A Review On Anti-Bacterial Activity Of Substituted Azetidinone, Benzothiazole, Thiazole, Thiadiazole, Triazole, Triazolothiazole And Naphthalene Derivatives

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Abstract
This review paper discusses the potential of different nitrogen-containing ring structures, including azetidinone, benzothiazole, naphthalene, thiadiazole, and triazole, in drug development for antibacterial medications. The paper highlights the unique structural characteristics and pharmacological properties of each moiety and their potential for combating antibiotic resistance. The authors emphasize the importance of structure-activity relationship studies in understanding how modifications to these ring structures can affect their efficacy, spectrum of action, and pharmacokinetic properties. The paper also provides examples of antibacterial drugs containing these moieties and their significant antibacterial activity against various bacterial species. Overall, the paper highlights the potential of these nitrogen-containing ring structures in the development of new antibacterial drugs.

Key words: -Azetidinone, Benzothiazole, Naphthalene, Triazolothiadiazole, Thiadiazole, Triazole, Antimicrobial medications, Nitrogen-containing Ring, Structural diversity, Pharmacological effects, Fused heterocyclic compound, Antibacterial pharmaceutical development.

Introduction

The field of drug development has seen a surge of interest in the azetidinone moiety, a nitrogen-containing ring with four members. This unique structural characteristic, combined with its pharmacological properties, has made it an appealing target for researchers in the quest for new antibiotics. With the rise of drug-resistant bacterial strains, there is an urgent need for novel approaches to combat antibiotic resistance. The small size and ease of synthesis of azetidinone, coupled with its potential for chemical modifications, make it a promising candidate for the development of antibacterial medications(Desai et al., 2014; Kaur & Kataria, 2016).

The benzothiazole moiety, a heterocyclic compound composed of a fused benzene and thiazole ring, is also garnering attention in medicinal chemistry and drug research. Researchers are exploring the medicinal chemistry of benzothiazole derivatives to create new molecules with improved therapeutic efficacy and pharmacokinetic properties. The aromatic structure and presence of an electronegative sulfur atom in the benzothiazole moiety allow it to interact with various biological targets, including nucleic acids, enzymes, and receptors. (Patel et al., 2015). By introducing different substituents to different positions on the benzothiazole ring, researchers can alter its pharmacological properties and enhance its binding affinity to specific molecules. (Pal et al., 2013). Similarly, the naphthalene moiety, a bicyclic aromatic hydrocarbon with two fused benzene rings, is being investigated for its chemical and pharmaceutical properties. The naphthalene moiety is highly adaptable and can interact with a wide range of biological targets through π-π stacking and π-π binding. (Saravanan et al., 2012) By modifying different parts of the naphthalene ring, researchers can influence its pharmacological properties, including antibacterial, antifungal, anti-inflammatory, antiviral, and anticancer effects. (Rani & Jha, 2017).

The thiadiazole moiety has also attracted widespread interest due to its unique chemical composition and diverse pharmacological effects. Substituents at various positions on the thiadiazole ring can alter its inclination and selectivity toward specific molecular targets. Thiadiazole derivatives have shown significant antibacterial activity against various bacterial species, (Bhatt & Mehta, 2014). making them promising candidates for the development of antibacterial medications. Understanding the structure-activity relationship of thiadiazole derivatives is crucial for maximizing their effectiveness and addressing the global issue of antibiotic resistance. (Sharma et al., 2016).Triazole compounds, known for their structural diversity and chemical stability, have also gained attention in medicinal chemistry and pharmaceutical research. These compounds exhibit a wide range of pharmacological effects, including antibacterial, antifungal, antiviral, anticancer, and anti-inflammatory properties. (Singh et al., 2018). Researchers have focused on essential bacterial enzymes or cellular processes required for bacterial growth and survival when studying triazole derivatives as potential therapeutic agents for bacterial infections. Modifying the triazole ring at different positions can significantly impact the

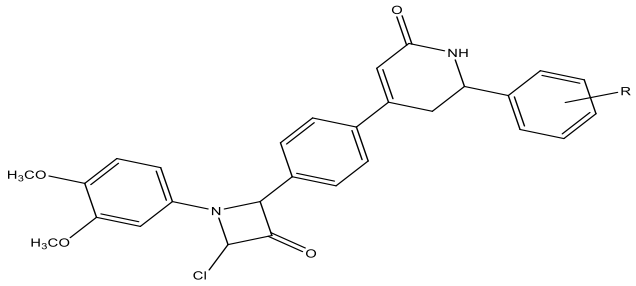
compound's antibacterial activity, range of activity, and pharmacokinetic properties. (Patel et al., 2017). Triazolothiadiazole, a fused heterocyclic compound containing both triazole and thiadiazole groups, is another intriguing pharmacophore being investigated for its chemical and biological properties. (Rana et al., 2015). Triazolothiadiazole derivatives have demonstrated significant antibacterial activity against pathogenic bacteria, making them promising candidates for antibacterial pharmaceutical development. Researchers have successfully improved the effectiveness of triazolothiadiazole derivatives by altering their structures to increase electron density or introduce functional groups that interact positively with bacterial targets(Kamble et al., 2018).In conclusion, the azetidinone, benzothiazole, naphthalene, thiadiazole,thiazole and triazole and triazolothiadiazole moieties are all promising candidates for the development of antibacterial medications. These moieties possess unique structural characteristics and pharmacological properties that make them appealing to researchers in the field of drug development. By understanding the structure-activity relationship of these moieties and exploring their chemical modifications, researchers can enhance their therapeutic efficacy and combat antibiotic resistance worldwide. (Zhang et al., 2019).

1. Azetidinone

The azetidinone moiety, which is a nitrogen-containing ring that is composed of four members, has garnered a substantial amount of attention from medicinal chemists and professionals in the field of drug development. Due to the fact that this chemical possesses both distinctive structural characteristics and a wide range of pharmacological capabilities, it is an appealing option for the creation of therapeutics. In this introduction, we will investigate the factors that have led to the growing fascination that researchers have with the azetidinone moiety, the biological functions that it possesses, the effectiveness that it has in combating bacteria, the relationship that exists between its structure and activity, and specific examples of antibacterial drugs that contain this moiety. Due to the growing incidence of drug-resistant bacterial strains and the pressing need for new antibiotics, researchers are investigating different chemical frameworks for the synthesis of antibacterial medications. This is being done in response to the urgent need for an antibiotic. The azetidinone moiety possesses a number of benefits, including its small size, the simplicity with which it may be synthesised, and the possibility of undergoing a wide variety of chemical changes. Because of these characteristics, it has become more appealing to researchers who are looking for novel approaches to combat antibiotic resistance and to solve medical needs that are now unfulfilled. One of the most diverse pharmacophores, the azetidinone group is responsible for a wide variety of active biological processes. It is possible for this chemical to interact with a wide variety of biological targets, including enzymes, receptors, and transport proteins, due to the distinctive structural properties that it possesses. Various pharmacological effects may be attributed to molecules that include azetidinone. These effects include antibacterial, antifungal, antiviral, anti-inflammatory, and anticancer actions. In many cases, the biological activity of azetidinone derivatives is affected by certain ring substitutions. These substitutions have the potential to alter the affinity and selectivity of the azetidinone derivatives for target molecules.

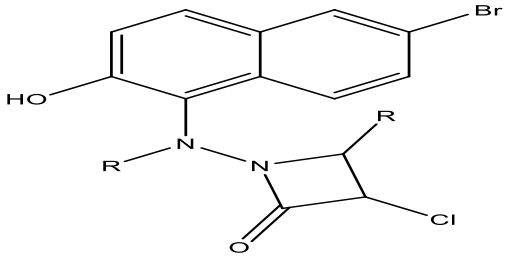
Compounds containing azetidinone exhibit significant antibacterial action against Gram-positive as well as Gram-negative organisms. It has been established through research on structure-activity relationships (SAR) that alterations made to the azetidinone ring at various places can have an influence on the antibacterial efficacy, spectrum of action, and pharmacokinetic properties of the antibacterial molecule. One example of this is the addition of electron-drawing groups to the C-3 position, which frequently results in an increase in antibacterial activity. This is accomplished by enhancing contacts with bacterial enzymes or components of the cell wall. On the other hand, changes that enhance steric hindrance lead to a reduction in activity because they reduce the capacity to connect to the bacterial target. For the purpose of treating bacterial infections, a variety of the antibacterial drugs that contain the structure of an azetidinone have been created and tested in clinical settings. The antibiotic ceftaroline is an example of a noteworthy cephalosporin antibiotic that belongs to the fifth generation. In addition to treating acute bacterial skin and skin structure infections, this medicine is licenced for use in the treatment of community-acquired pneumonia symptoms. As a result of its great effectiveness against methicillin-resistant Staphylococcus aureus (MRSA) and other infections that are often seen, ceftaroline is an important addition to the arsenal of antibiotics. Taking everything into consideration, the structure of azetidinone has the potential to operate as a framework for the development of antibacterial medications that demonstrate a wide range of pharmacological actions. This entity is a promising candidate for drug development attempts due to the fact that it possesses distinctive structural characteristics and a wide range of biological functions. The researchers intend to undertake more study on the structure-activity relationship (SAR) and investigate other chemical alterations in order to achieve their goals of improving the therapeutic efficacy of azetidinone derivatives and addressing the worldwide problem of antibiotic resistance.

I. ***Parth P. Patel et al in 2020*** synthesized a series of compounds derived from 3-chloro-4-(3,4-dimethoxyphenyl)-1-{4-[6-(2-hydrox-2-oxo-1,2,5,6-tetrahydropyrimidin-4-yl]phenyl}aze derived from 3-chloro-4-(3,4-dimethoxyphenyl)-1-{4-[3-(substitu-prop-2-enoyl]phenyl}-azetidin-2-one and urea. The compounds were characterized using element analysis and NMR spectral data, and tested for antibacterial and antifungal activities.



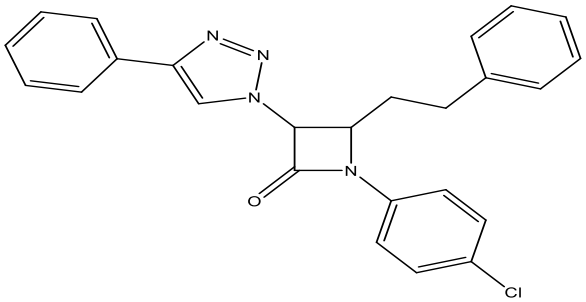
R = H, 2-OH , 2Cl, 4-OH , 3,4- OCH_3 , $N(CH_3)_2$

II. ***Chopde, H. N et al in 2020***study has synthesized 1-([6-bromo-2-hydroxy-naphthalen-1-yl]arylphenyl)m-3-chloro-4-(arylphenyl)-azetidin-2-ones via the Staudinger [2 + 2] ketene-imine cycloaddition reaction pathway. The compounds were tested for their antibacterial activity against gram-positive and gram-negative bacteria. The widest spectrum of antibacterial activities was found in compounds with more hydroxyl groups and β-lactam ring compared to other substituted azetidinones. The compounds were characterized by their dark brown color, 74% yield, and IR values.

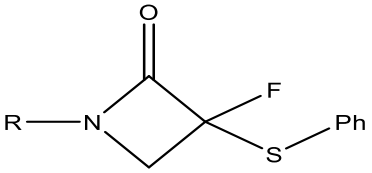


R = -C_6H_5, 2-OHC_6H_4, 4-OHC_6H_4, 3-$NO_2C_6H_4$

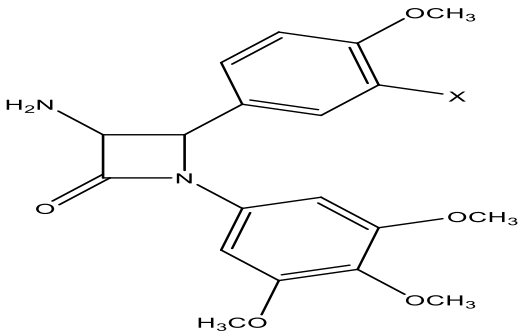
III. The study by ***Fu, D.-J et al in 2020*** explore the potential of β-lactams as anticancer agents, focusing on molecular hybrids, structure-activity relationships, and potential targets. β-lactams are known for their antibacterial properties and have been the subject of much discussion in chemistry, biology, and medicine. Recent research has focused on synthesis of novel β-lactam derivatives, such as thymine-bis-β-lactam hybrids, benzothiazole-β-lactam hybrids, and benzothiazole-β-lactam hybrids. The study also explores the molecular hybridization approach to design anticancer β-lactam hybrids, which involves rational design of prototypes based on the recognition of pharmacophoric sub-units in the molecular structure of known bioactive derivatives. The research highlights the importance of understanding the structural diversity of β-lactam analogues and their potential molecular targets for cancer treatment. Further research is needed for better efficacy and less side effects



IV. ***Wang, X et al in 2020*** Fluorine-substituted lactams, crucial in biomedicine, agriculture, and materials science, have gained interest due to their biological and pharmaceutical activities. Researchers Jiazhu Li and Kai Sun have developed strategies for synthesizing these lactams, including fluoro-β-lactams, fluoro-γ-lactams, and fluoro-δ-lactams. These strategies have shown effectiveness in inhibiting β-lactamases and human leukocyte elastas, and can be used as synthetic intermediates for fluorinatedβ-lactam antibiotics and building blocks for carbohydrates and amino acids. New methods and approaches in fluorochemistry present new opportunities and challenges. Fluorinated pyrrolidinones are also crucial in drug discovery.

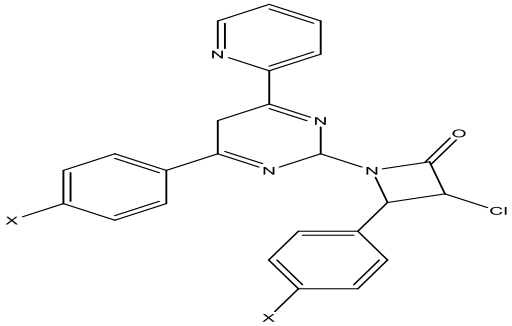


V. ***Malebari, A. M et al. in 2019*** have designed and evaluated a series of 1,4-diaryl-2-azetidinone analogues of combretastatin A-4 (CA-4) for their antiproliferative, antiapoptotic, and tubulin polymerization properties. These analogies, which are made to get rid of possible sites of ring B glucuronate conjugation, work better on CA-4-resistant HT-29 colon cancer cells and keep their effectiveness in MCF-7 breast cancer cells. Compound 46 stops tubulin from putting together and stops mitosis, which means that they could be used to treat breast and colon cancers that are not responding to chemotherapy.



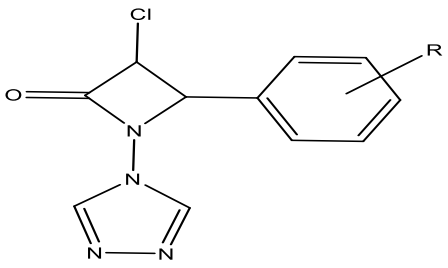
X = F, Cl

VI. ***A Bakr, R. B et al in 2019*** have developed novel thiazolidinones, imidazolinones, and azetidinones with pyridine and pyrimidine moieties for antimicrobial activity. The chemical structures of these derivatives were elucidated using spectral and elemental analyses. The most active derivative was the azetidin-2-one derivative. The antibacterial potential was limited to the thiazolidinone derivatives (12a and 12c) and the imidazolinone (13c). Docking studies of the most active agents recorded good scores with several binding interactions with the active site. The compounds were tested against Bacillus subtilis and Staphylococcus aureus, as well as Aspergillus flavus and Candida albicans. The study also focuses on the development of new target compounds for antimicrobial activity against Candida albicans. The compounds were categorized into three groups and analyzed for their binding modes and molecular formulas.



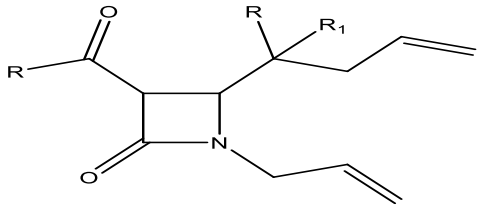
X = H, OH Cl, $N(CH_3)_2$

VII. ***Khan, T et al in 2018*** have developed an efficient synthesis and antibacterial activity of novel 2-azetidinone derivatives of 4H-1,2,4-triazoles using DABCO as a nontoxic, eco-friendly catalyst. The synthesis of active 2-oxo-azetidine was carried out using a highly electrophilic ketene intermediate. The compounds showed variable inhibitory effects against bacteria, with compounds 3b and 3dis showing better activity against E. coli. The DABCO catalyst is economically viable and readily available.



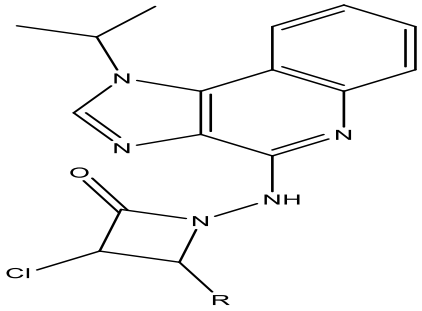
R = NO_2, Br, Cl, OMe, OH, Me

VIII. ***Zakaszewska, A et al in 2018*** developed a two-step method for preparing bicyclic β-lactam and bicyclic 1,3-oxazinone scaffolds using combined cycloaddition and metathesis processes. The method was applied to ring closing metathesis (RCM) of different heterocyclic substrates, demonstrating its versatility. The researchers focused on developing one- or two-step synthesis methods for bicyclic scaffolds with b-lactam moiety and a second major hetero ring, potentially acting as a new antiuropathogenicpilicide. The study focuses on the synthesis of selective cholesterol-absorption inhibitors, which showed a 94% inhibition rate.



