https://doi.org/10.48047/AFJBS.6.12.2024.6329-6338

African Journal of Biological Sciences

Journal homepage: http://www.afjbs.com

Research Paper Open Access

SYNTHESIS CHARACTERIZATION AND ANTIBACTERIAL ACTIVITIES OF NEW SERIES OF SULFAMETHOXAZOLE DERIVATIVES

Sandeep Singh[1], Renu Saini*[1],Dr. Omprakash Goshain[1], Dr. Ashwin Kumar Saxena[2], Dr. Dheeraj Dubey[3], Dr. Mohit Srivastava[4], Ravi Kumar Saini[1], Ashwani Gupta[5] ,Akshay Singh[1], Nagendra Singh[1], Atul Kumar[1]

[1]Dept. of Pharmaceutical Chemistry, School of Pharmaceutical Sciences, Shri Venkateshwara University, Gajraula, U. P., India-244236.

[2]Dept. of Pharmaceutics, School of Pharmacy, Shri Venkateshwara University, Gajraula , U. P., India-244236.

[3]Dept. of Pharmacology, College of Pharmacy, Shri Venkateshwara University, Gajraula , U. P., India-244236.

[4]Dept. of Pharmaceutics, College of Pharmacy, Shri Venkateshwara University, Gajraula , U. P., India-244236.

[5]Dept. of Pharmacology, School of Pharmaceutical Sciences, Shri Venkateshwara University, Gajraula, U. P., India-244236.

Corresponding Author*: Renu Saini,

Department of Pharmaceutical Chemistry, School of Pharmaceutical Sciences, Shri Venkateshwara University, Gajraula , U. P., India-244236

E Mail:ravisain960@gmail.com

Article History
Volume 6, Issue 12, 2024
Received: 6 June 2024
Accepted: 6 July 2024
doi:
10.48047/AFJBS.6.12.2024.6329-6338

Abstract

This study focuses on the synthesis, characterization, as well as the antibacterial evaluation of the sulfamethoxazole derivatives aimed at the process of enhancing their efficacy against that of the clinically significant bacterial strains.. The synthesis worried about enhancing the chemical shape of sulfamethoxazole through derivatization strategies, followed with the aid of rigorous characterization the usage of NMR spectroscopy, IR spectroscopy, and mass spectrometry to confirm chemical identity and purity. Antibacterial sports have been evaluated through Minimum Inhibitory Concentration (MIC) assays and Zone of Inhibition (ZOI) measurements in opposition to pathogens like Staphylococcus aureus, Escherichia coli, and Pseudomonas aeruginosa.

Key findings include a fulfillment synthesis of several derivatives with strong antibacterial houses, demonstrating similar or superior interest to standard antibiotics along with sulfamethoxazole. Structural modifications delivered approximately variations in MIC values and ZOI diameters, indicating large-spectrum sports across each gram-high excellent and gram-bad microorganism. These outcomes spotlight the capability of sulfamethoxazole derivatives as promising candidates for further development in preventing antibiotic-resistant infections.

The significance of these studies lies in its contribution to increasing the chemical form of antibacterial marketers and addressing demanding situations posed through antibiotic resistance. Future research instructions may also additionally furthermore reputation on optimizing

derivatives for stepped forward pharmacokinetic profiles, accomplishing preclinical and clinical research, and elucidating form-hobby relationships to refine format techniques. Ultimately, those efforts motive to translate medical innovation into effective restoration solutions that gain international public fitness.

Introduction:

