), and extract-metronidazole [33]. The checkerboard assay showed that there were 61.25 percent synergistic interactions, 23.75 percent additive/indifferent, and 15 percent antagonistic effects. Synergy was the most evident in combinations such as extract-tetracycline, metronidazole, ciprofloxacin, and amoxicillin against pathogens such as E.coli, S. aureus, K. pneumonia, and P. vulgaris [33]. The results of Vipin et al. (2020), who found that three combinations of plant extracts had a higher antibacterial activity against S. enterica in comparison to two- and four-component combinations, support the results of the present study [34]. Cefoxitin and coriander extracts were more effective in combination than cefoxitin alone in fighting K. pneumoniae, E. coli, and MRSA (Shariati et al., 2022). The various combinations of plant extracts exhibited different zones of antibacterial activity against K. pneumoniae, with the maximum inhibition being at 20 mg/mL of acetyl acetate and aqueous extracts [35]. In addition, the combined ethanolic leaf extracts of Chrysanthemum odoratum, Lawsonia inermis, and Catharanthus roseus were more effective against MRSA than individual leaf extracts. In general, the banana extracts of the study exhibited potent antibacterial activity against the human pathogens tested, which shows their versatility as bioactive agents.

Conclusion

Corynebacterium diphtheriae was identified in the upper respiratory tract samples, and the study of the application of plant extracts with the use of traditional antibiotics provided useful data on the potential treatment methods. The 23 clinical isolates were obtained, which proved the significant occurrence of C. diphtheriae in respiratory infections. The antibiotic susceptibility testing showed a high level of resistance to various commonly used drugs-clindamycin, ciprofloxacin, sulphonamide, and chloramphenicol, highlighting the increasing problem of antimicrobial resistance in this pathogen. The tested plant extracts, especially the ethanol extract of banana peels, showed good antibacterial properties, where ethanol extracts had better inhibitory effects than hexane extracts. The combination of these plant extracts with antibiotics such as erythromycin and tetracycline showed strong synergistic effects, which improved the overall antimicrobial action.

Acknowledgements:

The authors gratefully acknowledge the conducive environment of Bashir Institute of Health Sciences that enabled them to complete this study successfully. The authors would also like to express their sincere gratitude to the Faculty of Life Sciences, Sarhad Institute of Allied Health Sciences, in providing their academic support and guidance during the research work.

Ethical Approval:

The study was approved by the ethics committee and institutional review board of Sarhad Institute of Allied Health Sciences Sarhad University of Science and Information Technology, Peshawar. The ethical approval latter Ref No: was provided by institute to conduct his study.

Data Availability:

The data supporting the findings of current research study is available to provide on reasonable request.

Financial Support and Sponsorship:
No financial support or sponsorship was provided by any institution or person.

Conflict of Interest:
No conflict of interest among authors to declare.

Authors Contribution:
Mareeha Hayat was the main contributor to this study, including its design, experimental work, data collection, analysis, and manuscript preparation. Dr. Asif Mehmood supervised the research, providing guidance, critical review, and oversight throughout the process, participated in overall designing the study, collecting and analyzing data, compiling the final results and interpreting those results. Dr Nasir Ali co Supervised the research

REFERENCES

1. Eedee, K.F., et al., *Antimicrobial Activities of Ethanol Extract of Banana (Musa sapientum L.) Peels against Organisms Associated with Urinary Tract Infection.* Asian Journal of Research in Infectious Diseases, 2022. **9**(1): p. 1-7.
2. Okyere, J., et al., *Utilisation of traditional healers among older people living with HIV in South Africa: a WHO SAGE well-being of older people study.* AIDS Research and Therapy, 2023. **20**(1): p. 40.
3. SeyedAlinaghi, S., et al., *A systematic review on natural products with antimicrobial potential against WHO's priority pathogens.* Eur J Med Res, 2025. **30**(1): p. 525.
4. Lahiri, D., et al., *Microbiologically-synthesized nanoparticles and their role in silencing the biofilm signaling cascade.* Frontiers in microbiology, 2021. **12**: p. 636588.
5. Prygiel, M., et al., *New Corynebacterium species with the potential to produce diphtheria toxin.* Pathogens, 2022. **11**(11): p. 1264.
6. Sharma, N.C., et al., *Diphtheria.* Nature Reviews Disease Primers, 2019. **5**(1): p. 81.
7. Arcari, G., et al., *Multidrug-resistant toxigenic Corynebacterium diphtheriae sublineage 453 with two novel resistance genomic islands.* Microbial Genomics, 2023. **9**(1): p. 000923.
8. Arcari, G., et al., *Multidrug-resistant toxigenic Corynebacterium diphtheriae sublineage 453 with two novel resistance genomic islands.* Microb Genom, 2023. **9**(1).
9. Brémont, S., et al., *Multidrug-resistant Corynebacterium diphtheriae in people with travel history from West Africa to France, March to September 2023.* Euro Surveill, 2023. **28**(46).
10. Williams, M.M., et al., *Detection and Characterization of Diphtheria Toxin Gene-Bearing Corynebacterium Species through a New Real-Time PCR Assay.* J Clin Microbiol, 2020. **58**(10).
11. Forde, B.M., et al., *Fatal Respiratory Diphtheria Caused by β-Lactam-Resistant Corynebacterium diphtheriae.* Clin Infect Dis, 2021. **73**(11): p. e4531-e4538.
12. Atta, S., et al., *Antibacterial potential and synergistic interaction between natural polyphenolic extracts and synthetic antibiotic on clinical isolates.* Saudi J Biol Sci, 2023. **30**(3): p. 103576.
13. García-Villegas, A., et al., *Cosmeceutical potential of major tropical and subtropical fruit by-products for a sustainable revalorization.* Antioxidants, 2022. **11**(2): p. 203.
14. Otshudiema, J.O., et al., *Respiratory Illness Caused by Corynebacterium diphtheriae and C. ulcerans, and Use of Diphtheria Antitoxin in the United States, 1996-2018.* Clin Infect Dis, 2021. **73**(9): p. e2799-e2806.
15. TURAY, F.M., *Banana Peel can be Utilize as A Promising Alternative for Medicinal Activities (Cancer Treatment).* 2023, University of Sierra Leone.