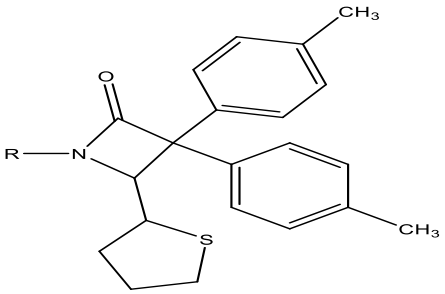
R = PhNH, 3-ClC_6H_4NH, 4 FC_6H_4NH R_1 = Me, -$(CH_2)_5$-

IX. ***Kayarmar, R et al in 2014*** Synthesized N-substitutedazetidinones showed good antibacterial and anticancer activities, with compounds 9a and 9b showing minimal binding energy and good affinity towards the active pocket, making them effective inhibitors of b-tubulin.



R = 4- chloro phenyl , Biphenyl , 2,4-dimethoxy phenyl , 2,4- diethoxy-5-nitrophenyl

X. ***Girija S. Singh; Boycie J. Mmolotsi in 2005*** study has reported the synthesis of 2-azetidinones from 2-diazo-1, 2-diarylethanones, and N-(2-thienylidene) imines as a potential antimicrobial agent. The compounds were screened in vitro for their antibacterial and antifungal activity against various bacteria and fungi. The study acknowledges the assistance of the Chemistry Department at the University of Botswana.



R =4-MePh, 4-MeOPh, Ph,

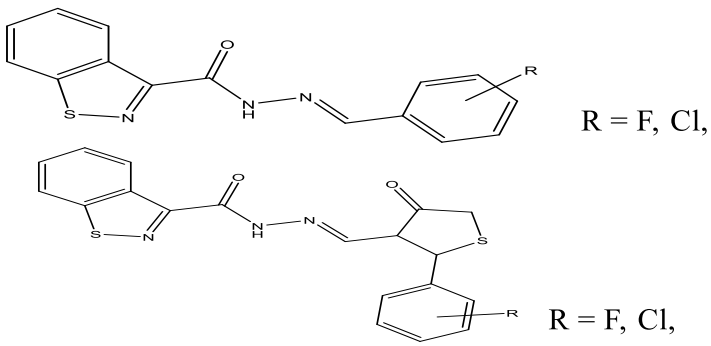
2.BENZOTHIAZOLE

A key focus in medicinal chemistry and medication research is the benzothiazole moiety, a heterocyclic compound comprising a fused benzene and thiazole ring. Scientists worldwide have focused on the distinctive chemical composition and diverse pharmacological characteristics of this substance. In this introduction, we will explore the reasons behind the increasing interest in the benzothiazole moiety. We will examine its role as a biologically active component and its antibacterial properties, including the relationship between its structure and activity. Additionally, we will provide examples of antibacterial drugs that contain this moiety.

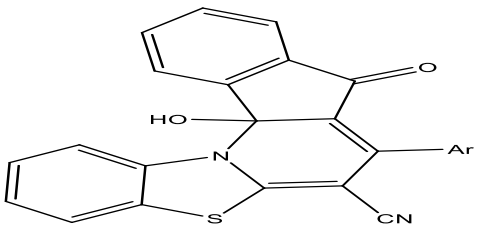
The remarkable flexibility of the benzothiazole structure, along with its diverse range of pharmacological effects, has piqued the interest of researchers. Due to its inflexible and flat structure, as well as its capacity to engage in a diverse array of molecular interactions, it has the potential to function as a dependable framework for the creation and advancement of medications. Researchers are interested in exploring the medicinal chemistry of benzothiazole derivatives to develop new molecules with improved therapeutic effectiveness and pharmacokinetic properties. The benzothiazole moiety not only

functions as an effective pharmacophore, but also exhibits a wide range of biological activity. Its aromatic makeup, along with the presence of an electronegative sulphur atom, allows it to effectively interact with many biological targets, such as nucleic acids, enzymes, and receptors. Moreover, the existence of substituents at different positions on the benzothiazole ring has the capacity to alter its pharmacological characteristics, which might subsequently impact its affinity and specificity for distinct molecular targets when administered. Therefore, compounds containing benzothiazole exhibit a diverse array of pharmacological properties, such as antiviral, antibacterial, antifungal, anticancer, and anti-inflammatory activities. They have exhibited substantial antibacterial efficacy against a diverse range of bacterial species, rendering them optimal candidates for the development of antibacterial medications. Benzothiazole derivatives have demonstrated efficacy against. Studies on structure-activity relationship (SAR) have shown that modifying the benzothiazole ring at various positions can greatly affect the antibacterial potency, spectrum of activity, and pharmacokinetic properties of the molecule. For example, adding electron-withdrawing or electron-donating substituents at certain locations has the potential to increase antibacterial activity. This is achieved by enhancing the contacts with elements of bacterial cell walls or targets inside the cells that are essential for bacterial development. Conversely, alterations that enhance steric hindrance or alter the overall molecular shape might lead to a reduction in the efficacy of antibacterial medicines. Several antibacterial medicines containing the benzothiazole moiety have been created and tested in clinical settings for the treatment of bacterial infections. An example of a widely known antibiotic is cefixime, a cephalosporin with a broad range of activity against both Gram-positive and Gram-negative bacteria. Cefixime exerts its antimicrobial activity by inhibiting the synthesis of bacterial cell walls by binding to penicillin-binding proteins. This leads to an interruption in the formation of cell walls, ultimately leading to the demise of bacterial cells. Cefixime is commonly used to treat sexually transmitted diseases, urinary tract infections, and respiratory tract infections because to its strong antibacterial properties and favourable pharmacokinetic profile. Overall, the benzothiazole structure is a fascinating pharmacophore that might be used to create antibacterial drugs with diverse pharmacological properties. Because of its distinct chemical characteristics and diverse range of biological effects, it becomes an appealing candidate for the development of medications. By gaining a more profound understanding of the link between the structure and activity of benzothiazole derivatives, and by discovering new chemical changes, researchers want to fully uncover the therapeutic capabilities of these compounds and address the worldwide issue of antibiotic resistance.

I. ***Kumar, M et al in 2022*** study developed a QSAR model and molecular modeling of benzothiazole analogues for antibacterial drug discovery. Validated on 21 analogues, the model identified compounds with significant activity, potentially controlling E. coli infections. QSAR modeling is used in biochemistry, pharmaceuticals, and medicine

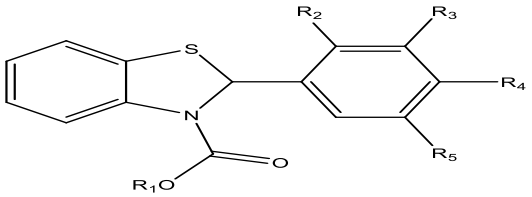


II. ***Mohamed, K. S et al in 2021*** synthesize novel heterocycles containing the benzothiazole moiety and evaluate their antimicrobial properties. They used 2-cyanomethylbenzothiazole (1) or its arylidene derivatives under different reaction conditions. The compounds were tested against Staphylococcus aureus and Escherichia coli bacteria. Benzothiazole derivatives are a valuable platform in synthetic and medicinal chemistry, with various properties including antimicrobial, antioxidant, and anti-tumor activities. The study also explored the use of a pyrazole derivative in pyridobenzothiazole derivatives.

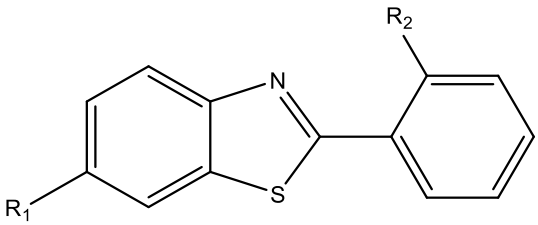


III. ***Stremski, Y et al in 2020*** have studied the synthesis and antibacterial activity of hydroxylated 2-arylbenzothiazole derivatives. These derivatives are used in various biologically active compounds and medicines, including cytotoxic agents and calcium antagonists. The researchers used an alkylative coupling approach to screen benzothiazoline

derivatives against Gram-positive and Gram-negative strains using Mueller-Hinton agar. Although oxidative rearomatization attempts were unsuccessful, the compounds showed promising antibacterial properties.

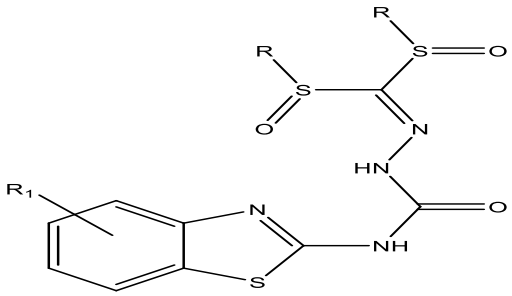


IV.***Racané, L et al in 2020*** a green synthetic protocol has been developed to introduce substituents to the C-6 position of 2-arylbenzothiazole nuclei, resulting in compounds with potential antioxidant, antibacterial, and antitumor properties. The compounds were designed to study the influence of hydroxy and methoxy groups on the 2-arylbenzothiazole scaffold and the type of substituents placed on the benzothiazole moiety on biological activity. The tested compounds exhibited moderate to strong antiproliferative activity against four human tumor cell lines. Compounds 5a-5f and 6a-6f showed strong antioxidant and antioxidative properties, while compounds 5c, 5f, 6c, and 6f exerted promising antioxidant and antioxidative properties as potential suppressors of the hypoxia-inducible factor-1 (HIF-1) protein.



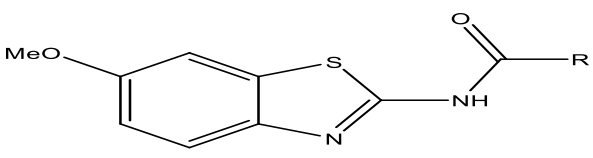
R_1= H, NO_2, CN
R_2=OH OCH_3

V.**Zhang, J et al. in 2020** conducted a study to synthesize 24 bis-sulfoxide derivatives with acylhydrazone and benzothiazole moieties as potential antibacterial agents. The bioactivity assay results showed that many compounds had significant in vitro inhibitory effects against Xanthomonas oryzae pv. oryzae (Xoo) and Xanthomonas citripv. citri(Xac). Compound 4b showed the best in vitro antibacterial activity against Xoo, with curative and protection activities of 42.5% and 40.3%, respectively. It can influence biofilm formation, inhibit extracellular polysaccharide production, and reduce Xoo's pathogenicity.



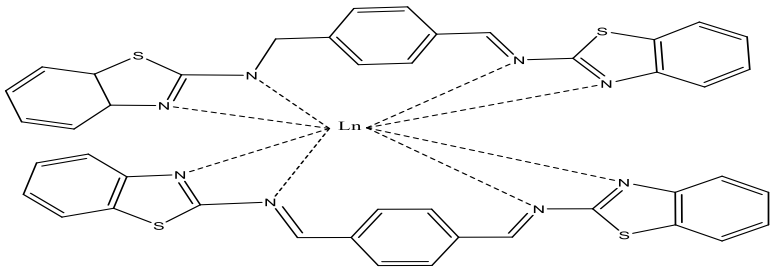
R_1 = 4-CH_3, 6-F, 6-OCH_3
R = CH_3, CH_2CH_3

VI.***Williams, N et al in 2020***study has developed a series of N-acyl benzothiazoles that have shown selective and potent cytotoxicity against cancer cell lines expressing cytochrome P450 4F11. The prodrug form (R)-27 was identified as an active inhibitor of stearoyl-CoA desaturase (SCD) by cancer cells. The researchers synthesized compounds with a polar linker at C4 attached to a lipophilic group, which were found to be potent against H2122 cells with an IC50 of 11 nM and 100-fold selectivity toward H2009 cells. The toxicity of both drug and prodrug forms was rescued by the addition of the unsaturated fatty acid oleate, supporting the hypothesis that toxicity arises from the inhibition of SCD. The study also tested the in vivo activity of (R)-27, which inhibits cytotoxicity against cancer cell lines expressing certain cytochrome P450 isoforms.

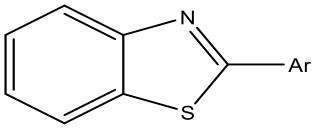


R = 4-HN_2, H, 4-OMe, 3-OMe, 4-F, 4-NO_2, 4-OBn, 4-COPh

VII. ***Mishra, N et al in 2020*** study explores the synthesis, characterization, optical, and anti-bacterial properties of benzothiazole Schiff bases and their lanthanide complexes. Two new Schiff base ligands, L1 and L2, have been synthesized and characterized using various techniques. These ligands form lanthanide complexes with Ce(III), Nd(III), and Pr(III) ions in a 1:2 stoichiometry. The UV/vis spectra of L1,L2, and 1–6 show characteristic ligand-centered absorptions in the 230–350 nm range. Both ligands and complexes show significant emissions and good anti-bacterial activity against pathogenic bacteria. The study also explores the synthesis, characterization, optical, and anti-bacterial properties of thiazole-containing Schiff base ligands and their complexes with Ce(III), Nd(III), and Pr(III) ions.

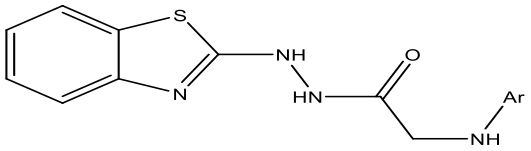


VIII. ***Irfan, A et al in 2019*** review highlights the broad biological activities of benzothiazole (BTA) derivatives, including anticancer, antioxidant, anti-inflammatory, anti-tumour, viral, bacterial, anti-proliferative, diabetic, convulsant, analgesic, anti-tubercular, antimalarial, anti-leishmanial, anti-histaminic, and anti-fungal properties. BTA derivatives are particularly effective against cancer cell lines and tumor-associated carbonic anhydrase (CA), potentially leading to hypoxic tumor treatments.



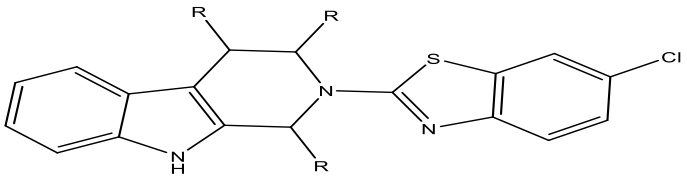
Ar = Idole 2 carboxaldehyde
bealdehyde , napthaldehyde , 2-chloro benzaldehyde ,2-methyl benzaldehyde

IX. ***Fadda, A. A et al in 2019*** synthesized antimicrobial compounds using benzothiazole-linked carboxamide, acetohydrazide, and sulfonamide systems. These compounds were formed by interacting diethylethoxymethylene malonate with 2-cyanomethylbenzothiazole. Compounds 22a,b displayed the highest antimicrobial activity against tested organisms, providing insights into the synthesis of biologically active compounds.



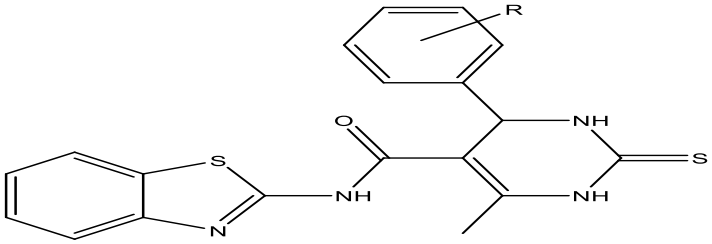
Ar = 4-C_6h_4Cl, 4-C_6H_4-SO_3H, 4-C_6H_4-OCH_3

X. ***Wang, X et al in 2019*** a new class of resistance-modifying agents (RMAs) has been discovered using a tryptoline-based benzothiazole scaffold. The most potent compound (4ad) re-sensitizes multiple MRSA strains to cephalosporins at low concentrations and has low mammalian cytotoxicity. The study aimed to explore whether functionalization of the tricyclic-indoline core with motifs could enhance RMA activity or decrease cytotoxicity. The researchers synthesisedtryptoline-based benzothiazoles, benzimidazoles, and benzoxazoles using a one-step reaction or two-step method. The benzothiazole core motif had the most optimal RMA activity, while the thiourea motif had good antibacterial activity and moderate RMA activity. Further investigation is ongoing to determine the compounds' mode of action and efficacy in vivo.



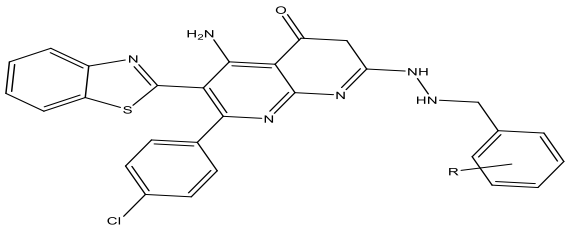
R = H, Cl OMe
R_1 = H, CO_2Me

XI.***Gjorgjieva, M et al in 2018*** Benzothiazole-based compounds have shown promising antibacterial activities against Gram-positive and Gram-negative bacteria, including Mycobacterium tuberculosis. These compounds inhibit enzymes essential for bacterial cell processes, such as cell-wall synthesis, cell division, and DNA replication. However, research in antibacterial compounds is facing a crisis due to the resistance of Gram-positive bacteria and the less permeable bacterial cell wall in Gram-negative bacteria. Benzothiazole-based compounds have shown potential in antibacterial drug discovery, with compounds 16 and 17 showing potent antibacterial activities against drug-resistant bacteria. Potential targets for tuberculosis drug research include inhibitors of HisG, nitrobenzothiazole compounds, and biotin. Further research is needed to identify new targets and develop effective antibacterial compounds.



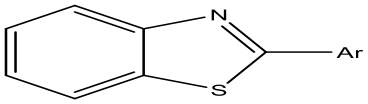
R= H, 4-F, CF_3, 4-$N(CH_3)_2$

XII.***Maddila, S et al in 2016*** study explores the synthesis and antibacterial and antifungal properties of novel benzothiazole pyrimidine derivatives. Researchers synthesized compounds with moderate to high yields and tested them against various organisms. The compounds were characterized using IR, 1H NMR, 13C NMR, LCMS mass, and C, H, N analyses. Compounds with electron-withdrawing substituents displayed greater antibacterial activity. The study also focuses on the preparation of compounds from a mixture of DMF, potassium carbonate, and benzyl bromide. The compounds have excellent antibacterial and antifungal activities, making them potential lead series for further efficacy evaluation.