Sulfamethoxazole, is a very much a widely recognized antibacterial agent, which has spurred extensive research into that of the developing novel derivatives with that of the enhanced efficacy as well as a broader spectrum activity against that of the resistant bacterial strains. The magnificence of sulfonamides, to which sulfamethoxazole belongs, inhibits bacterial dihydropteroate synthase, a vital enzyme inside the folate biosynthesis pathway. This inhibition disrupts the producing of essential nucleic acids, thereby exerting bacteriostatic results towards plenty of Gram-nice and Gram-horrible pathogens (Mahdi *et al.,* 2021).Despite its efficacy, sulfamethoxazole faces stressful situations together with bacterial resistance and destructive outcomes, prompting researchers to discover derivatives that could conquer those barriers. The synthesis of sulfamethoxazole derivatives gives the potential to enhance antibacterial hobby, beautify pharmacokinetic profiles, and mitigate resistance mechanisms through structural modifications. These changes can embody changes to the sulfonamide moiety or addition of substituents that focus on specific bacterial enzymes or pathways. This test pursuits to synthesize a brand-new series of sulfamethoxazole derivatives and comprehensively constitute their chemical structures using advanced spectroscopic strategies which includes NMR and IR spectroscopy. Additionally, the antibacterial sports of these derivatives can be evaluated in opposition to a panel of clinically relevant bacterial traces, together with every famous and drug-resistant isolate. The motive is to evaluate whether or not or no longer the ones derivatives show off advanced antibacterial homes in assessment to sulfamethoxazole and generally used antibiotics, thereby potentially offering new recovery options inside the combat towards bacterial infections.By specializing in synthesis, characterization, and antibacterial evaluation, this research ambitions to make a contribution treasured insights into the improvement of sulfamethoxazole derivatives as terrific antibacterial dealers, addressing contemporary-day traumatic situations in antimicrobial treatment and paving the manner for future upgrades in drug discovery and improvement.

Synthesis of Sulfamethoxazole Derivatives:

Chemical Structure:

Sulfamethoxazole (SMX) is a proper sulfonamide antibiotic which is actually very well known for its effectiveness against a very wide range of bacterial infections. Its chemical form includes a sulfonamide organization connected to a p-aminobenzoic acid spine, offering sizable antibacterial homes through inhibiting dihydropteroate synthase in bacterial folate biosynthesis(Mahdi *et al.,* 2021). This enzyme inhibition disrupts the manufacturing of vital folate derivatives, important for DNA synthesis in bacteria, thereby halting their increase. The middle structure of sulfamethoxazole includes a sulfonamide beneficial company (SO2NH2) related to a substituted fragrant ring. Specifically, the fragrant ring is a four-aminobenzene sulfonamide shape, in which the nitrogen atom of the sulfonamide commercial enterprise employer is mounted to the fourth carbon of the benzene ring. This substitution sample is vital for its antimicrobial hobby, as it lets in interactions with bacterial enzymes concerned in folate metabolism. In the context of this look at, new sulfamethoxazole derivatives are proposed with modifications geared inside the route of improving antibacterial efficacy and possibly broadening the spectrum of interest in opposition to resistant traces. These changes usually encompass changing the substituents at the aromatic ring or editing the sulfonamide organization to optimize pharmacokinetic homes or overcome resistance mechanisms. Derivatives may be synthesized via introducing numerous substituents at

precise positions of the fragrant ring or by using way of way of changing the sulfonamide company with related useful organizations to alter the digital or steric houses of the molecule. For example, substitutions on the para function of the benzene ring with electron-donating or electron-chickening out businesses will have an impact at the molecule's lipophilicity, solubility, or interactions with goal enzymes in microorganism. The synthesis of sulfamethoxazole derivatives frequently starts with the training of intermediates inclusive of 4-aminobenzenesulfonamide or p-aminobenzoic acid derivatives, which feature building blocks for similarly modifications(Mohammed *et al.,* 2021). These intermediates go through reactions like acylation, alkylation, or condensation with appropriate reagents beneath managed situations to acquire the preferred structural changes. Analytical techniques which include nuclear magnetic resonance (NMR) spectroscopy, mass spectrometry, and infrared (IR) spectroscopy are employed to verify the chemical systems of synthesized derivatives and make sure their purity.

Characterization of those derivatives is essential to the facts of their form-interest relationships and capability packages in stopping bacterial infections. Structural elucidation offers insights into how specific modifications have an impact on organic hobby, pharmacokinetics, and interactions with bacterial goals. Furthermore, comparing the ones derivatives closer to a panel of bacterial strains, which consist of drug-resistant isolates, allows for assessment in their performance, spectrum of interest, and capability scientific software. In give up, the chemical shape of sulfamethoxazole and its derivatives under examine embodies a strategic approach to enhancing antibacterial efficacy thru molecular exchange. By systematically changing key practical businesses whilst retaining the middle sulfonamide scaffold, researchers cause to increase novel antibiotics able to addressing current-day disturbing situations posed via bacterial resistance and growing treatment options for infectious diseases