16. Akhtar, S., et al., *Review of Traditional and Phytochemical Compounds in Herbs, Shrubs, Climbers, and Trees from Jammu and Kashmir Union Territory of Indian Subcontinent Used in Management of Respiratory Disorders.* Natural Product Communications, 2025. **20**(4): p. 1934578X251338522.
17. Balouiri, M., M. Sadiki, and S.K. Ibnsouda, *Methods for in vitro evaluating antimicrobial activity: A review.* J Pharm Anal, 2016. **6**(2): p. 71-79.
18. Al-Dhabaan, F.A., *Morphological, biochemical and molecular identification of petroleum hydrocarbons biodegradation bacteria isolated from oil polluted soil in Dhahran, Saud Arabia.* Saudi Journal of Biological Sciences, 2019. **26**(6): p. 1247-1252.
19. Church, D.L., et al., *Performance and Application of 16S rRNA Gene Cycle Sequencing for Routine Identification of Bacteria in the Clinical Microbiology Laboratory.* Clin Microbiol Rev, 2020. **33**(4).
20. Lau, C.L., et al., *Performance of direct-from-blood-culture disk diffusion antibiotic susceptibility testing and its impact on antibiotic adjustment in bloodstream infections at a Malaysian tertiary center.* Microbiol Spectr, 2025. **13**(8): p. e0286324.
21. Zeleke, B., et al., *Phytochemical screening and antimicrobial activity of Polygala sadebeckiana Gürke extracts on bacterial isolates from Wound samples of patients with "Shimetere".* BMC Complement Med Ther, 2024. **24**(1): p. 72.
22. Limboo, K.H. and B. Singh, *Antibiotic potentiating effect of Bauhinia purpurea L. against multidrug resistant Staphylococcus aureus.* Frontiers in Microbiology, 2024. **Volume 15 - 2024**.
23. Hennart, M., et al., *A global Corynebacterium diphtheriae genomic framework sheds light on current diphtheria reemergence.* Peer Community Journal, 2023. **3**.
24. Hoefer, A., et al., *Molecular and epidemiological characterization of toxigenic and nontoxigenic Corynebacterium diphtheriae, Corynebacterium belfantii, Corynebacterium rouxii, and Corynebacterium ulcerans isolates identified in Spain from 2014 to 2019.* Journal of clinical microbiology, 2021. **59**(3): p. 10.1128/jcm. 02410-20.
25. Saeed, M., et al., *Diphtheria in Pakistan post-COVID-19, a potential public health threat: an update.* Tropical Medicine and Health, 2023. **51**(1): p. 24.
26. Schaeffer, J., et al., *Assessing the genetic diversity of Austrian Corynebacterium diphtheriae clinical isolates, 2011 to 2019.* Journal of clinical microbiology, 2021. **59**(3): p. 10.1128/jcm. 02529-20.
27. Otshudiema, J.O., et al., *Respiratory illness caused by Corynebacterium diphtheriae and C. ulcerans, and use of diphtheria antitoxin in the United States, 1996–2018.* Clinical Infectious Diseases, 2021. **73**(9): p. e2799-e2806.
28. Crestani, C., et al., *Corynebacterium ramonii sp. nov., a novel toxigenic member of the Corynebacterium diphtheriae species complex.* Research in Microbiology, 2023. **174**(7): p. 104113.
29. Sharma, A., et al., *Medicinal plants and their components for wound healing applications.* Future Journal of Pharmaceutical Sciences, 2021. **7**(1): p. 1-13.
30. Santos, L.M., et al., *Activity of ethanolic and supercritical propolis extracts in Corynebacterium pseudotuberculosis and its associated biofilm.* Frontiers in Veterinary Science, 2021. **8**: p. 700030.
31. Narayanan, M., et al., *Antibacterial and antioxidant efficacy of ethyl acetate extract of Cymodocea serrulata and assess the major bioactive components in the extract using GC-MS analysis.* Process Biochemistry, 2023. **124**: p. 24-32.

32. Saquib, S.A., et al., *Synergistic antibacterial activity of herbal extracts with antibiotics on bacteria responsible for periodontitis.* The Journal of Infection in Developing Countries, 2021. **15**(11): p. 1685-1693.
33. Magryś, A., A. Olender, and D. Tchórzewska, *Antibacterial properties of Allium sativum L. against the most emerging multidrug-resistant bacteria and its synergy with antibiotics.* Archives of microbiology, 2021. **203**(5): p. 2257-2268.
34. Odabaş Köse, E., et al., *Quercetin: synergistic interaction with antibiotics against colistin-resistant Acinetobacter baumannii.* Antibiotics, 2023. **12**(4): p. 739.
35. Shariati, A., et al., *The resistance mechanisms of bacteria against ciprofloxacin and new approaches for enhancing the efficacy of this antibiotic.* Frontiers in public health, 2022. **10**: p. 1025633.