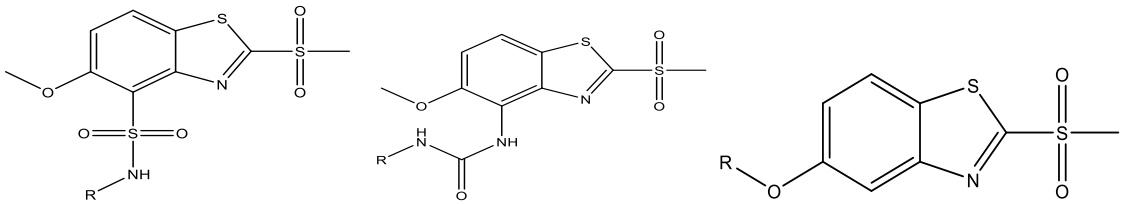
R = H, 4Cl, 2-Cl, 2-CH_3, 4-F, 4-NO_2, 4-NH_2

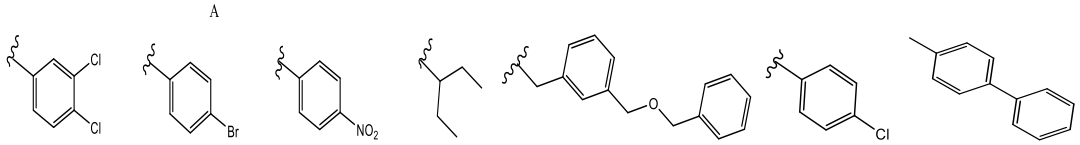
XIII.***Chhabra, M et al in 2015*** have developed an efficient green synthesis of 2-arylbenzothiazole analogues as potent antibacterial and anticancer agents. They synthesized 2-aryl & heteroaryl benzothiazole scaffolds using Amberlite IR-120 resin under microwave irradiation. The scaffolds were tested against various bacterial strains and cancer cell lines, and found novel 2-aryl benzothiazole derivatives with significant anticancer activities. The study highlights the importance of free nitrogen, planarity of molecules, and halogen and alkyl functions for the activity of these compounds.



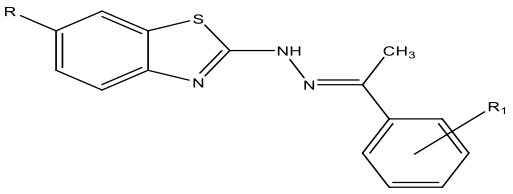
Ar = Idole 2 carboxaldehyde
bealdehyde , napthaldehyde , 2-chloro benzaldehyde ,2-methyl benzaldehyde

XIV.***Lad, N. P et al in 2015*** aimed to synthesize new 2-(alkylsulfonyl)benzothiazoles (MSBT) derivatives and investigate their antimicrobial and anticancer activities. The compounds were screened against antimicrobial activity and selected for anticancer activity. The compounds were found to be potent against Gram-negative organisms and Candida species, with some showing dose-dependent reduction of cell viability in HeLa cancer cell lines. These compounds were effective against both bacterial and fungal species.



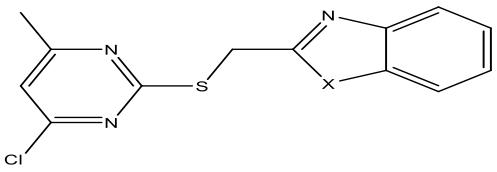


XV. ***Gabr, M. T in 2015*** study investigates the synthesis, antimicrobial, antiquorum-sensing, and cytotoxic activities of new benzothiazole derivatives. It focuses on predicting solubility and Lipinski's rule of five for synthesizing compounds with antibacterial and antifungal activity. Compounds 4c, 5a, and 6j show higher drug-likeness values.



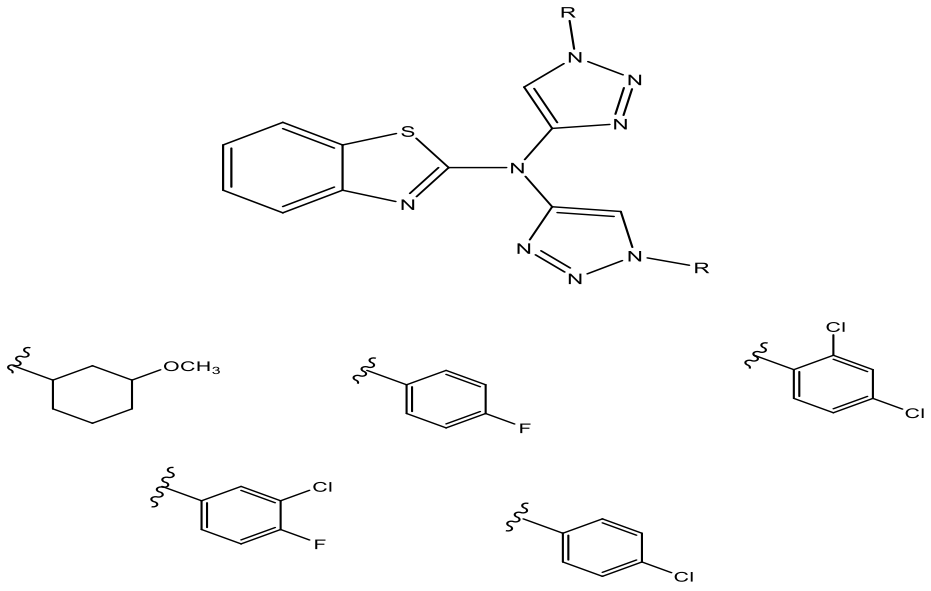
R = H, F, CF_3
R_1 = 2-F, 3-F, 2-Cl, 4-OH, 2,5-$(OH)_2$

XVI. ***Seenaiah, D et al in 2014*** study investigates the synthesis, antimicrobial, and cytotoxic properties of pyrimidinyl benzoxazoles, benzothiazoles, and benzimidazoles linked by thio, methylthio, and amino moieties. Results show more activity against Gram-positive bacteria, with tris heterocyclic compounds showing greater activity. The synthesis process is complex, providing insights into their chemistry and properties.

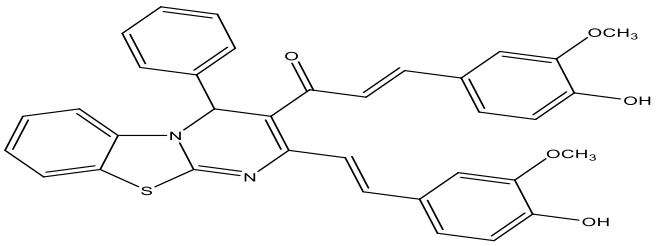


X = NH, S O.

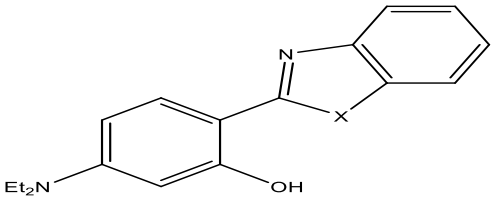
XVII. ***Singh, M. K et al in 2013*** synthesized benzothiazole 1,2,3-triazole analogs using click chemistry to create a new class of antimicrobials. The compounds were tested against various bacterial strains and molds. The study found that electron-withdrawing groups significantly impacted antibacterial activity. To confirm this hypothesis, more systematic design and synthesis of diversified compounds using multifunctional substituted benzene ring are needed. 2nd and 3rd generation compounds should be synthesized to establish meaningful structure-activity relationships.



XVIII. ***Sahu, P. K et al in 2012*** conducted a study on the antimicrobial properties of 4H-pyrimido[2,1-b]benzothiazole, pyrazole, and benzylidene derivatives of curcumin using a microwave-based method. The compounds were tested for their antibacterial and antifungal properties using in-vitro tests. The study aimed to develop novel curcumin derivatives by synthesizing substituted aromatic aldehydes, curcumin, and 2-amino benzothiazole in a microwave under solvent-free conditions. The pyrazole derivatives were collected as yellow crystals.

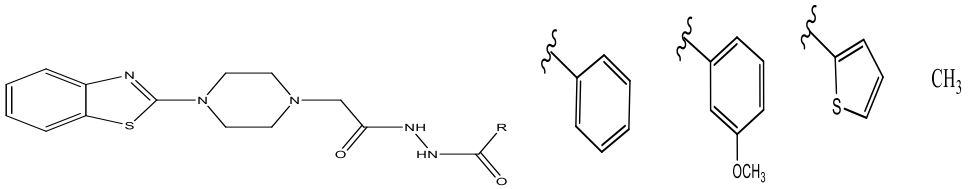


XIX.***Padalkar, V. S et al in 2011*** aimed to create new antimicrobial agents by synthesizing 2-substituted benzimidazole, benzoxazole, and benzothiazole derivatives. The compounds were characterized using FT-IR, 1H NMR, and LC-MS. They were tested against Escherichia coli and Staphylococcus aureus strains and Candida albicans and Aspergillus nigerstrains. The synthesized compounds showed variable inhibitory effects on these strains. The findings could be useful for developing potential drug candidates derived from these compounds for novel anti-infective agents.

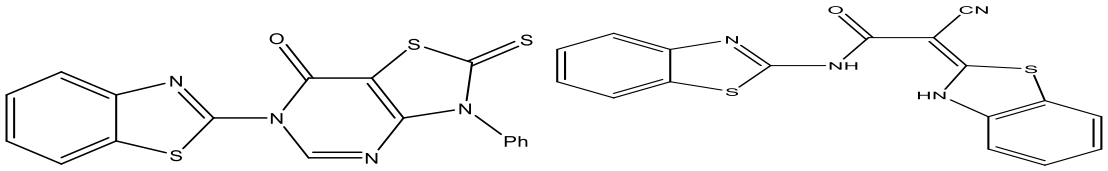


X = NH, S, O
R = H, NO_2

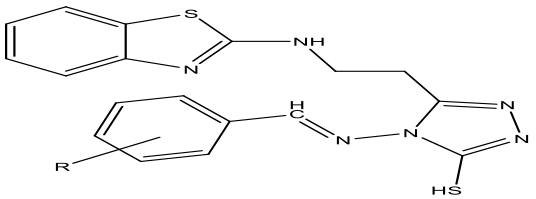
XX.***Al-Talib, M et al in 2011*** A new series of hydrazide derivatives were synthesized, characterized, and biologically evaluated. The compounds showed similar aromatic H-atom patterns and piperazine ring resonances. In vitro antibacterial activity was tested against Staphylococcus aureus, Escherichia coli, and Candida albicans bacteria. The study also focused on the synthesis and biological evaluation of new benzothiazoles as antimicrobial agents, with the title compound prepared from compound4 and furan-2-carbonyl chloride.



XXI.***Bondock, S et al in 2010*** study investigates the synthesis and antimicrobial activity of new thiazole, thiophene, and pyrazole derivatives with benzothiazole moiety. These compounds were tested against Gram-positive and Gram-negative bacteria, as well as Fusarium oxysporum and Aspergillus fumigatus, with the aim of designing potent, selective, and less toxic agents.

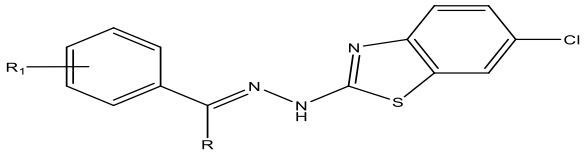


XXII.***Soni, B et al in 2010*** explores the synthesis and evaluation of new benzothiazole derivatives as potential antimicrobial agents. It synthesized Schiff bases of these derivatives, revealing their diverse biological activities. The compounds were screened for their antimicrobial activity, with the most active being compounds 6b, 6f, and 6g. These compounds showed a minimum inhibitory concentration (MIC) of 100mg/ml, suggesting their potential as novel drugs.



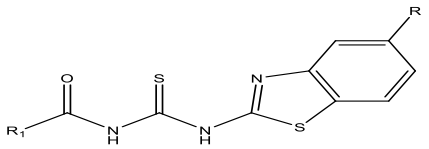
R =H, 4-OH, 2-NO_2, 3-NO_2, 3-Cl, 3,4-OCH_3

XXIII.***Asati, V et al in 2010*** study aimed to synthesize new compounds with nucleus substitution on the 2 and 6 position of the heterocyclic ring to enhance their biological properties. The compounds were characterized using IR, HNMR, and NMR and showed moderate activity against four pathogenic bacterial strains and two different fungal strains. Compounds 3a and 3b showed maximum activity against B. subtilis due to the substitution of electron donating and electron withdrawing groups.



R = H, CH_3, C_6H_5
R_1 = H, NO_2, Br, OCH_3, OH, CH_3, Cl, F

XXIV.***Saeed, S et al in 2010*** study explores the synthesis, characterization, and biological evaluation of five thiourea derivatives with benzothiazole moiety as potential antimicrobial and anticancer agents. The compounds showed broad antimicrobial activity against microorganisms, with higher activity against fungi than bacteria. Compounds 1b, 2b, 3b, and 4band5b exhibited the greatest antimicrobial activity. The cytotoxicity of synthesized thiourea derivatives on human cancer cells, specifically MCF-7 and HeLa cells, was found to be more sensitive to these cells. The study identifies compounds 2d, 5c, and 5das as potential anticancer candidates, offering a new template for developing a new class of antimicrobial agents.



R = 4-NITRO PHENYL, 2-THIOPHENE PHENYL, n-BUTYL
R_1 = H, O_2, NH_2, Br

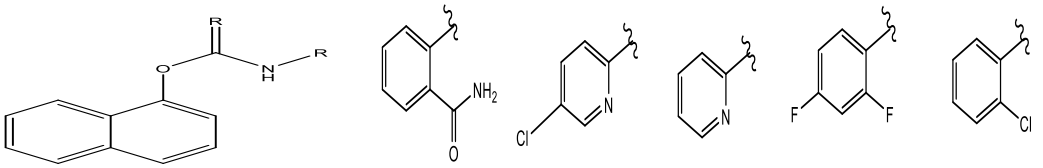
3.NEPHTHALINE

Professionals in the domains of medical chemistry and medication development have shown great interest in the naphthalene moiety. This moiety is a bicyclic aromatic hydrocarbon that consists of two fused benzene rings. It is a promising candidate for the development of new treatments since it has a distinct chemical composition and a wide range of pharmacological characteristics. This introduction will examine the factors that have contributed to the growing interest among researchers in the naphthalene moiety. It will also explore the biological activities of this moiety, particularly its antibacterial properties, including the structure-activity relationship (SAR). Additionally, it will provide examples of antibacterial drugs that incorporate this moiety. Researchers are interested in the naphthalene moiety because it has a wide range of pharmacological actions and might potentially be used as a framework for drug development. Due to its inflexible and flat configuration, together with its electron-rich aromatic system, it presents possibilities for systematic drug development and chemical alteration. Researchers are interested in exploring the medicinal chemistry of naphthalene derivatives to develop innovative molecules with improved therapeutic effectiveness and less unfavourable side effects.

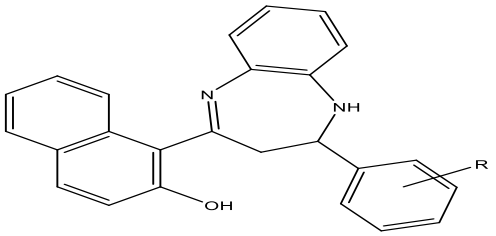
The naphthalene moiety is a highly adaptable pharmacophore that exhibits a diverse range of characteristics found in biological systems. The compound's aromatic properties enable it to engage with biological entities such as enzymes, receptors, and nucleic acids by means of a phenomenon referred to as π-π stacking. Furthermore, the addition of electron-donating or electron-withdrawing substituents to the naphthalene ring has the ability to alter its pharmacological characteristics, hence impacting its affinity and selectivity for specific targets. Naphthalene-containing compounds have diverse pharmacological actions, encompassing antibacterial, antifungal, anti-inflammatory, antiviral, and anticancer properties. Due to the observed substantial antibacterial activity of naphthalene derivatives against a broad spectrum of bacterial species, these chemicals hold promise for the development of antibacterial drugs. Studies on the structure-activity relationship (SAR) have shown that modifying the naphthalene ring at various places can affect the antibacterial effectiveness, range of action, and pharmacokinetic properties of the molecule. For example, adding electron-drawing groups to certain locations might potentially increase antibacterial effectiveness by strengthening contacts with components of bacterial cell walls or enzymes that are essential for the development of bacteria. Conversely, alterations that enhance steric hindrance or alter the overall molecular shape might lead to a reduction in the efficacy of antibacterial medicines. Several antibacterial medicines containing the naphthalene moiety have been created and tested in clinical settings for the treatment of bacterial infections. An illustrative instance that is widely recognised is chloramphenicol, an antibiotic with a wide range of effectiveness that targets both Gram-positive and Gram-negative bacteria. Chloramphenicol hinders bacterial protein synthesis via binding to the 50S ribosomal subunit. This is achieved by inhibiting the formation

of peptide bonds. Despite its strong efficacy against germs, chloramphenicol is notorious for its substantial adverse effects. However, it is commonly employed to address serious infections that have shown resistant to other antibiotics. Overall, the naphthalene structure is a very versatile framework that may be effectively employed in the synthesis of antibacterial medications with diverse pharmacological properties. Because of its specific chemical features and diverse range of biological effects, it becomes an appealing candidate for the development of medications. The researchers want to harness the whole therapeutic capabilities of naphthalene derivatives while also addressing the worldwide issue of antibiotic resistance. Their strategy involves doing more investigations into the structure-activity link and generating additional chemical changes.

I. ***Kalariya, R et al in 2022*** study explores the development of novel amide-coupled naphthalene scaffolds as potent inhibitors of bacterial recombinase. The scaffolds were synthesized using acid-amine coupling reactions of 2-(naphthalen-1-yloxy)acetic acid with various amines. The scaffolds were evaluated for their antibacterial, antifungal, and anti-malarial actions. The highest binding affinity was found for compound 4c, which interacted well with GLY 3071 and THR 3073 amino acids. The naphthalene scaffolds were characterized using 1H NMR, 13C NMR, FT-IR, and mass spectroscopic techniques. The findings could be used to develop new RecA inhibitors or antibiotic adjuvants. The synthesis of naphthalene scaffolds was characterized using tetramethylsilane (TMS) and other analytical reagents.