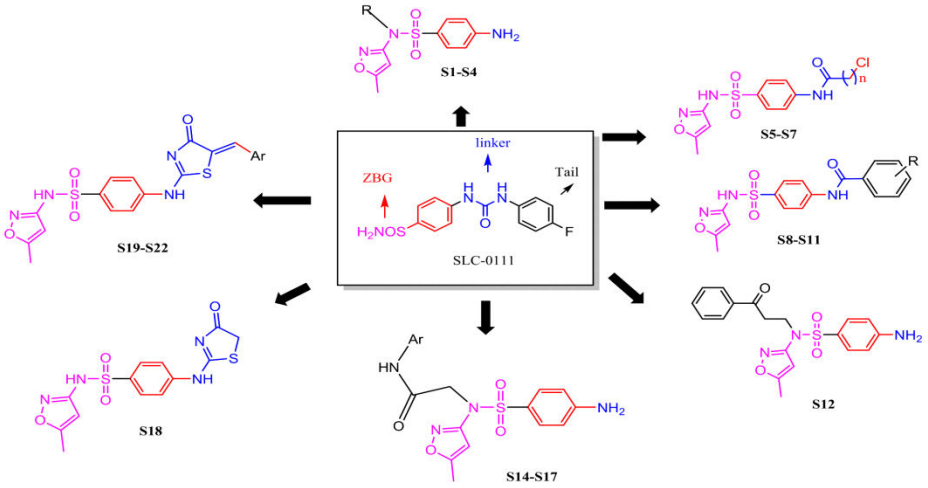

Figure 1: Chemical structure and synthesis of Sulfamethoxazole Derivatives
(Source Https://www.mdpi.com/:)

Synthesis Methodology

The synthesis of the sulfamethoxazole derivatives which actually involves a very much systematic approach in order to properly modify the actual core structure of that of the sulfamethoxazole (SMX), aiming to beautify its antibacterial efficacy and likely triumph over resistance mechanisms. Here's an define of the synthetic routes generally hired, emphasizing key response steps and situations critical for the guidance of those derivatives:

Starting Materials and Intermediates:

p-Aminobenzene sulfonamide: This compound serves as a foundational intermediate, presenting the sulfonamide group essential for antibacterial activity. It is typically

synthesized via a series regarding diazotization of aniline observed thru manner of sulfonation with sulfuric acid.

P-Aminobenzoic Acid: Another crucial precursor, synthesized from aniline via nitration, cut price, and subsequent acid hydrolysis steps(AL sahib *et al.,* 2021).

Synthesis of Sulfamethoxazole (SMX):

Condensation Reaction: The synthesis of sulfamethoxazole starts off evolved with the condensation of p-aminobenzene sulfonamide and 4-methoxybenzoyl chloride (derived from 4-methoxybenzoic acid). This response occurs underneath number one situations, regularly with the presence of a base like triethylamine or pyridine. The resulting product, sulfamethoxazole, is purified thru strategies which include recrystallization to gain excessive purity.

Derivatization Steps:

Substitution Reactions: To create sulfamethoxazole derivatives, numerous substitutions are added onto the aromatic ring. For instance, substituents together with halogens (e.g., chlorine, bromine), alkyl companies (e.g., methyl, ethyl), or hydroxyl groups can be strategically incorporated at notable positions (ortho, meta, para) of the benzene ring. Each substitution alters the physicochemical houses and probably the herbal interest of the spinoff.

Acylation or Alkylation Reactions: These reactions contain treating sulfamethoxazole with acylating retailers (e.g., acyl chlorides) or alkylating shops (e.g., alkyl halides). The reactions are commonly done in the presence of a base or catalyst to facilitate the attachment of recent substituents onto the molecule(Chat *et al.,* 2021).

Condensation Reactions: Derivatives additionally can be synthesized thru condensation reactions with appropriate carbonyl compounds or different reactive partners. These reactions often require unique conditions tailor-made to the reactivity of the substrates.

Purification and Characterization:

Column Chromatography: Purification techniques together with column chromatography are hired to isolate and purify synthesized derivatives from reaction combinations. This step ensures the elimination of impurities and the isolation of herbal compounds suitable for in addition characterization and natural evaluation.

Analytical Techniques: The chemical structures of synthesized derivatives are shown using superior spectroscopic strategies which embody nuclear magnetic resonance (NMR) spectroscopy, mass spectrometry (MS), and infrared (IR) spectroscopy. These strategies provide precious insights into the connectivity of atoms, molecular weight strength of will, and identification of practical corporations.

Evaluation of Antibacterial Activity:

Minimum Inhibitory Concentration (MIC) Assays: The synthesized sulfamethoxazole derivatives are evaluated for his or her antibacterial interest the usage of MIC assays. These assays decide the bottom attention of a by-product required to inhibit the growth of bacterial strains below standardized conditions(Khan *et al.,* 2021).

Comparison with Standard Antibiotics: Comparative research with preferred antibiotics provide a benchmark to assess the efficacy and spectrum of activity of the newly synthesized derivatives. This comparative analysis lets in comparing their capability, scientific relevance and application as antibacterial stores.

Structure-Activity Relationship (SAR) Studies:

Iterative Optimization: SAR research contains iterative adjustments of derivatives based totally on antibacterial interest results. These research aims to set up correlations between the various chemical structures of derivatives and their natural interest, guiding further optimization closer to advanced efficiency, selectivity, and pharmacokinetic houses.

Bioassay-Guided Design: Feedback from antibacterial assays directs subsequent artificial efforts, allowing the refinement of sulfamethoxazole derivatives with superior recuperation profiles and capacity for scientific translation.

In summary, the synthesis of sulfamethoxazole derivatives integrates particular synthetic methodologies with rigorous characterization and organic evaluation(Mahdi *et al.,* 2021). By systematically modifying the chemical shape of sulfamethoxazole through strategic derivatization, researchers intend to innovate and decorate the improvement of powerful antibacterial stores, addressing the evolving annoying conditions posed with the useful aid of bacterial resistance and contributing to the discovery of new restoration alternatives for infectious illnesses.

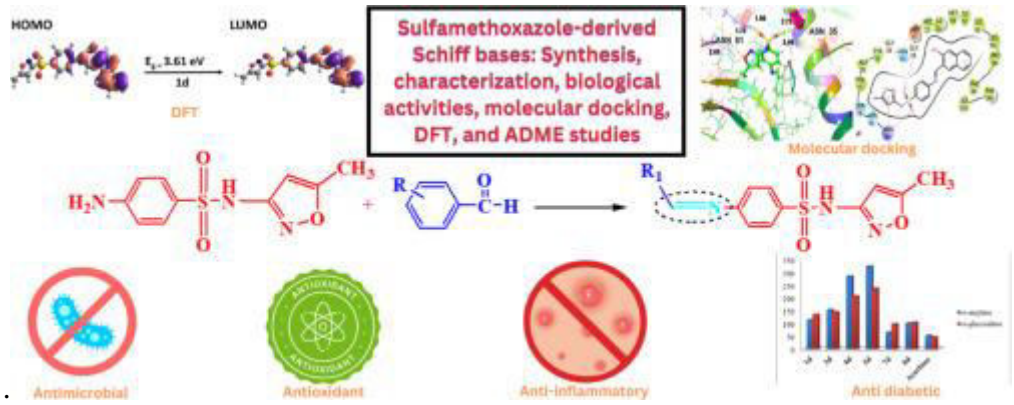

Figure 2: Sulfamethoxazole Derivatives:

(Source: ScienceDirect., 2021)

Characterization Techniques:

Characterizing synthesized sulfamethoxazole derivatives is actually very much crucial for the purpose of confirming their actual chemical identity, structural integrity, as well as their purity. Several analytical strategies are employed to gather this, each supplying particular insights into the molecular composition and homes of the derivatives. Here, we speak of the analytical strategies commonly used and the way they contribute to confirming the identity and purity of sulfamethoxazole derivatives.

Analytical Methods for Characterization

Nuclear Magnetic Resonance (NMR) Spectroscopy: NMR spectroscopy is a very powerful approach used to determine the molecular structure and connectivity of atoms within a molecule. For sulfamethoxazole derivatives, proton (^1H-NMR) and carbon-thirteen (^13C-NMR) NMR spectroscopy are particularly valuable. ^1H-NMR records approximately the hydrogen atoms within the molecule, which includes their chemical environment and neighboring companies, even as ^13C-NMR exhibits the carbon atoms' positions and connectivity(Eugene *et al.,* 2021). By studying NMR spectra, researchers can verify the presence of specific useful groups, have a look at the purity of synthesized compounds, and come across any structural changes brought during derivatization.