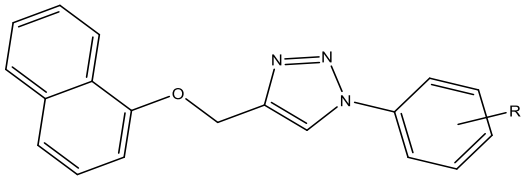


II. ***Kottapalle, G., & Shinde, A. et al in 2021*** study focuses on synthesizing 1-(2-substitutedphenyl-2,3-dihydro-1H-benzo[b][1,4]diazepin-4-yl)naphthalene-2-ol (3a-3 h) as a potent antimicrobial agent. The compounds were tested for their in vitro antimicrobial activity and found that electron withdrawing and electron releasing groups at the para position on the phenyl ring and the 1:2 molar ratio of chalcones and benzene-1,2-diamine in 2-ethoxy ethanol were key factors in increasing antimicrobial activity and yield. The study highlights the importance of selecting solvents from renewable sources to provide a sustainable environment and suggests that the combination of substitution patterns on anticipated biological activities could add synergistic biological significance to target compounds. The study also explores the design, synthesis, computational, and biological evaluation of new benzodiazepines as CNS agents.



R = H, CN, OH, CH_3, I, Br, OCH_2CH_3

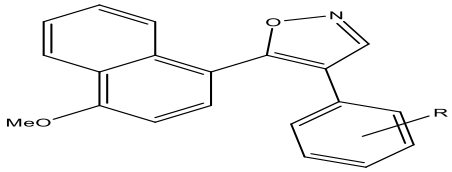
Kaushik, C. P., & Luxmi, R in 2020 study synthesized 15 naphthyl-linked disubstituted 1,2,3-triazoles through click synthesis between 1-(prop-2-yn-1-yloxy) naphthalene and aromatic azides. The compounds were characterized using FTIR, 1H NMR, 13C NMR, and HRMS techniques. The compounds were tested against bacteria B. cereus, S. aureus, and E. coli, and their antibacterial and antioxidant properties were evaluated. Compound 7f, which has significant medicinal importance, showed moderate to good antibacterial activity against the tested strains. The compounds also exhibited remarkable free radical scavenging activity using the DPPH assay. The study focuses on the synthesis of aromatic azides and ether-linked 1,4-disubstituted 1,2,3-triazoles.



R = 2/3/4 -OH , 2/3/4 -$OCH_2C_6H_5$, 2/3/4 - $OCH_2C_6H_4NO_2$

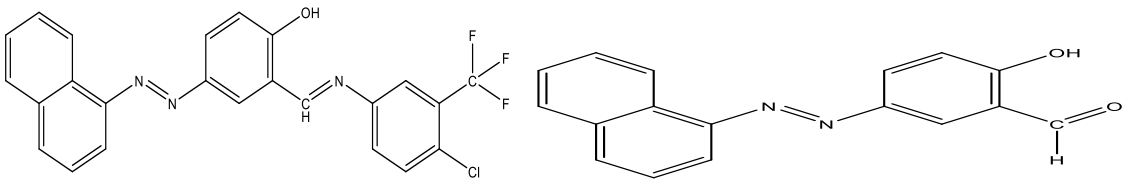
III. ***Wang, G et al in 2020*** investigates the synthesis and biological evaluation of isoxazole-naphthalene derivatives as anti-tubulin agents. Researchers synthesized a series of compounds containing isoxazole and naphthalene moiety in a single molecule, which were evaluated for their antiproliferative activities against human breast cancer cell line MCF-7. The most potent compound was compound5j, which contained a 4-ethoxy substitution at the phenyl ring.

The most active compound was compound5j, which inhibited cell cycle at the G2/M phase and induced apoptosis. The study highlights the importance of developing new anti-tubulin agents to disrupt microtubule dynamics and induce tumor cell death by apoptosis.

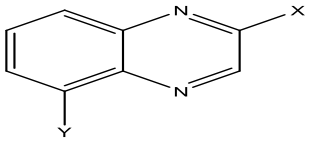


4-Cl, 2-Cl, 2-OMe, 2-F, 4-Br, 3=NH_{2-4}-OMe, 4-OEt, 4-OMe

IV. ***Parchegani, F et al in 2019*** A novel receptor, CTNP, based on azo derivatives of naphthalene, has been successfully synthesized for simultaneous measurement of hydrogen carbonate and acetate anions. The compound, prepared by dissolving 1-Naphthylamine in a solution of hydrochloric acid and ultrapure water, showed hydrogen-bonding between CTNP and incoming anions, resulting in significant changes in the visible region and color change. CTNP exhibited excellent antifungal and antibacterial activity against Aspergillus brasiliensis and Aspergillus niger. The study also explored the use of biologically active 2,4-dinitrophenyl hydrazones as colorimetric sensors for selective detection of acetate ions, sodium bicarbonate nanoparticles in tumor treatment, and azo dye-based colorimetric chemosensors for detecting acetate content in pharmaceutical peptides. The researchers also explored the antioxidant and antifungal activity of chitosan derivatives bearing Schiff bases and quaternary ammonium salts.

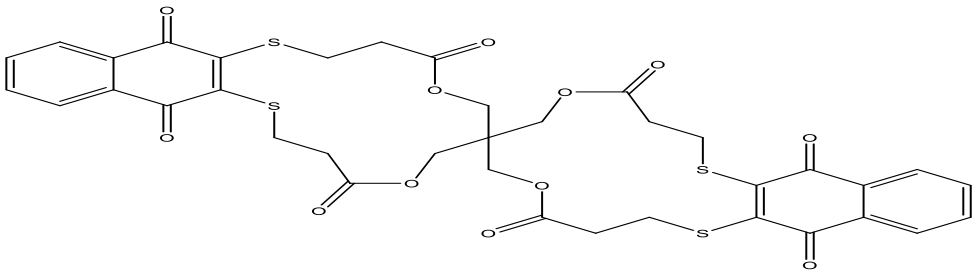


V. ***Parhi, A. K et al in 2013*** discusses the antibacterial properties of various phenyl substituted quinoxalines, quinazolines, and 1,5-naphthyridines. The study evaluates the antibacterial activity of these compounds against methicillin-sensitive and methicillin-resistant Staphylococcus aureus and vancomycin-sensitive and vancomycin-resistant Enterococcus faecalis. The results show that certain compounds exhibit significant antibacterial activity, with differences observed between nonquaternized and quaternized quinoxaline derivatives. The study also explores the bactericidal and bacteriostatic activities of these compounds and their impact on FtsZ protein polymerization.



X= H, phenyl, fluorophenyl, bipheyl, 3-t-Butyl phenyl
Y= H, $CH_2N(NH_2)_2$

VI. ***Ibis, C et al. in 2011*** synthesized and evaluated novel nitrogen- and sulfur-containing hetero-1,4-naphthoquinones as potent antifungal and antibacterial agents. The compounds showed high reactivity in nucleophilic vinylic substitutions and other transformations. The study aims to discover new drugs for fungal and bacterial infections. The compounds were tested against fungi, bacteria, and viruses, showing promising biological activity in chemistry. The study also focused on the antifungal activities of Nystatin and C. tenuisA. niger.



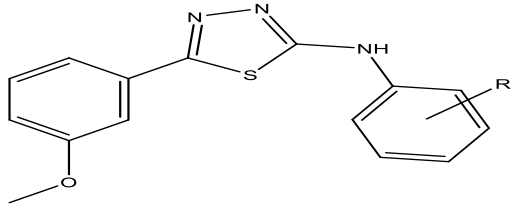
4.THIADIAZOLE

The thiadiazole moiety has attracted significant interest, especially in the realms of medicinal chemistry and drug development, because of its fused ring structure including one sulphur atom and two nitrogen atoms. The unique chemical composition of this drug, together with its wide array of pharmacological impacts, has captivated the attention of researchers worldwide. This section will provide an overview of the reasons behind the increasing interest in the thiadiazole moiety, its role as a biologically active component, its antibacterial properties, including the relationship between its structure and activity, and a few examples of antibacterial drugs that contain this moiety. Researchers have shown considerable interest in the thiadiazole moiety because of its remarkable flexibility and potential medicinal applications. Due to its inflexible and flat configuration, as well as its ability to form hydrogen bonds and interact with diverse biological targets, it serves as an ideal framework for the creation and advancement of pharmaceuticals. Researchers are interested in the medicinal chemistry of thiadiazole derivatives due to their potential to possess enhanced pharmacological properties and therapeutic efficacy.

The thiadiazole molecule exhibits a diverse range of biological activities and serves as an effective pharmacophore. The inclusion of electronegative sulphur and nitrogen atoms in its composition allows it to engage with a diverse range of biological targets, such as nucleic acids, enzymes, and receptors. Moreover, the pharmacological properties of the thiadiazole ring can be modified by substituents located at various positions. This can influence the ring's inclination and selectivity towards certain molecular targets. Compounds containing thiadiazole have diverse pharmacological effects, including antiviral, antifungal, antibacterial, and anticancer activities. Thiadiazole derivatives have been scientifically demonstrated to possess substantial antibacterial activity against a diverse range of bacterial species, rendering them promising candidates for the development of antibacterial medications. Based on the results of a structure-activity relationship (SAR) study, modifications to the thiadiazole ring can significantly impact the antibacterial effectiveness, range of activity, and pharmacokinetic properties of the compound. For example, the addition of substituents that either donate or withdraw electrons at certain locations has the potential to increase antibacterial effectiveness. This is achieved via promoting interactions with intracellular targets that are essential for bacterial growth or with constituents of bacterial cell walls. The antibacterial activity of these compounds can be reduced by alterations that either modify the overall molecular structure or enhance the steric hindrance.

Several antimicrobial medicines containing the thiadiazole moiety have been developed and are now being used in clinical settings to treat bacterial infections. An illustrious instance is the antibiotic cefazolin, which pertains to the initial generation of cephalosporins and exhibits efficacy against an extensive range of Gram-positive and Gram-negative bacteria. Cefazolin hinders the formation of bacterial cell walls by binding to penicillin-binding proteins. This can lead to the interference with cell wall synthesis and eventually the demise of bacterial cells. Cefazolin is commonly used to treat skin and soft tissue infections and to prevent surgical complications due to its potent antibacterial properties and favourable pharmacokinetic characteristics. the thiadiazole moiety is a highly effective pharmacophore that may be utilised in the production of antibacterial compounds with diverse pharmacological characteristics. It is a fascinating target for therapeutic research since it has unique chemical characteristics and a broad spectrum of biological effects. The researchers want to address the global problem of antibiotic resistance and maximise the medicinal benefits of thiadiazole derivatives. Their objective is to do this by discerning distinctive chemical alterations and comprehending the correlation between structure and function.

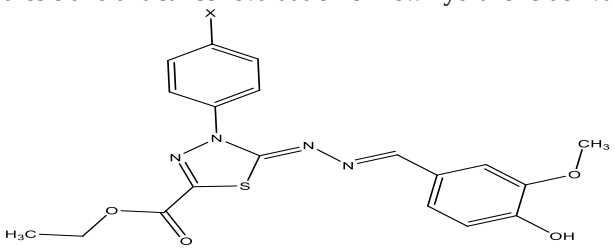
I. ***Janowska, S et al in 2022*** synthesized thiosemicarbazide and 1,3,4-thiadiazole derivatives and tested their antibacterial activity. In vitro tests showed moderate antimicrobial response, depending on the substituent on the phenyl ring. The highest activity towards all Gram-positive bacteria strains was demonstrated by linear compounds with a trifluoromethylphenyl group. The study also attempted to explain the antibacterial activity of the compounds using molecular docking to DNA gyrase and topoisomerase IV. Docking simulations allowed for the purposing dual mechanism of antibacterial activity.



R = 2-Cl, 3Cl, 4-F, 2-F, 3-F, 4-F, 2-OCH_3, 3OCH_3, 4-OCH_3, 2-CF_3, 3-CF_3, 4CH_3, 2,4-diCl

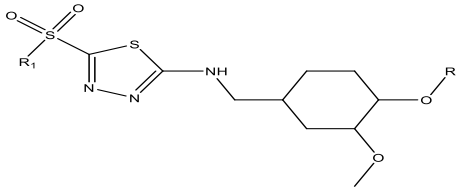
II. ***Shehadi, I. A et al in 2022*** presents the synthesis and antibacterial activities of novel imidazo[2,1-b]-1,3,4-thiadiazoles, synthesized by reacting 2-aryl-2H-1,2,3-triazol-4-yl acids with thiosemicarbazide and phenacyl bromides. Some compounds showed slight to moderate activity against microorganisms. The study also discusses the effectiveness of hydrolytic enzymes in preventing radiation therapy-induced side effects in head and neck cancer patients, the use of

chemotherapy for advanced breast cancer, and the antimelanoma activity of 1,3,4-thiadiazolium mesoionics. The study also discusses the synthesis and anticancer evaluation of new hydrazone derivatives.



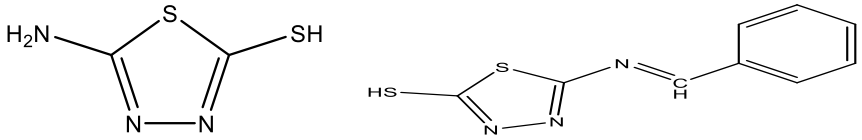
X = H, CH_3

III. ***Wu, Qiong et al in 2020*** synthesizes 1,3,4-thiadiazole derivatives with benzimidazole moiety, revealing their wide biological activity. The compounds were confirmed through physical and spectral data, and their antibacterial activity against various bacteria was screened. The compounds showed good activity against staph. and were resistant to the aqueous extract of azitidin-2-ones.

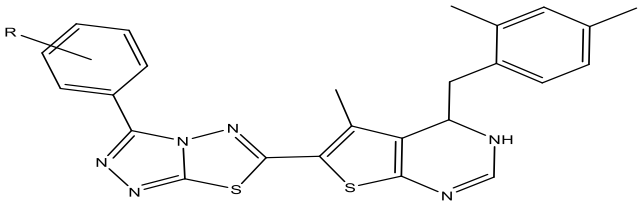


R_1 = 2-Cl-thiazole-5-CH_2, 3-Cl-5-CF_3-2-Py, 2-CH#-Bn, 4-Cl-Bn
R_2 = CH_3, CH_2CH_3, CH_2CH_2Cl, 2-Cl-Benzyl

IV. ***Akram, E et al in 2019*** study published in the Al-Nahrain Journal of Science investigated the synthesis and evaluation of 1, 3, 4-thiadiazole derivatives as antibacterial agents against common pathogenic bacteria. The Schiff base compound, prepared from a condensation reaction, showed higher activity proportional to the chosen antibiotics, highlighting the growing burden of antimicrobial-resistant pathogens on healthcare systems and global economic costs.

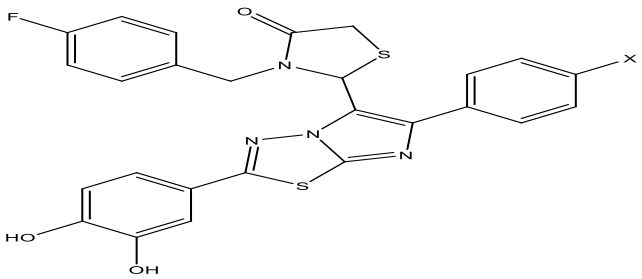


V. ***Settypalli, T et al in 2019*** a series of 1,2,4-triazolo[3,4-b]1,3,4-thiadiazole-linked thieno[2,3-d]pyrimidine derivatives have been synthesized for neuroprotective and antibacterial activities. The compounds derived from 4-methylphenyl(10a) and 4-nitrophenyl(10c) showed good neuroprotective activity against H2O2-induced PC12 cell death. In silico docking studies were performed for all synthesized compounds. The study reveals that substitutuents like -NO2 in thienopyrimidine-triazolothiadiazole derivatives significantly reduce neuroprotectivity. The compounds exhibited strong antibacterial activity against four bacterial strains, suggesting potential for further development. The study explores the use of antimicrobial agents in treating infections and the role of adiposity in the regulation of cellular metabolism.



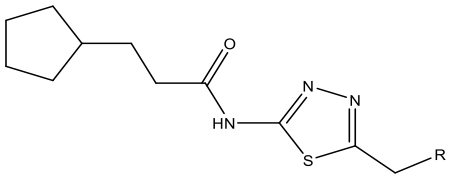
R = Me, H.
R_1= H, Me
R_2 = NO_2, Cl, Me, OMe

VI. ***Taflan, E et al in 2019*** synthesized novel imidazo[2,1-b][1,3,4]thiadiazole (ITD) compounds and studied their antimicrobial and antioxidant properties. The compounds showed high anti-tuberculosis activities at low concentrations, while 3b showed moderate activity. The compounds were effective against Gram-negative, Gram-positive, and fungi. The synthesis of compounds 6a-6g and 7a-7g involved adding corresponding compounds in dimethylformamide containing indium (III) chloride and Norfloxain or Ciprofloxacin. The study also focused on the synthesis of 1,3-thiazolidin-4-one derivatives from the oily product.



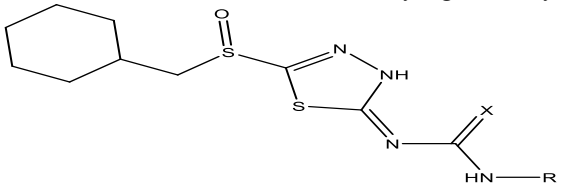
X = Cl, H

VII. ***Zhang, M et al in 2019*** synthesized a series of environmentally friendly 1-(5-(benzylsulfinyl)-3-methyl-1,3,4-thiadiazol-2(ylidene)-thiourea/urea derivatives. These compounds showed moderate to excellent antibacterial and antifungal activities against various bacterial and fungal strains. The 1,3,4-thiadiazole moiety significantly enhanced their activity. The compounds were tested against various strains and fungi, with thiourea-based derivatives showing the most activity. The work aims to aid in new drug discovery and development programs.