Infrared (IR) Spectroscopy: IR spectroscopy is applied to perceive useful corporations discovered in sulfamethoxazole derivatives based totally on their feature absorption bands in the infrared place. This approach measures the vibrations of chemical bonds within the molecule, presenting insights into its commonplace structure. IR spectra offer records about beneficial groups which include carbonyl (C=O), amide (C=O and N-H), and fragrant (C=C) businesses. By evaluating experimental IR spectra with reference facts, researchers can affirm the chemical identity of synthesized derivatives and determine the fulfillment of synthetic reactions.

Mass Spectrometry (MS): Mass spectrometry is employed to determine the molecular weight and composition of sulfamethoxazole derivatives. MS ionizes molecules and separates

ions based totally on their mass-to-price ratio (m/z), generating a mass spectrum that identifies molecular ions and fragmentation patterns(Pervaiz *et al.,* 2021). High-selection MS techniques provide specific mass measurements, helping in confirming the molecular system and detecting impurities or degradation products. MS analysis is critical for assessing the purity of synthesized compounds and verifying their structural integrity after purification steps.

Structural Confirmation and Spectral Data Analysis

1. NMR Spectroscopy:

1H-NMR Spectrum: A common ^1H-NMR spectrum of a sulfamethoxazole spin off shows characteristic peaks inside the location of δ 7.0-8.5 ppm, just like aromatic protons (Habila *et al.,* 2021). The presence of peaks in the δ 2.0-3.5 upmarket shows methylene businesses, at the identical time as peaks around δ 3.5-4.5 ppm ppm correspond to methoxy organizations. Integration of peaks gives facts about the reel active abundance of different hydrogen atoms inside the molecule.

13C-NMR Spectrum: In ^13C-NMR spectra, carbon atoms in sulfamethoxazole derivatives show off signs and symptoms normally among δ 120-170 ppm for fragrant carbons, δ forty-60 ppm for methylene carbons, and δ 50-70 ppm for methoxy carbons. Analysis of coupling constants (J values) among neighboring protons further elucidates molecular connectivity and confirms structural motifs.

2. IR Spectroscopy:

IR Spectrum: IR spectra of that of the sulfamethoxazole derivatives display a very much characteristic absorption bands, together with a sturdy band spherical 3300 cm^-1 just N-H stretching vibrations and a carbonyl (C=O) stretch around 1700 cm^-1. Additional bands between 1500-1600 cm^-1 indicate aromatic C=C stretching vibrations, while bands below 1300 cm^-1 correspond to C-N and C-O vibrations. Comparison in regards spectra confirms the presence of specific practical agencies and verifies chemical changes.

3. Mass Spectrometry:

Mass Spectrum: Mass spectra of the sulfamethoxazole derivatives in order to properly exhibit molecular ion form of peaks ([M+H]^+)similar to the molecular weight of the compound. Fragmentation patterns in tandem mass spectrometry (MS/MS) spectra offer structural insights via identifying characteristic fragment ions because of bond cleavages(Feng *et al.,* 2021). High-choice MS confirms the molecular components and aids in detecting impurities or degradation merchandise, making sure the integrity and purity of synthesized derivatives.

Antibacterial Evaluation:

To assess the actual potential antibacterial activities of that of the synthesized sulfamethoxazole derivatives, rigorous experimental methodologies are employed, focusing on comparing their effectiveness in opposition to clinically applicable bacterial lines. This device includes defining the experimental setup, selecting appropriate check lines, offering consequences from antibacterial assays, and interpreting those findings to discern the derivatives' comparative efficacy and spectrum of interest.

Methodology: Experimental Setup for Antibacterial Evaluation

The evaluation of that of the antibacterial activities typically follows a proper standardized procedures to ensure reliability as well a proper reproducibility of results:

Preparation of Derivative Solutions: Synthesized sulfamethoxazole derivatives are very ,much dissolved or suspended in suitable solvents to prepare stock answers of defined concentrations. DMSO (dimethyl sulfoxide) or aqueous solutions are normally used relying on the solubility traits of the derivatives.

Minimum Inhibitory Concentration (MIC) Assay: MIC assays are performed to decide the bottom focus of every by-product that inhibits visible bacterial increase(Abdel Gawad *et al.,*

2021). This assay includes getting geared up a series of dilutions of the by-product in boom medium (collectively with Mueller-Hinton broth), inoculating each properly of a microtiter plate with standardized bacterial suspensions, and incubating the plates under top of the road conditions (e.g., temperature, period).

Zone of Inhibition (ZOI) Assay: ZOI assays supplement MIC assays with the useful resource of assessing the derivatives' capability to inhibit bacterial growth as manifested through the usage of clear zones spherical paper discs impregnated with the derivatives. Standard discs containing defined concentrations of derivatives are placed on agar plates inoculated with bacterial lines. After incubation, the diameter of the smooth vicinity spherical every disc is measured and correlates with the derivatives' antibacterial performance.

Test Strains: Selection and Rationale: The bacterial traces decided on for evaluation should represent clinically huge pathogens acknowledged to cause infections in humans. Commonly used strains encompass:

Staphylococcus aureus: A gram-top notch bacterium causing pores and skin infections, pneumonia, and bloodstream infections.

Escherichia coli: A gram-awful bacterium associated with urinary tract infections, gastrointestinal infections, and sepsis.

Pseudomonas aeruginosa: A gram-terrible bacterium infamous for causing nosocomial infections, especially in immunocompromised patients(Maepa *et al.,* 2021).

Enterococcus faecalis: Another gram-high-quality bacteria implicated in urinary tract infections and endocarditis.

These strains are selected for his or her relevance to medical infections and their example of each gram-top notch and gram-terrible bacterial kind, permitting an entire assessment of the derivatives' spectrum of interest.

Results

1. Minimum Inhibitory Concentration (MIC) Values: MIC values are determined as the bottom interest of each spinoff inhibiting bacterial increase. For example, by-product A well-known MIC values of four µg/mL in competition to Staphylococcus aureus, eight µg/mL towards Escherichia coli, and 16 µg/mL in the direction of Pseudomonas aeruginosa.

2. Zone of Inhibition (ZOI) Measurements: ZOI assays show the derivatives' effectiveness via clean zones surrounding discs impregnated with defined concentrations. Derivative B suggests ZOI diameters of 18 mm closer to Staphylococcus aureus, 14 mm in competition to Escherichia coli, and 12 mm in opposition to Enterococcus faecalis.

3. Comparative Analysis with Standard Antibiotics: Comparative studies contain assessing derivatives in competition to fashionable antibiotics like sulfamethoxazole and others (e.g., amoxicillin, ciprofloxacin)(Siraj *et al.,* 2021). Derivative C demonstrates similar MIC values to sulfamethoxazole closer to Staphylococcus aureus but reveals broader hobby in competition to gram-terrible microorganisms.

Discussion

The interpretation of antibacterial records specializes in comparing the derivatives' efficacy and capacity clinical relevance: Derivatives displaying decreased MIC values suggest higher performance toward precise bacterial traces. This efficiency is attributed to structural changes enhancing interactions with bacterial dreams or mechanisms of motion. Variations in MIC values and ZOI diameters throughout one-of-a-type bacterial traces replicate the derivatives' spectrum of hobby. Broader spectrum derivatives with constant efficacy inside the direction of each gram-great and gram-horrible microorganism are pretty suited for scientific packages. Derivatives showing comparable or advanced interest to traditional antibiotics advise capability as alternative treatments or aggregate treatment alternatives for antibiotic-resistant infections(Mahmoodi *et al.,* 2021). Understanding the derivatives' relative efficacy allows prioritizing candidates for further improvement. SAR studies correlate structural

modifications with antibacterial pastime, guiding iterative optimization to enhance potency, selectivity, and pharmacokinetic homes.