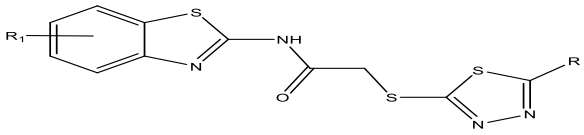
R = CH_3, $CH_2CH_2CH_3$, $CH_2CH{=}CH_2$, $CH(CH_3)_2$ BANZYL, 3-CN-BENZYL, 3-F-BENZYL, 4-Cl-BENZYL

VIII. ***Mannam, M. R et al. in 2019*** synthesized a series of 1-(5-(benzylsulfinyl)-3-methyl-1,3,4-thiadiazol-2(3H)-ylidene)-thiourea/urea derivatives. They developed a new process for N-methylation of the 1,3,4-thiadiazole moiety using dimethyl carbonate and selectively oxidized the sulfide to sulfoxide using chlorine. The compounds were tested for their antimicrobial activities, showing moderate to excellent antibacterial and good antifungal activities against both Gram-positive and Gram-negative bacterial strains. Compounds 1b, 1d, 1h, and 1i were particularly promising, exhibiting both antibacterial and antifungal activities compared to standard drugs like ciprofloxacin and fluconazole. The presence of the 1,3,4-thiadiazole moiety significantly enhances antimicrobial activity.



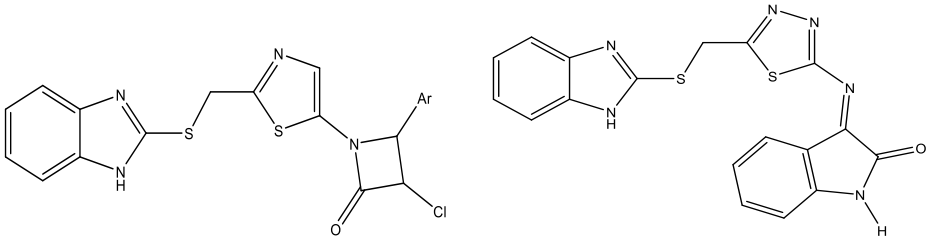
X = S, O. R= aryl, alkyl, aralkyl

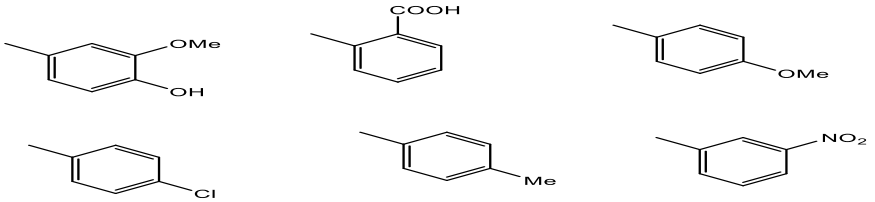
IX. ***Tang, Xu et al in 2018*** a series of benzothiazole derivatives with a 1,3,4-thiadiazole moiety were designed, synthesized, and evaluated for their antibacterial, antifungal, and antiviral activities. The bioassay results showed that most target compounds showed good antiviral activities against tobacco mosaic virus (TMV) and Xanthomonas oryzae pv. oryzae (Xoo) and Rastonia solanacearum (Rs). The structure-activity relationships of antibacterial activities showed that the changes of substituted groups could greatly affect the inhibition effects against plant bacteria. The study provides valuable insights into the structure-activity relationships of antiviral activities in benzothiazole derivatives.



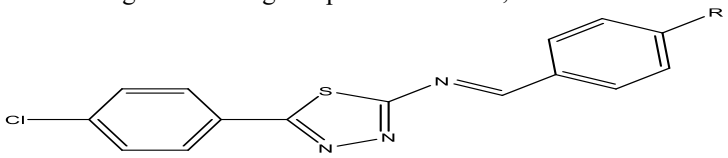
R = 4-CF_3Ph, 2-MePh, 2-OHPh, 2,4-diClPh
R_1 = 5-NO_2, 5-OMe

X. ***In 2017, Al-Jawady, M. S., & Younis, S. A*** conducted a study on synthesizing 1,3,4-thiadiazole derivatives to combat multidrug resistance in microbial pathogens. They tested compounds against Gram-positive, Gram-negative, yeast, and Candida albicans. Compounds 3 and 5 showed wide-spectrum antimicrobial activity against all tested pathogens, with Compound 3 showing the best antibacterial activity due to its six hydrogen bonds. Compounds 4 and 6 are recommended for further development as antibacterial agents.



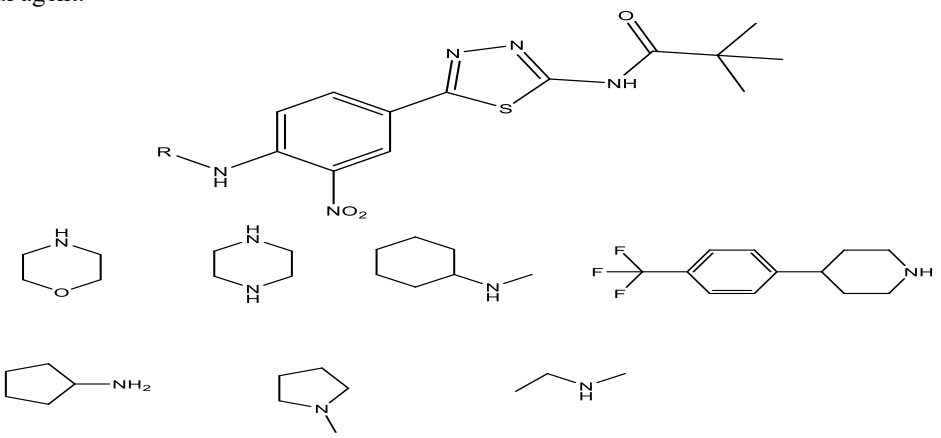


XI. ***In 2017, Mousa, M. N*** synthesized six compounds containing 1,3,4-thiadiazole and Schiff base. The compounds were tested for antibacterial activity against four microorganisms: S. aureus, B. Cereus, and E. coli and P. Aeroginosa. The disc diffusion method was used, and two concentrations of the compound and the standard drug were used. Compound 5f showed the highest activity, while compound 5b had the least. Compounds 5d, 5e, and 5f showed more powerful or equivalent effects than the standard drug. Compounds 5a and 5c showed higher antibacterial activity than compound 5b, while compound 5d, 5e, and 5f had less. The effect on gram-negative bacteria was higher than on gram-positive bacteria, while the weakest effect was observed on P. Aeroginosa.

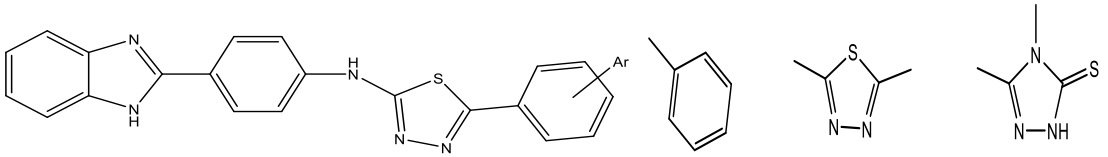


R = H, CH_3, OH, NO_2, Cl, Br

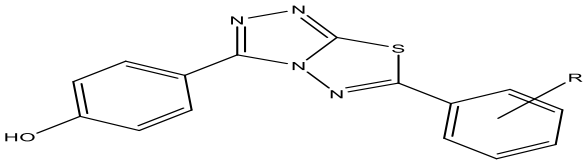
XII. ***Chandrakantha, B et al in 2013*** have developed a new series of compounds, including N-[5-(4-(alkyl/aryl)-3-nitro-phenyl)-[1, 3, 4-thiadiaol-2-yl]-2, 2-dimethyl propionamide 4(a-l) and 6-(4-Methoxy-phenyl)-2-(4-alkyl/aryl)-3-nitro-phenyl)-Imidazo [2, 1b] [1, 3, 4] thiadiazole 6 (a-l) from 5-(4-Fluoro-3-nitro-phenyl)-[1, 3, 4] thiadiazole-2-ylamine. These compounds were characterized using IR, NMR, mass spectral, and elemental analysis, and tested for antibacterial and antifungal activities. The compounds showed moderate to good activity in in-vitro antimicrobial screening. The new class of compounds holds greater promise in discovering a potent antimicrobial agent.



XIII. ***Barot, K. P et al in 2013*** synthesized novel 1,3,4-thiadiazole, 1,2,4-triazole-5-thione, and 1,3-thiazolan-4-one derivatives of benzimidazole, evaluating their structure-activity relationship and antimicrobial activities. The compounds were tested against Candida albicans, Aspergillus niger, and Fusarium oxyspora. The minimum inhibitory concentration (MIC) was determined to be the lowest concentration of the drug inhibiting the growth of bacteria and fungi. The study highlights the importance of understanding the structure-activity relationship in the treatment of fungal infections and highlights the importance of combining benzimidazole with various compounds for effective antimicrobial activities.

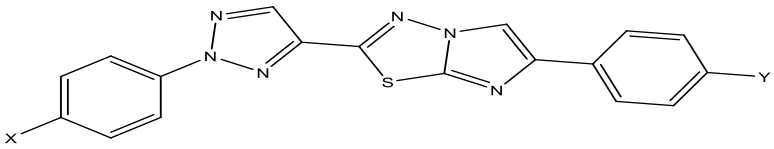


XIV. ***Rajput, S. S in 2012*** explores the synthesis, characterization, and antibacterial activity of mercapto 1,2,4-triazole, 1,3,4-thiadiazoles, mercaptobenzaldehydehydrazones, and thiazolidinone derivatives of 4-hydroxybenzhydrazide. The compounds were evaluated for antimicrobial activity against Escherichia coli and Pseudomasaeruginasa. The research also highlights the importance of mercaptotriazoles in various compounds.



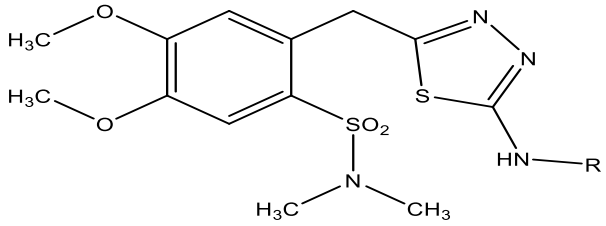
R = H, 2-Cl, 2-CH_3, 4-CH_3, 2-OH, 2-NH_3

XV. ***Atta, Kamal F. M et al in 2011*** has found that nitroaryl thiadiazole-gatifloxacin hybrids, containing 5-nitroheteroaryl groups, exhibit high antibacterial activity against Gram-positive and Gram-negative bacteria. Nitrofuran analog 6a showed the most potent inhibitory activity against Gram-positive bacteria. The study also assessed the cytotoxic activity of compounds 6a-fin and gatifloxacin against mouse fibroblast cells using MTT assay. The findings suggest the need for novel gatifloxacin derivatives with better activity profiles and tolerability to overcome gatifloxacin's limitations.



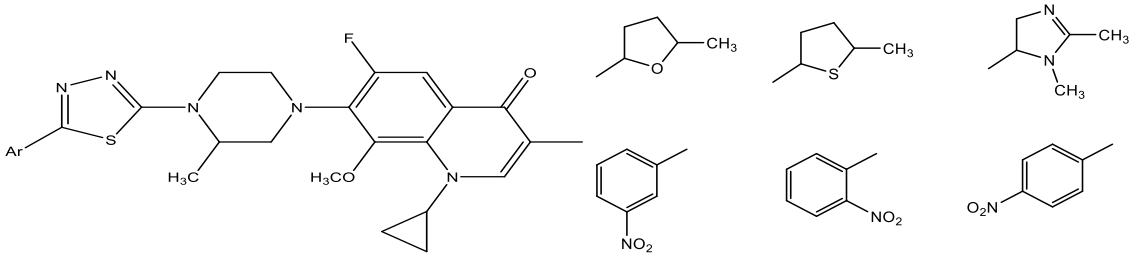
X = H, Br, Cl
Y = H, Br, Cl

XVI. ***P. Zoumpoulakis et al in 2011*** at Karadeniz Technical University and Rize University in Turkey have synthesized new 1,3,4-thiadiazol-2-ylmethyl-1,2,4-triazole derivatives and investigated their antimicrobial activities. The compounds were characterized using elemental analyses, IR, NMR, CNMR, and mass spectral studies. The 1,2,4-triazole nucleus has been used in various therapeutic agents, including ribavirin, rizatriptan, alprazolam, vorozole, letrozole, and anstrozole. The study highlights the importance of synthesizing new antimicrobial compounds to address the global problem of multi-drug resistant microorganisms. The compounds were obtained from the reaction of compound 2-[4-amino-3-(4-methylphenyl)-5-oxo-4,5-dihydro-1H-1,2,4-triazol-1-yl]ac with 4-fluorophenyl-(for compound2a), phenyl-(for compound2b), or 4-methoxyphenyl isocyanate. The compounds were found to have antimicrobial activity.

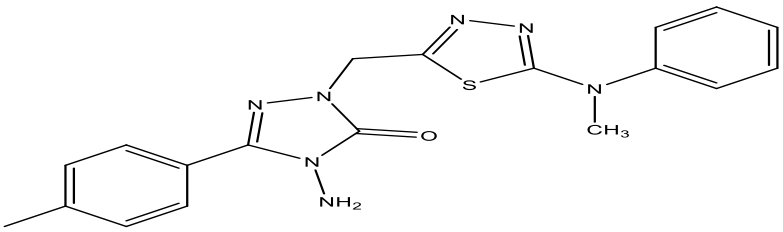


R = -CH_3, -CH_2CH_3, -$CH(CH_3)_2$, -$C(CH_3)_3$

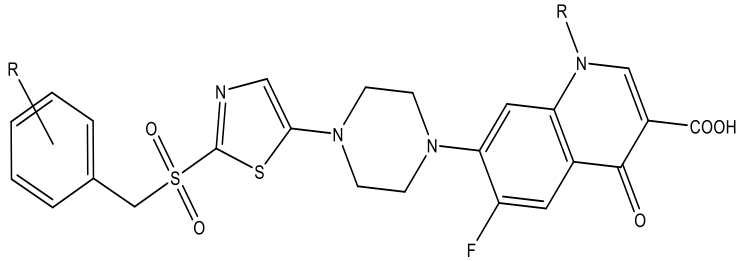
XVII. ***In 2009, Jazayeri, S et al***. conducted a study to develop effective antifungal agents for clinical research. They synthesized and evaluated novel substituted 1, 3, 4-Thiadiazole and 2, 6-di aryl substituted imidazo [2, 1-b] [1, 3, 4]-thiadiazole derivatives. The compounds were characterized using IR, NMR, mass spectral, and elemental analysis. Compounds 4a, 4c, and 6e, 6g showed significant activity at concentrations 0.5-1.0 mg/mL. The compounds bind to the amine ring, indicating potential drug delivery targets.



XVIII. ***Demirbas, A et al in 2009*** investigates the antibacterial activity of 1,3,4-thiadiazole derivatives containing Schiff bases. The compounds showed noticeable antimicrobial activity, with compound 5f showing the best results. The synergistic activity between the Schiff base and the 1,3,4-thiadiazole moieties is attributed to their potential. Further studies are needed to determine the mechanism of antimicrobial activity and evaluate their biological and physico-chemical properties.

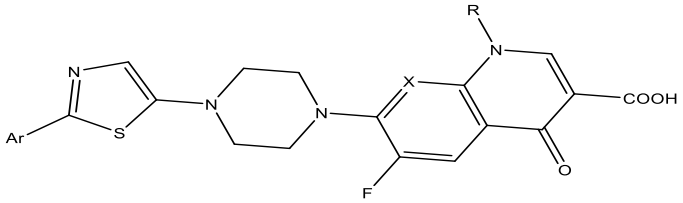


XIX. ***Foroumadi, A et al in 2005*** synthesized N-substituted piperazinyl quinolone derivatives (3and4) showed high antibacterial activity against Gram-positive and Gram-negative bacteria, comparable or more potent than their parent drugs, norfloxacin and ciprofloxacin. The structure of the benzyl unit and the S or SO2 linker significantly impact antibacterial activity. The study suggests that 1,3,4-thiadiazole bearing a certain dependent group is well tolerated at the N-4 position of the piperazine ring.



$R = CH_2CH_3, C_3H_5,$
$R_1 = H, 2\text{-}NO_2, 3\text{-}NO_2, 4\text{-}NO_2$

XX. ***Foroumadi, A in 2003*** involving the synthesis and evaluation of N-(5-aryl-1,3,4-thiadiazole-2-yl)piperazinyl quinolone derivatives was conducted. The results showed that all nitroimidazole derivatives showed significant antibacterial activity against Gram-positive bacteria, while all nitrophenyl analogues were inactive against both. The most active compound was the ciprofloxacin analogue in the nitroimidazole series. The study contributes to the understanding of quinolone antibacterials and their potential applications.