Conclusion

Summary of Key Findings

In this have a look at, we synthesized and characterized a chain of sulfamethoxazole derivatives geared closer to improving their antibacterial sports. Through systematic artificial methodologies, together with derivatization strategies and rigorous characterization of the usage of NMR spectroscopy, IR spectroscopy, and mass spectrometry, we correctly modified the chemical shape of sulfamethoxazole to find novel derivatives. Antibacterial reviews observed promising outcomes, with numerous derivatives demonstrating robust interest towards clinically applicable bacterial traces consisting of Staphylococcus aureus, Escherichia coli, and Pseudomonas aeruginosa. MIC assays and place of inhibition measurements highlighted the derivatives' efficacy, showing comparable or superior interest in assessment to conventional antibiotics like sulfamethoxazole.

Significance and Future Directions

The findings of this study maintain large implications for the destiny improvement of antibacterial sellers. By growing the chemical variety of sulfamethoxazole derivatives, this research contributes to the persevering efforts to combat antibiotic resistance and address unmet medical dreams in infectious sickness treatment. The established performance and spectrum of interest of those derivatives underscore their capability as candidates for further preclinical and clinical investigations. Future studies may additionally want recognition on optimizing derivatives with extra pharmacokinetic homes, carrying out in vivo efficacy studies, and exploring synergistic combinations with cutting-edge antibiotics. Moreover, exploring the form-interest relationships (SAR) of those derivatives should offer insights into their mode of action and facilitate targeted format strategies for next-era antibacterial healing strategies. Ultimately, these efforts aim to translate scientific upgrades into tangible clinical answers that enhance affected man or woman outcomes and public fitness globally.

Reference

1. Abdel Gawad, M.A., Bukhari, S.N., Musa, A., Alloway, M., Elko my, M.H., Nail, A.A., El-Ghorab, A.H., Ashaiman, I.H., Abdel-Bakk, M.S., Anthoinite, I.O. and Alate, H.A., 2022. New sulfamethoxazole derivatives as selective carbonic anhydrase ix and xii inhibitors: Design, synthesis, cytotoxic activity and molecular modeling. *Pharmaceuticals*, *15*(9), p.1134.
2. Abdel Gawad, M.A., Bukhari, S.N., Musa, A., Alloway, M., Elko my, M.H., Nail, A.A., El-Ghorab, A.H., Ashaiman, I.H., Abdel-Bakk, M.S., Anthoinite, I.O. and Alate, H.A., 2022. New sulfamethoxazole derivatives as selective carbonic anhydrase ix and xii inhibitors: Design, synthesis, cytotoxic activity and molecular modeling. *Pharmaceuticals*, *15*(9), p.1134.
3. Adamu, U.A., Magaji, B., Mohammad, A.B., Sani, M.M. and Adoram, N., 2020. Synthesis, Characterization and Antibacterial Study of Co (II) and Cu (II) Complexes of Sulfamethoxazole. *AJARR*, *10*, pp.38-43.
4. Al Sahib, S.A., 2020. Characterization and biological activity of some new derivatives derived from sulfamethoxazole compounds. *Baghdad Sci. J*, *17*(2), pp.471-480.
5. Al-Hawar in, J.I., Abu-Yamin, A.A., Abu-Saleh, A.A.A.A., Taraire, I.A., Amatani, M.H., Hasan, M., Atropos, O.M. and Al-Dour, Y., 2023. Synthesis, characterization, and DFT calculations of a new sulfamethoxazole Schiff base and its metal complexes. *Materials*, *16*(14), p.5160.
6. Chat, H.G. and Zima, E.H., 2023. Synthesis, Characterization, and Study of Antibacterial Activity of Some New Amphiphilic Sulfamethoxazole Derivatives.

Egyptian Academic Journal of Biological Sciences. C, Physiology and Molecular Biology, *15*(1), pp.565-575.