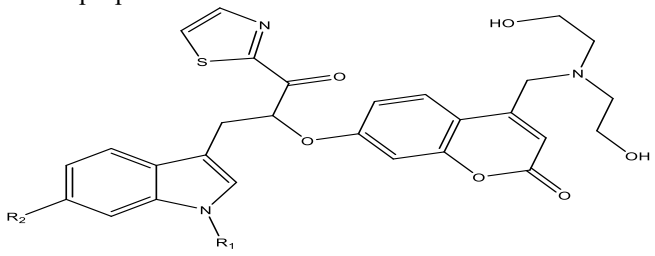
X- CN, N
$R = CH_2CH_3, C_3H_5,$
$R_1 = H, 2\text{-}NO_2Ph, 3\text{-}NO_2Ph, 4\text{-}NO_2Ph$

5.THIAZOLE

The field of medicinal chemistry has given great importance to the thiazole moiety, a heterocyclic ring consisting of five members and containing both nitrogen and sulphur atoms. Experts worldwide have shown interest in it because of its unique molecular structure and wide variety of pharmacological effects. In this introduction, we will examine the reasons behind the growing interest in the thiazole moiety. Additionally, we will explore its role as a biologically active component and its antibacterial properties as determined by the structure-activity relationship (SAR). Finally, we will provide examples of antibacterial medications that incorporate this moiety. Scientists have displayed significant interest in the thiazole moiety because of its remarkable flexibility and potential therapeutic applications. Due to its heterocyclic structure consisting of sulphur and nitrogen atoms, this compound may undergo chemical changes and be adjusted to specifically target a diverse range of molecular targets and biological processes. Furthermore, thiazole compounds have a diverse array of pharmacological properties, encompassing antiviral, antifungal, antibacterial, and anticancer activities. Due to these characteristics, the thiazole moiety serves as a viable foundation for drug discovery and design, which has therefore led to increased research into the pharmacological and medicinal chemistry of this molecule. The thiazole molecule exhibits a wide range of biological impacts in addition to its strong pharmacological properties. The unique chemical composition of this drug enables it to interact with a diverse array of molecular targets present in biological systems. The molecular targets encompass nucleic acids, enzymes, and receptors. By making structural and chemical changes, researchers may manipulate these interactions, resulting in the development of compounds containing thiazoles that have improved therapeutic efficacy, selectivity, and potency. Thiazole compounds have being investigated as potential therapeutic alternatives for bacterial infections. This is because they specifically target crucial bacterial enzymes or cellular processes that are vital for the growth and survival of bacteria. Thiazole compounds have been scientifically demonstrated to possess potent antibacterial properties against a diverse range of bacterial species. These chemicals have great potential for the development of antibacterial medications. Based on the results of a structure-activity relationship (SAR) study, modifications to the thiazole ring can significantly influence the antibacterial efficacy, range of activity, and pharmacokinetic properties of the compound. Research has shown that substituting thiazole rings at the C2 and C4 positions can enhance the effectiveness of antibacterial agents. This is achieved by facilitating interactions with bacterial

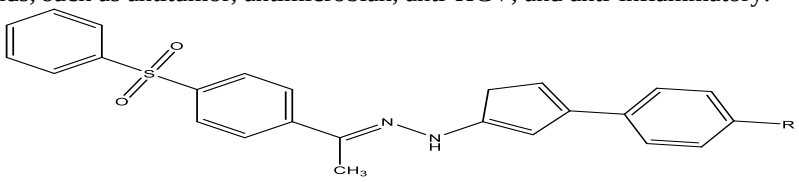
enzymes or cell wall components that are crucial for bacterial growth. Incorporating certain functional groups or substituents might potentially improve antibacterial activity and also boost pharmacokinetic properties like bioavailability and metabolic sustainability. In the field of treating bacterial infections, a number of antimicrobial drugs containing the thiazole component have been developed and are now being used in medical settings. Cefixime is a prominent cephalosporin antibiotic from the third generation that has efficacy against both Gram-positive and Gram-negative bacteria. Cefixime inhibits the synthesis of bacterial cell walls by interacting with penicillin-binding proteins, resulting in the lysis and demise of bacterial cells. Cefixime is commonly given to treat respiratory tract infections, sexually transmitted infections, and urinary tract infections caused by susceptible bacterial strains. The reason for this is that cefixime has potent antibacterial properties, a broad range of actions, and advantageous pharmacokinetic qualities. In conclusion, the thiazole moiety is a highly effective pharmacophore that may be utilised in the synthesis of antibacterial compounds with a wide range of pharmacological characteristics. It is an interesting target for drug discovery and development since it has a unique chemical structure, a broad spectrum of biological effects, and the potential for structural enhancements. Researchers want to address the global issue of antibiotic resistance and maximise the medical benefits of thiazole derivatives by identifying new chemical alterations and understanding the relationship between their structure and action.

I. ***In 2021, Ibrahim, S. A et al*** conducted the creation and synthesis of new magenta dyestuffs using thiazole. This was done due to its antibacterial properties.



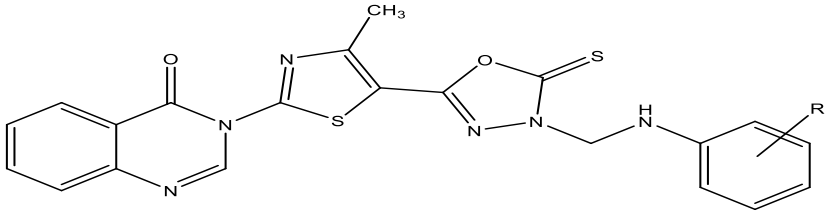
R_1 = H, CH_2CH_3 R_2 = H, Cl, CH_3

II. ***Shaaban, M. R et al in 2020*** investigates the synthesis, antimicrobial, and anticancer evaluations of novel thiazoles containing phenylsulfone moiety. It synthesized a series of thiazoles from the treatment of N-(1-(4-(phenylsulfonyl)-phenyl)ethylidene)hydrazi carbothioamide with various a-halo-carbonyl compounds under microwave irradiation. The antimicrobial activity of some derivatives was found to be potent, with some exceeding the activity of reference drugs. The study also investigated the anticancer activities against HepG-2 and HCT-116 cell lines. Thiazole and phenyl sulfone moieties are important pharmacological scaffolds in heterocyclic compounds, such as antitumor, antimicrobian, anti-HCV, and anti-inflammatory.

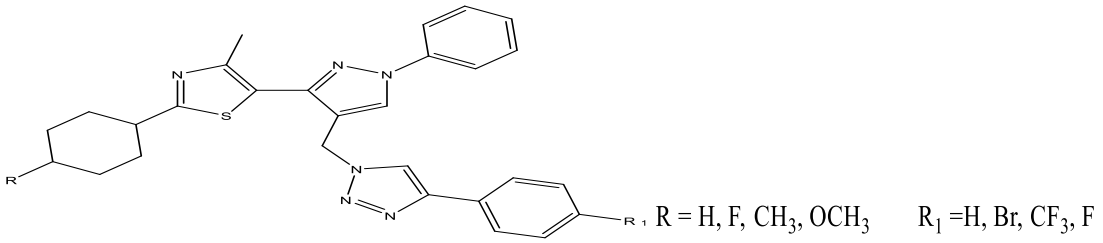


R= Cl, CH_3, Br

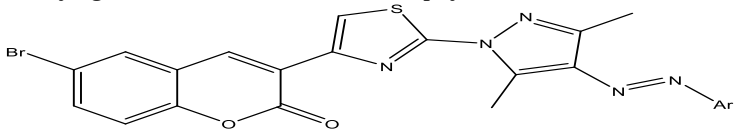
III. ***In 2020, Desai, N et al*** conducted a study on the synthesis, characterization, antibacterial evaluation, and molecular docking analysis of substituted quinazolines including thiazole and oxadiazole heterocyclic groups.



IV. ***Jagadale, S. M et al***synthesised novel thiazole and pyrazole chemicals, which were named 1,2,3-triazole. These compounds have the capacity to function as antibacterial and antimycobacterial agents.

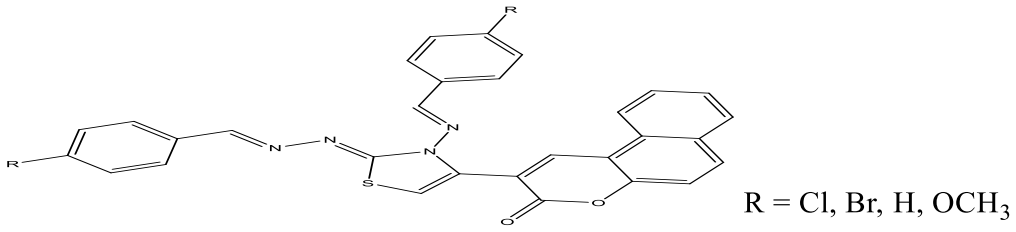


V. ***Abdel-Aziem, A et al in 2020*** found that 1,3-thiazoles and arylazothiazoles 3-6 were produced by reacting thiosemicarbazide with derivative 2. Pyrazolyl thiazolyl coumarin derivatives 9a-c and 11a-c were prepared by reacting hydrazinylthiazole 8 with acetylacetone, trifloroacetylacetone, ethyl acetoacetate, and/or arylazoa-city Thiazolotriazine derivative 12 was made by reacting 8 with ethyl 2-(2-phenyhydra-Zono)-2-chloroacetate. Spectral measurements revealed complex structures. After screening eleven compounds, compounds 5a, 5b, 9a, 9c, 11b, and 12 showed high activity against Enterococci faecalis, Staphylococcus aureus, and Pseudomonas aeruginosa.

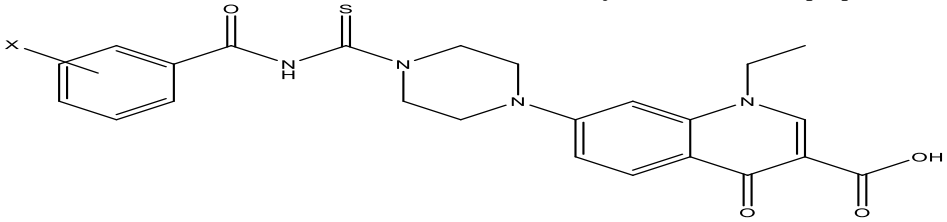


Ar = C_6H_5, 4-$CH_3C_6H_4$, 4-FC_6H_4

VI. ***Mamidala, S et al in 2020*** have reported that a new series of hybrid cumain-based thiazoles would be synthesised for use as an antibacterial agent.

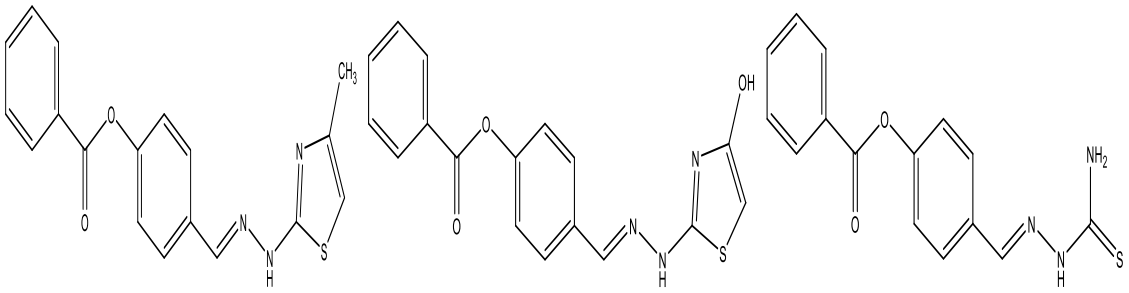


VII. ***Ahmed, A et al in 2020***Compounds with anti-inflammatory, anti-infective, and gastrointestinal selectivity are being developed. Trisubstituted thiazole compounds (AR-17a to AR-27a) were tested for inflammation reduction and microorganism killing. Against S. aureus, E. coli, and P. aeruginosa. AR-17a and AR-27a at 20 mg/kg protected 59% and 61% of the inflamed paw model. Low minimum inhibitory concentrations and broad inhibition zones made these compounds antimicrobial. New trisubstituted thiazole compounds may treat chronic inflammatory illnesses and bacterial infections alone due to their anti-inflammatory and antibacterial properties.

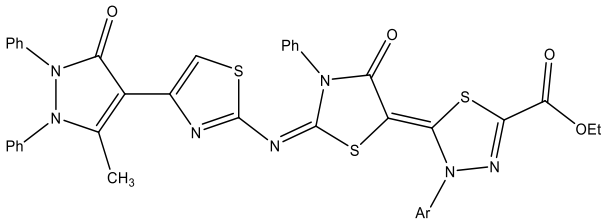


X =H, p-Cl, C_6H_5

VIII. ***Abdel-Galil, E et al in 2018*** used the compound 4-Formylphenyl benzoate as a flexible starting material to create a range of novel heterocyclic structures, including thiazole and thiazolidin-5-one rings. We assessed the antibacterial efficacy of these scaffolds against two bacterial strains, and found that most of them demonstrated significant activity. Compounds 5, 6, and 8a showed antibacterial activity similar to the common chemotherapy drug ampicillin among the thiazole derivatives that were made.

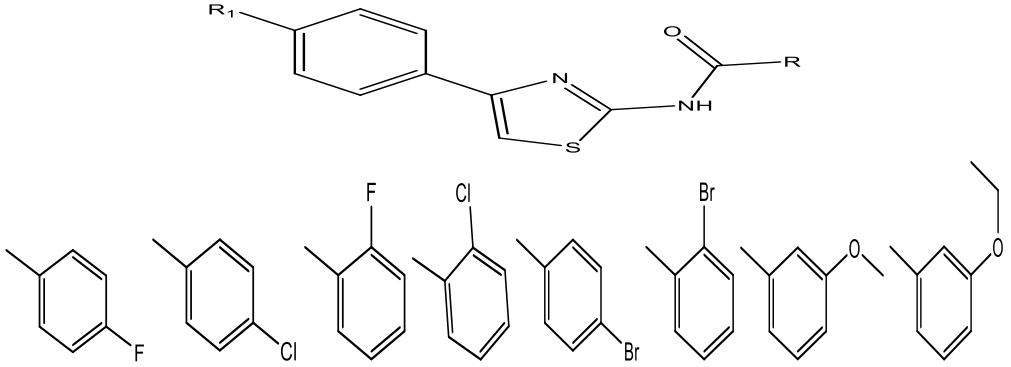


IX. ***Dawood, K. M et al in 2015*** synthesized bis-1,3-thiazole derivatives combining pyrazole and thiadiazole moieties to test their efficacy as potential antiviral agents. The most active structure was 1,3,4-thiadiazole. The study aimed to discover novel antiviral scaffolds by focusing on compounds of repeated azole units. In-vitro antiviral screening was conducted in the USA, targeting Poliovirus, Influenza A (H1N1) virus, Hepatitis B virus, and Hepatitis C virus. The results showed significant resistance against Polio and Hepatitis B viruses, while compound 22 showed an effective effect against H1N1. The synthesis of 5-(2,4-diphenyl-1,3,4-thiadiazol-5-ylidene)-2-(4-() and 5-(1,3-thiazol-2-ylidene)-2-(4-(pyrazol-4-yl)thiaz involved stirring a mixture of thiazolidin-4-one derivative and KOH in DMF for 10 minutes.

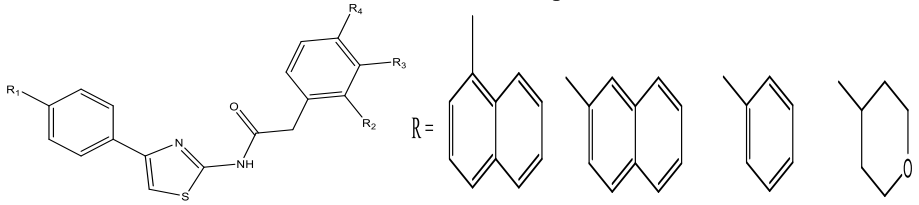


Ar = C_6H_5, 4-ClC_6H_4, 4-MeC_6H_4, 4OMe-C_6H_4

X. ***Li, J et al in 2014***synthesised novel anti-inflammatory, anti-infective, and gastrointestinal-selective monotherapies using thiazole compounds (AR-17a to AR-27a). These compounds were tested against Staphylococcus aureus, Enterococcus faecalis, Escherichia coli, and Pseudomonas. The compounds showed antibacterial activity, with the lowest minimum inhibitory concentration and largest inhibition zone. These compounds can be used alone to treat bacteria and chronic inflammation, providing a potential solution for various health conditions.



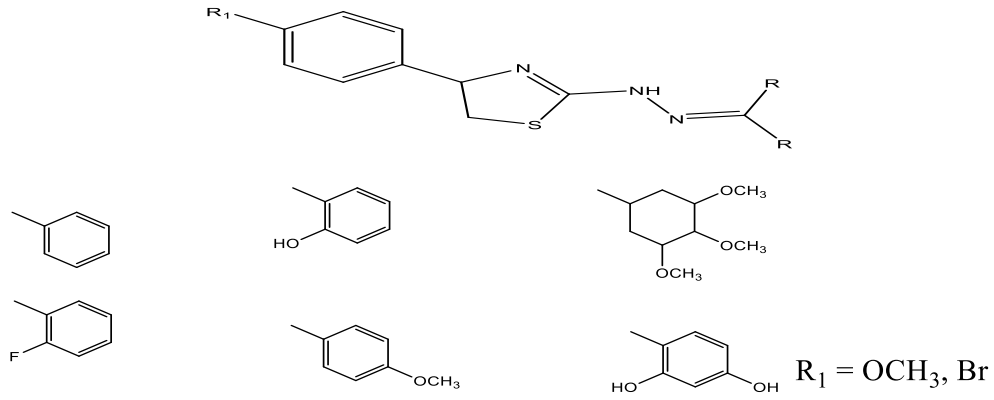
XI. ***Cheng, K. et al in 2013***synthesised two sets of thiazole compounds with an amide structure as effective inhibitors of Escherichia coli B-ketoacyl-acyl-carrier-protein synthase III (eckKAS I). We tested the antibacterial activity of the 24 newly synthesised compounds against various bacterial strains, including Escherichia coli, Pseudomonas aeruginosa, Bacillus subtilis, and Staphylococcus aureus. Compound 4e demonstrated the strongest inhibition of ecKAS III activity, with an ICso of 5.3 pM. The study also conducted a docking simulation to accurately anticipate the binding mode between the small molecule and the eckAS III protein.



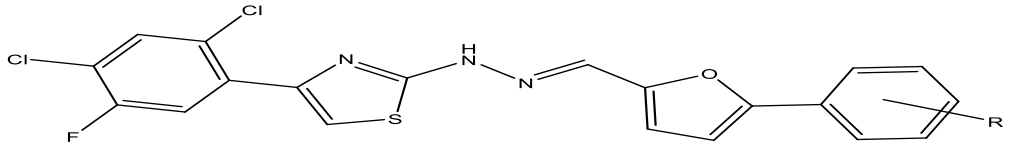
R1= H, Br,R2 = H R3= H, Br, Cl, OMe, OEt R4 = H, Cl, Br, OEt

XII. ***Bharti, S. K et al in 2010*** investigates the synthesis, anti-bacterial, and anti-fungal activities of novel Schiff bases containing 2,4-disubstituted thiazole rings. The compounds were synthesized, characterized, and screened for their

antimicrobial activities. The most effective compounds were found in Candida albicans, Cryptococcus neoformans, and Aspergillus flavus. Thiazole ring systems play a crucial role in biologically active molecules, such as thiazole derivatives used for antibiotic synthesis. The researchers also explored the potential of thiazole nucleus as a pharmacophore in various pharmacologically active agents. They synthesized a Schiff base of thiosemicarbazone, which showed good activity against all four fungal strains. The study provides valuable insights into the anti-fungal activity of newly synthesized compounds and their potential applications in various fungi.



XIII. ***Holla, B*** et al in 2003 reacted Arylthioureas, aromatic aldehyde thiosemicarbazones, and 5-aryl-2-furfuraldehyde thiosemicarbazones with 2,4-dichloro-5-fluorophenacyl bromide to synthesisearylaminothiazoles and arylidene/5-ary-2-furfurylidene hydrozinothiazoles. We characterized the compounds using IR, H-NMR, and mass spectrum investigations, and then evaluated their antibacterial and anti-inflammatory properties.

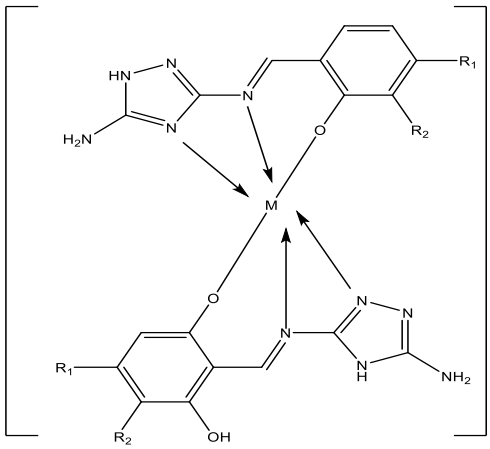


6.TRIAZOLE

Triazole compounds, characterised by the inclusion of three nitrogen atoms inside a five-membered heterocyclic ring, have garnered significant attention in the realms of medicinal chemistry and pharmaceutical research. This is mainly attributed to the multitude of pharmacological properties and structural adaptability that they possess. This introduction will examine the factors contributing to the growing interest in the triazole moiety, its role as a biologically active component, the antibacterial properties of the triazole as demonstrated by the structure-activity relationship (SAR), and provide examples of antibacterial drugs that incorporate it. Researchers have attributed great significance to the triazole moiety due to its remarkable structural diversity, chemical stability, and wide range of pharmacological effects. Due to its unique heterocyclic structure, it is feasible to apply various chemical and structural modifications to improve its biological properties and therapeutic effectiveness. Triazole compounds have a wide range of pharmacological actions, including antibacterial, antifungal, antiviral, anticancer, and anti-inflammatory characteristics, among others. Due to these specific attributes, the triazole moiety is a compelling structure for the exploration and development of drugs, hence promoting more investigation into the pharmacological and medicinal chemistry of the triazole motif. The triazole moiety exhibits a diverse range of biological effects while also serving as a powerful pharmacophore. Its structural properties enable it to interact with a wide range of molecular targets found in biological systems. The molecular targets encompass nucleic acids, enzymes, and receptors. To enhance the therapeutic effectiveness, selectivity, and pharmacological potency of triazole-containing medicines, researchers can adjust these interactions by structural and chemical alterations. Triazole derivatives have been investigated as potential therapeutic agents for the treatment of bacterial infections. These chemicals demonstrate antibacterial activity by specifically targeting essential bacterial enzymes or cellular processes required for bacterial growth and survival. Triazole derivatives are regarded promising candidates for the development of antibacterial drugs due to their shown outstanding antibacterial activity against a wide range of bacterial species. The results of a structure-activity relationship (SAR) study indicate that altering the triazole ring at various positions can significantly affect the antibacterial efficacy, range of activity, and pharmacokinetic properties of the compound. Triazole ring substitutions at positions C1 and C4 have been shown to enhance antibacterial effectiveness by facilitating interactions with bacterial enzymes or cell wall components essential for bacterial growth. Incorporating certain functional groups or substituents might potentially improve antibacterial activity while also boosting pharmacokinetic factors like bioavailability and metabolic durability. Scientists have developed many antibacterial drugs containing the triazole moiety to effectively treat bacterial infections. These drugs are currently being used in clinical settings. A widely recognised

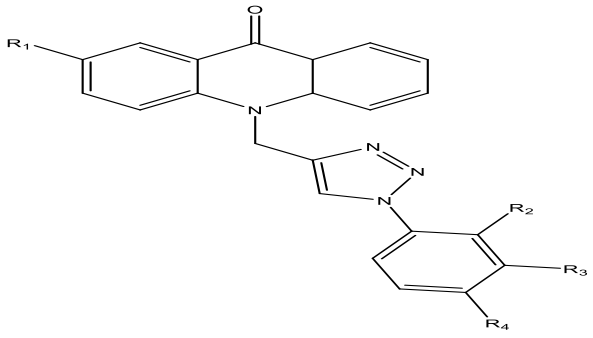
example is fluconazole, a triazole antifungal agent that also exhibits antibacterial properties against some bacterial strains. Fluconazole induces the demise of fungal cells by inhibiting the synthesis of ergosterol, a vital component of the fungal cell membrane. Moreover, studies have shown that fluconazole effectively hinders the proliferation of some strains of bacteria, particularly those associated with urinary tract infections, nosocomial infections, and other diseases. The triazole component is a highly effective pharmacophore that may be used in the creation of antibacterial drugs with diverse pharmacological characteristics. It is an interesting target for drug discovery and development since it has a unique chemical structure, a broad spectrum of biological effects, and the potential for structural enhancements. This study aims to address the global issue of antibiotic resistance and maximize the therapeutic benefits of triazole derivatives. This will be achieved by acquiring comprehension of the relationship between structure and action, and by producing alternative chemical modifications.

I. ***Sumrra, S. H et al in 2021*** investigates the molecular structures, spectroscopic properties, cholinesterase inhibition, and antibacterial activities of triazole Schiff bases endowed metal chelates. Researchers synthesized two mono-Schiff bases and one bis-Schiff base, and evaluated their complexes of transition metals. The results showed that the complexes (15) and (1) were the most active inhibitors of BChE and AChE enzymes with 94.60% and 90.90% activity, respectively. The study also investigated the antibacterial action of synthesized triazole ligands and their transition metal complexes on five bacterial strains. The ligands were prepared by condensation reaction using equimolar amounts of 3,5-diamino-1,2,4-triazole and 2,4-dihydroxybenzaldehyde, respectively. The study confirmed the synthesis of the Schiff base and the coordination of ligands with the metals. The fluorescence properties of Schiff bases and their derived metal complexes were also investigated.



M= Cr, Mn, Fe, Co, Ni, Cu, Zn X = CH_3COO^- R_1= H, OCH_3 R_2 = OH , H

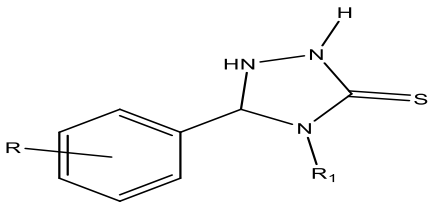
II. ***Aarjane, M et al in 2021*** create new antibiotics with antibacterial properties, specifically 1,2,3-triazole derivatives from acridone. The synthetic approach involves preparing the acridone skeleton, functionalizing the nucleus with propargyl bromide, and clicking the reaction with aromatic azides. The compounds were tested for their antibacterial activity against Staphylococcus aureus and three gram-negative bacteria. The most potent inhibitory activity was found in 2-methyl-10-((1-(o-tolyl)-1H-1,2,3-triazol-4-yl)me (4e). In silico molecular docking and ADMET prediction studies were performed to rationalize the results. The compounds were synthesized using a mixture of aniline, o-bromobenzoic acid, anhydrous potassium carbonate, metallic copper powder, and copper oxide. The study contributes to understanding acridone's potential for cancer treatment and developing novel isoxazole derivatives.



R_1= H, CH_3 R_2 = COOH, CH_3 R_3 = CH_3, H. R_4= COOH, H

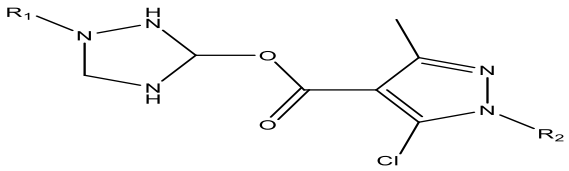
III. ***Kosikowska, U et al in 2020*** developed a library of ortho-, meta-, and para-fluorobenzoylthiosemicarbazides and their cyclic analogues with a 1,2,4-triazole scaffold for antibacterial activity against Gram-positive bacteria strains. The

antibacterial response of these compounds was highly dependent on substitution patterns at the N4 aryl position. The optimum activity for these compounds was found for trifluoromethyl derivatives, such as 15a,15b, and16b, which were active against both the reference strains panel and pathogenic methicillin-sensitive and methicillin-resistant Staphylococcus aureusclinical isolates at minimal inhibitory concentrations (MICs) ranging from 7.82 to 31.25µg/mL. The study also investigated the antibacterial activity of various thiosemicarbazides, including meta electron-withdrawing substitutions, and found that the linear NH-NH-C(=S)-NH core is a key structural element for antibacterial activity.



R_1= Ph, 1-Naph, p-FPh, p-ClPh, m-CF_3Ph

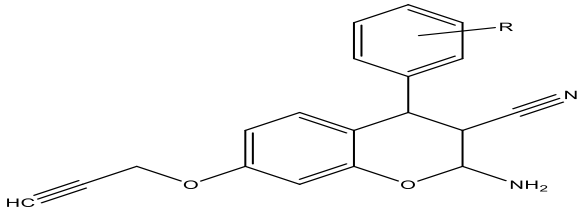
IV. ***In 2019, Chu, M et al*** synthesized novel triazole-containing pyrazole ester derivatives to develop new antibacterial agents. Compound4d showed the most potent antibacterial activity against Staphylococcus aureus, Listeria monocytogenes, Escherichia coli, and Salmonella gallinarum. The study focused on compounds 4d, 4g, and 4k, with Compound 4d showing more potent inhibition against DNA gyrase and topoisomerase IV enzymes. Recent developments in anticancer amonafide derivatives have shown promising potential for treating various diseases, including cancer, atopic dermatitis, and bacterial infections.



R_1= H, F, Cl, CH_3

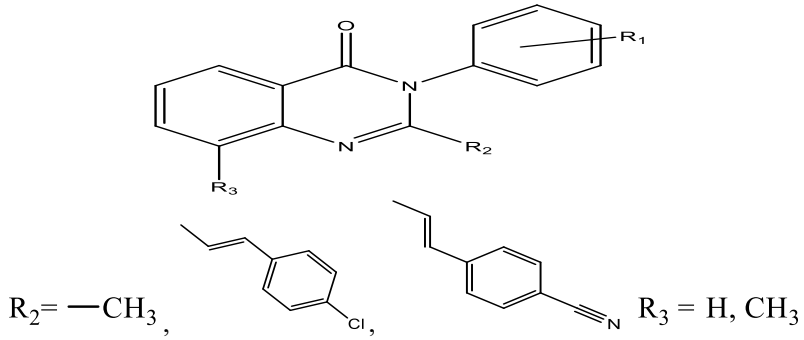
R_2 = H, F, Cl, CH_3

V. ***Thanh, N. D et al in 2019*** developed 1H-1,2,3-triazole-tethered 4H-chromene-3-d-glucose conjugates with antibacterial, MRSA, and antifungal activities, yielding 80-97.8% yields.



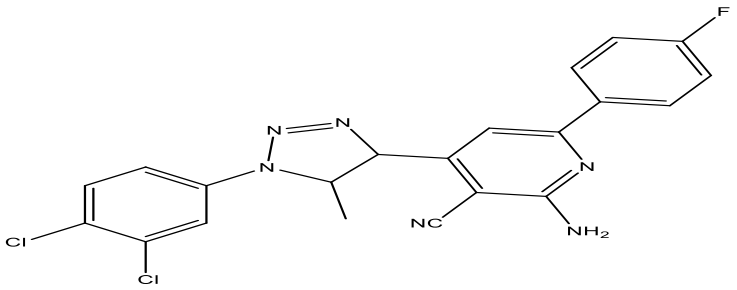
R= H, 4-NO_2, 3-NO_2, 2',3'-diChloro, 4-OMe

VI. A study by***Gatadi, S et al in 2018*** found that 1,2,3-triazole linked 4(3H)-quinazolinones are potent antibacterial agents against multidrug-resistant Staphylococcus aureus. The compounds were designed and synthesized, with compounds 7a, 9a, 7b, 7c, 7e, 7f, 7g, 7h, 7i, 9a, 9c, 9d, and 9e exhibiting selective inhibitory activities against Staphylococcus aureus. The study emphasizes the need for new antibacterial agents to combat methicillin and vancomycin-resistant Staphylococcus aureus infections.

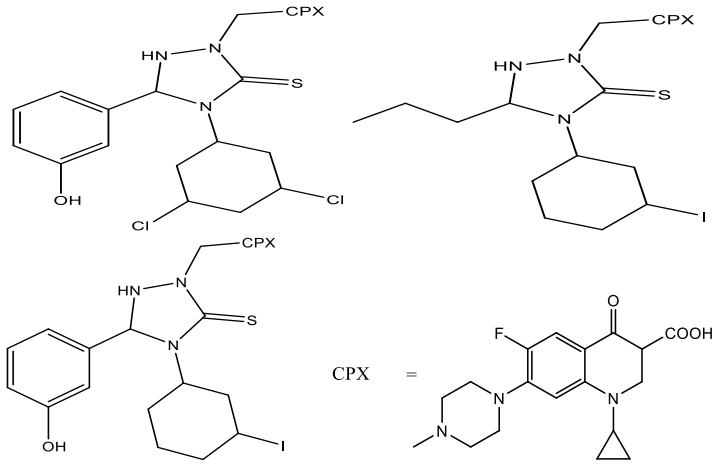


R_2= —CH_3, , R_3 = H, CH_3

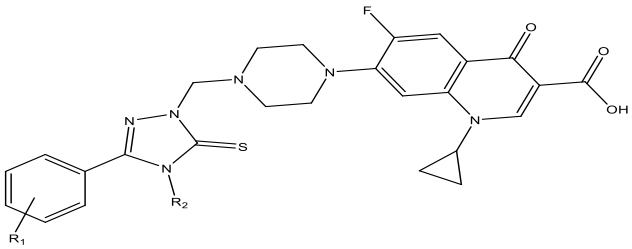
VII. ***Santosh, R et al in 2018*** study published in ChemistrySelect explored the synthesis, scharacterization, and antibacterial and antioxidant properties of heterocyclic compounds from triazole-linked chalcone derivatives. They discovered a promising antimicrobial molecule and modified it to create new antibacterial and antioxidant chemicals. The study also tested DNA binding and docking site interaction, suggesting these compounds could be used for developing new antibiotics.



VIII. ***Plech, T et al in 2015*** A series of 1,2,4-triazole-based compounds were designed as potential antibacterial agents using a molecular hybridization approach. The target compounds were synthesized by the Mannich reaction of 1,2,4-triazole-3-thione derivatives with ciprofloxacin (CPX) and formaldehyde. The potent antibacterial effect on Gram-positive bacteria was accompanied by similarly strong activity against Gram-negative strains. The toxicity of the CPX-triazole hybrids for bacterial cells was even up to 18930 times higher than the toxicity for human cells. The researchers aimed to trace the way in which further modification of the structure of the synthesized compounds affects the antibacterial activity and check whether there is an interrelation between the structure of the synthesized compounds and their toxicity for human cells. The newly obtained CPX-triazole hybrids were found to be much more potent than CPX itself in microbiological tests conducted on reference strains of Gram-positive and Gram-negative bacteria. The antibacterial activity of the CPX-triazole hybrids is not dependent solely on the degree of their affinity to DNA gyrase and topoisomerase IV.

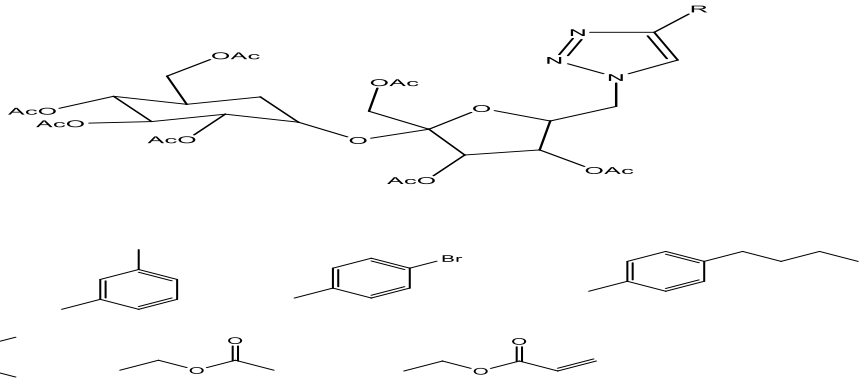


IX. ***Plech, T et al in 2015*** has synthesized and examined the antibacterial activity, toxicity, and affinity towards bacterial type II topoisomerases of 1,2,4-triazole-ciprofloxacin hybrids. The majority of novel hybrids were more active than the initial antibiotic, with enhanced antibacterial effects concerning both types of bacteria. The strongest inhibitory effect on P. aeruginosa was demonstrated by derivatives with the 2,4-disubstituted phenyl ring connected to the 1,2,4-triazole skeleton. Most of the synthesized compounds also demonstrated strong antibacterial effects against the remaining two Gram-negative strains. The study focuses on the antibacterial activity of newly synthesized compounds, specifically CPX-triazole hybrids, against Gram-positive bacteria and methicillin-resistant S. aureus (MRSA). The strongest antibacterial activity of the novel CPX derivatives cannot be attributed to the increased affinity towards bacterial type II topoisomerases. The study suggests that the increased antibacterial activity of the newly synthesized CPX-triazole hybrids is likely a result of various factors, including the change in affinity towards primary and secondary molecular targets.