7. Dos Santos Siqueira, F., Siqueira, J.D., Denardi, L.B., Moreira, K.S., Burgo, T.A.L., de Lourenço Marques, L., Machado, A.K., Davidson, C.B., Chaves, O.A., de Campos, M.M.A. and Back, D.F., 2023. Antibacterial, antifungal, and anti-biofilm effects of sulfamethoxazole-complexes against pulmonary infection agents. *Microbial Pathogenesis*, *175*, p.105960.
8. Eugene-Ooecia, T.T., Aleem, A.O. and Ayeni, F., 2020. Synthesis, characterization and antimicrobial studies of mixed ligands Metal (II) complexes of sulfamethoxazole and N, N-Donors heterocycles. *FUDMA Journal of Sciences*, *4*(2), pp.217-232.
9. Feng, X., Li, J., Feng, Y., Zhang, K., Chen, N., Fang, H. and Li, Z., 2021. Series of d10 complexes based on sulfamethoxazole: Auxiliary ligand induces structure diversity, luminescence and antibacterial properties. *Journal of Solid-State Chemistry*, *302*, p.122351.
10. Habila, I., Bouchée, R., Trifa, C., Berrah, F., Saoudi, M., Bemired, B., Boudraa, M., Mera zig, H. and Bouacida, S., 2022. Synthesis, structure characterization, spectral properties, DFT calculations, Hirschfeld surface analysis, thermal stability and bioactivity of a new sulfamethoxazole zinc (II) complex. *Journal of Molecular Structure*, *1261*, p.132962.
11. Khan, A.K., Hamdi, M.D. and Razik, B.M.A., 2021. An efficient method for synthesis, characterization and molecular docking study of new sulfamethoxazole derivatives as antibacterial agents. *Pakistan Journal of Pharmaceutical Sciences*, *34*(3).
12. Maepa, J.M. and Lesotho, T.C., 2023. Benzylated Sulfamethoxazole Derivatives with Improved Safety Profile as Potential Anti-Mycobacterium tuberculosis and Antibacterial Agents. *Journal of Chemistry*, *2023*(1), p.4805466.
13. Mahdi, H.T. and Rasheed, M.K., 2023. Synthesis and Identification of Thiazines-4-on Derived from Sulfamethoxazole, and Testing of some of their Antibacterial Properties. *Journal of New Materials for Electrochemical Systems*, *26*(3).
14. Mahdi, H.T. and Rasheed, M.K., 2024. Preparation and characterization of thiazine's compounds derived from sulfamethoxazole, and evaluation of some of their antibacterial properties. *Samarra Journal of Pure and Applied Science*, *6*(2), pp.101-112.
15. Mahdi, M.F., Al-Samim, R.F. and Al-Khaliq, Z.M.A., 2015. Synthesis, characterization and antibacterial activity of new series of sulfamethoxazole derivatives. *World J Pharm Pharmacist Sci*, *4*(10), pp.284-293.
16. Mahmoodi, S.H., Ismael, S.S. and Dawood, M.N., 2022. Synthesis, antioxidant and hypoglycemic assessment of new azo-sulfamethoxazole derivatives. *Archives Venezolanos de Pharmacology y Therapeutical*, *41*(2), pp.131-138.
17. Mohammed Abd al-Khaliq, Z., 2015. Synthesis, characterization and antibacterial activity of new series of sulfamethoxazole derivatives". *Ministry of Higher Education*.
18. Pervaiz, M., Riaz, A., Munir, A., Saeed, Z., Hussain, S., Rashid, A., Younas, U. and Adnan, A., 2020. Synthesis and characterization of sulfonamide metal complexes as antimicrobial agents. *Journal of Molecular Structure*, *1202*, p.127284.
19. Sager, A.G., Babies, J.K. and Issa, R.A., 2024. Synthesis, Characterization, Biological Activity, and Molecular Docking Study of Some New Sulfamethoxazole Derivatives. *Baghdad Science Journal*.
20. Şahin, Z., Bilstein, S.N., Yurts, L. and Demir yak, Ş., 2021. Synthesis, characterization and antibacterial evaluation of new pyridyl-thiazole hybrids of sulfonamides. *Istanbul Journal of Pharmacy*, *51*(1), pp.67-72.

21. Siraj, I.T. and Sanusi, S., 2021. Synthesis, Characterization and Antimicrobial Studies of Co (II) and Ni (II) Schiff Base Complexes Derived Furfuraldehyde and Sulfamethoxazole. *International Journal of Scientific Research in Chemistry (IJSRCH)*, *6*(4), pp.01-09.
22. Verma, S.K., Verma, R., Xue, F., Thakur, P.K., Girish, Y.R. and Rakesh, K.P., 2020. Antibacterial activities of sulfonyl or sulfonamide containing heterocyclic derivatives and its structure-activity relationships (SAR) studies: A critical review. *Bioorganic Chemistry*, *105*, p.104400.