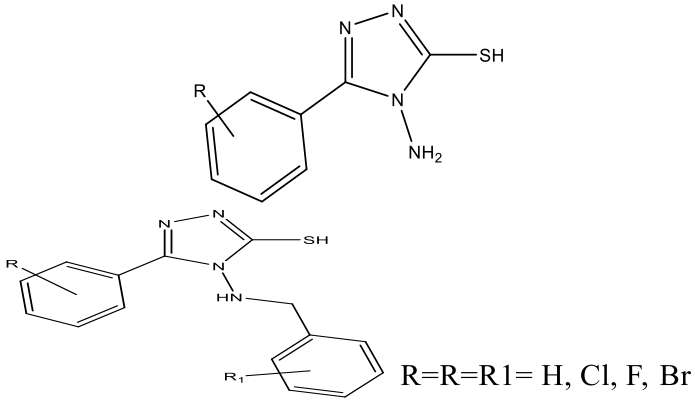


R1 =2-OH, 3-OH, 4-OH.
R2 = CYCLOHEXYL, 3,4-diCl-C6H3, 3-CF3,

X. ***Petrova, K. T et al in 2015*** A library of 1,2,3-triazole-sucrose derivatives was investigated for their antibacterial, antifungal, and cytotoxic activities. Most target compounds showed good inhibitory activity against various microbial pathogens, with 1-(1′,2,3,3′,4,4′,6-hepta-O-acetyl-6′-deoxy-sucros triazole (5) being highly active against all tested bacteria. Compound 3 showed moderate cytotoxicity against some tumor cell lines, but without toxicity for non-tumor liver cells. The compounds represent promising leads for the development of new generation sugar-triazole antifungal agents. The study focuses on the pharmacological properties of a compound and its potential applications in cancer treatment.

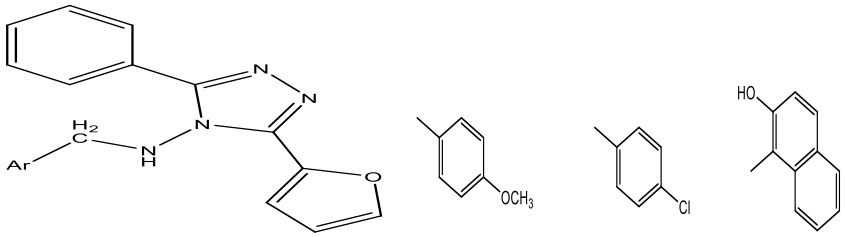


XI. ***Gupta, D., & Jain, D. K in 2015*** has synthesized a series of Schiff bases containing 1,2,4-triazole derivatives, which were tested for antifungal and antibacterial activity. The compounds showed strong antifungal effects against fungal species Microsporumgypseum and Staphylococcus aureus, with six showing superior antifungal activity to ketoconazole and one showing superior antibacterial activity to streptomycin. The study highlights the need for exploring these pharmacophores for developing novel molecules, such as triazole derivatives, which may be a safe antimicrobial agent.

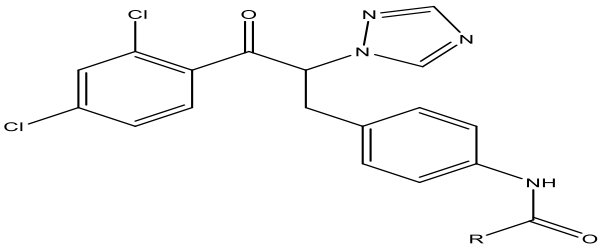


R=R=R1= H, Cl, F, Br

XII. ***Sokmen, B. B et at in 2015*** synthesized ethyl N′-furan-2-carbonylbenzohydrazonate, an acylhydrazone compound, by combining ethyl benzimidate hydrochloride with furan-2-carbohydrazide. The compounds were evaluated for their antibacterial, antiurease, and antioxidant activities. The compounds were found to inhibit urease and reduce infection stones in the urinary tract. The antioxidant activity of the compounds was found to be high, with Compound 3 having the best value. These compounds are suitable for pharmaceutical and agriculture industries.

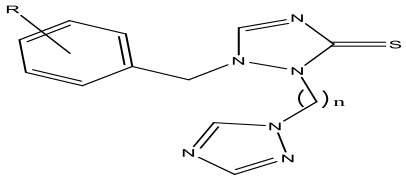


XIII. ***Tang, R et al in 2013*** have synthesized novel amide derivatives containing a triazole moiety to develop new bioactive molecules and pesticides against plant fungi and bacteria. The compounds exhibited moderate antifungal activity, with some showing more potent activity. Some compounds showed high antibacterial activity, with 71% and 65% inhibitory rates, respectively. Amide derivatives are a research hot spot in pesticide development due to their high-efficiency active features and broad spectrum bioactivities. Further studies are underway to establish a definite SAR for these compounds.



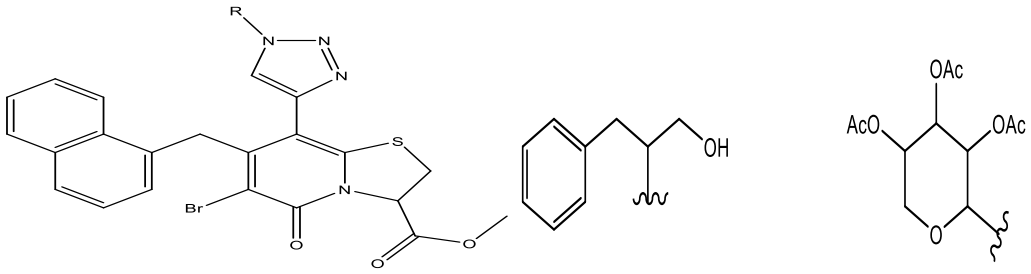
CH_3,OCH_3, NO_2, NH_2

XIV. **Wang, Q et al in 2012**synthesized novel thio-triazole derivatives, including thiols, thioethers, thiones, and triazolium compounds. These compounds were characterized using HNMR, CNMR, FTIR MS, and HRMS spectra. They were tested against Gram-positive, Gram-negative, and two fungi, with 3,4-dichlorobenzyl triazole-thione and its triazolium derivatives showing the most potent activity.

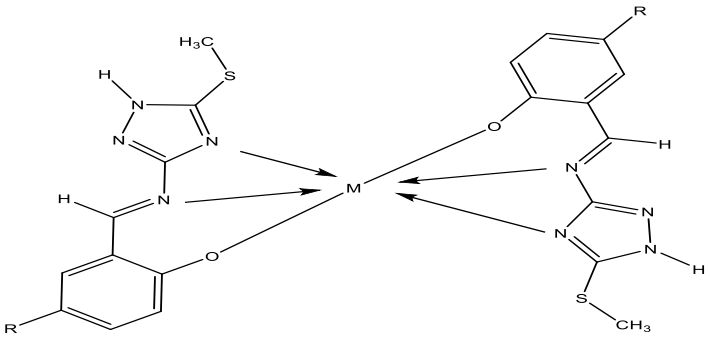


R = Cl, F, 3,4-diCl, 2,4-diF n =2, 4,,6,8

XV. ***Bengtsson, C et al in 2012*** have developed a method to introduce triazoles in position 8 and 2 of ring-fused bicyclic 2-pyridones as antibacterial agents. The method was developed through Sonogashira couplings followed by Huisgen 1,3-dipolar cycloadditions. The researchers tested twenty-four candidates, most of which showed low to no activity. Three compounds, one 8-substituted and two 2-substituted, showed promising activities with EC50 values between 9 and 50mM. The study aims to develop new antibacterial agents that inhibit pilus assembly, an important virulence factor for bacteria. The efficacy of the compounds depends on their direct interaction with the target and their ability to enter the bacteria. The best pilicide was 7g, active in the lower mM range. Further fine-tuning of the substitution pattern in this position could result in more potent pilicides.

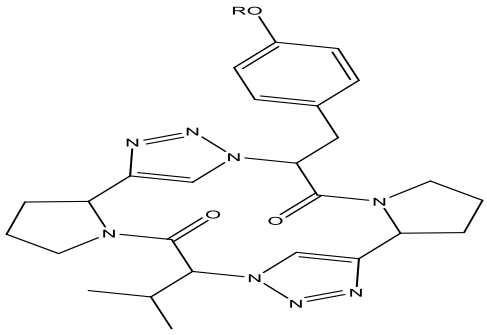


XVI. ***Chohan, Z. H et al in 2012*** a new class of Schiff base derivatives and their cobalt, nickel, copper, and zinc metal chelates have been synthesized and investigated for in vitro antibacterial activity against four Gram-negative and two Gram-positive bacterial strains, and antifungal activity against six fungal strains. The study outlines a procedure for synthesizing complexes, including cobalt(II) complexes with 2-[(E)-{[5- (methylsulfanyl)-1H-1,2,4-triazol-3-yl]imino}methy (l). The ligands were prepared by reacting 3-amino-5-methylthio-1H-1,2,4-triazole with chloro-, bromo-, and nitro-substituted 2-hydroxybenzaldehyde under reflux. The metal(II) complexes were found to be more potent against bacterial and fungal species than the parent Schiff bases. The antibacterial activity data of newly synthesized Schiff bases and their corresponding metal(II) complexes were determined against various bacterial strains.



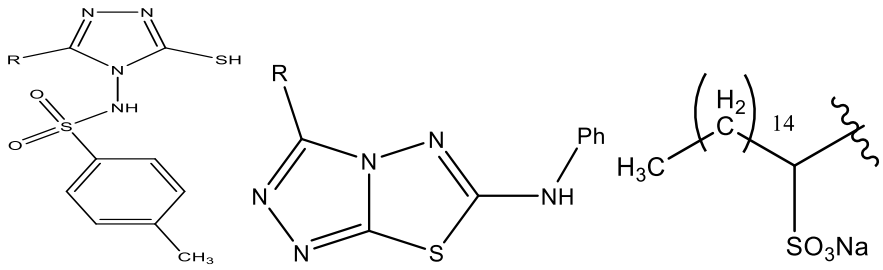
R = H, Cl, NO_2, Br M = Co (II), Ni(II), Cu(II)

XVII. ***Bock, V. D in 2007*** has reported the synthesis of triazole-containing analogues of the naturally occurring tyrosinase inhibitorcyclo-[Pro-Val-Pro-Tyr], demonstrating the effectiveness of a 1,4-connected 1,2,3-triazole as a transpeptide bond isostere. The study also focuses on the synthesis of two other triazole analogues and compares their inhibitory activity to the natural cyclotetrapeptide. The researchers used a modular approach to prepare azido alkyne linear precursors, which were then converted into cyclotetrapeptide analogues. The study provides the strongest evidence to date that 1,4-disubstituted 1,2,3-triazoles can serve as transoid amide bond mimics in natural compounds without compromising biological activity.

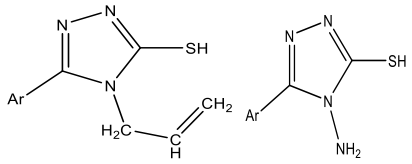


R = Bn, H

XVIII. ***El-Sayed, R in 2006*** explores the use of sodium 1-(4-amino-5-mercapto-4H-[1,2,4]triazol-3-yl) and heptadecane-1-sulfonate (2) as precursors for synthesizing biologically active heterocycles. The reactions yielded 1,2,4-triazole derivatives with antimicrobial activity and surface active agents. The preparation of Schiff bases and their derivatives was also studied. The synthesis of sodium triazole-1-sulfonate yielded various properties, including a long alkyl chain and a sulfonic acid hydrophilic center. The compounds have pronounced surface activity, with compounds 2, 6, 7, 12, and 13 being highly active against selected pathogens. The study highlights the potential of these anionic surfactants in the textile industry and their applications in dye baths and emulsion paints.

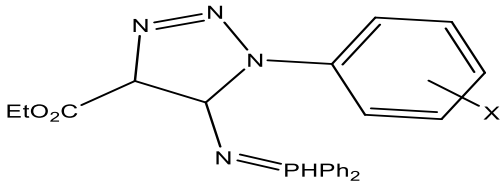


XIX. ***Colanceska-Ragenovic, K et al in 2001*** investigates the antibacterial and antifungal properties of 4-substituted-5-Aryl-1,2,4-triazoles, testing their effectiveness against bacteria and using various spectral data. Compounds with free NH 2 groups showed the most inhibitory effect.



2-OH-C_6H_4, 4-OH-C_6H_4, 2-OH-5-Cl-C_6H_3, 4-C_2H_5O-C_6H_4, 4-OH-C_6H_4-CH_2-

XX. ***Chen, M et al in 2000*** have developed new heterocyclic ß-enamino ester derivatives with 1,2,3-triazole, which are highly biologocal and pharmacologically valuable. These compounds are used in research on viruses, inflammation, antishock, anesthesia, and antitumor and antimicrobial activity. The researchers prepared esters with a 1,2,3-triazole core, reducing the amino group's activity. They also created new iminophosphoranes with better reactivity through the ester's reaction with triphenylphosphine. The results showed that various bacteria propagation was inhibited in varying degrees, with weak inhibitory action of other compounds. Further experiments on bacteria inhibition are currently in progress.



X = 4-F, p-OCH_2H_5, m-Br, m-NO_2, p-NO_2, p-Cl, p-CH_3, p-OCH_3, p-$COCH_3$

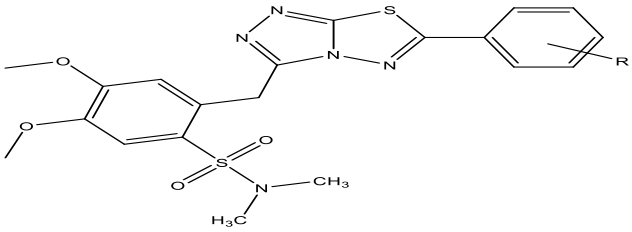
7. TRIAZOLOTHIAZOLE

Medicinal chemists and drug developers have displayed significant interest in triazolothiadiazole, a fused heterocyclic compound that incorporates both triazole and thiadiazole groups. This introduction explores the growing interest among researchers in triazolothiadiazole, its role as a biologically active component for various diseases, its antibacterial properties with structure-activity relationships (SAR), the specific substitutions that enhance its antibacterial activity, and provides examples of antibacterial drugs that incorporate this component.

Triazolothiadiazole has attracted the attention of researchers because of its unique structural features and possible pharmacological abilities. The presence of both triazole and thiadiazole components leads to the creation of triazolothiadiazole derivatives, which exhibit unique chemical and biological properties. Consequently, these molecules have demonstrated themselves to have intriguing medicinal potential. Researchers find triazolothiadiazole intriguing due to its potential as a versatile framework for creating bioactive molecules with diverse medicinal uses, such as antibiotics. Triazolothiadiazole exhibits a diverse range of biological activities and serves as an effective pharmacophore for treating many diseases. Triazolothiadiazole derivatives has the ability to exert pharmacological effects on various targets involved in different clinical conditions, depending on their chemical structure and substitution pattern. This category encompasses a wide range of traits, including antibacterial, anticancer, antiviral, anti-inflammatory, and anti-diabetic properties. Triazolothiadiazole derivatives have exhibited significant antibacterial efficacy against pathogenic bacteria, rendering them viable candidates for the development of antibacterial pharmaceuticals. Studies on the structure-activity relationship (SAR) have revealed valuable information about the specific structural characteristics that enhance the antibacterial effectiveness and range of action of these compounds. Modifying the triazolothiadiazole ring structure at different positions can greatly affect the antibacterial properties of the molecule. Electron-donating or electron-withdrawing substituents placed strategically might potentially improve the effectiveness of antibacterial medicines by optimising interactions with bacterial targets and increasing the stability of compounds. Over the years, researchers have enhanced the antibacterial effectiveness of triazolothiadiazole derivatives by exploring various structural alterations. A significant association exists between increased antibacterial effectiveness and alterations that elevate the electron density of the molecule or introduce functional groups capable of generating advantageous interactions with bacterial targets.

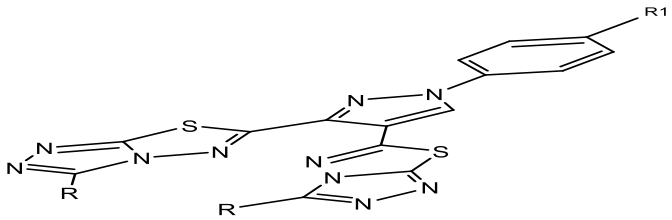
Additionally, it is possible that alterations aimed at improving the drug's solubility, bioavailability, and metabolic stability might potentially lead to an augmentation in its antibacterial efficacy. The triazolothiadiazole moiety is a crucial pharmacophore that is employed in the chemical composition of several antibacterial medicines. An example of a widely recognised antibiotic is ceftriaxone, which is classified as a third-generation cephalosporin. The antibacterial activity of ceftriaxone is enhanced by the presence of a triazolothiadiazole ring structure. This structure inhibits the synthesis of bacterial cell walls. In summary, triazolothiadiazole is a potential pharmacophore that might be employed in the creation of potent antibacterial drugs with a wide range of effectiveness. Its particular structural properties, diverse pharmacological action, and potential for structural optimisation make it an appealing candidate for the discovery and development of antibacterial medicines. The researchers want to explore the complete therapeutic capabilities of triazolothiadiazole derivatives and tackle the increasing difficulties posed by bacterial illnesses and antibiotic resistance. Their objective is to do this by acquiring a more profound understanding of the relationship between structure and action, and by investigating innovative chemical changes.

I. ***Kamoutsis, C et a in 2021*** examines the antimicrobial properties of nineteen synthesized 3,6-disubstituted-1,2,4-triazolo[3,4-b]-1,3,4-thia derivatives against bacteria, resistant strains, and fungi. The compounds showed more potent activity than ampicillin and streptomycin, with compounds 2 to 19 showing higher antibiofilm activity.



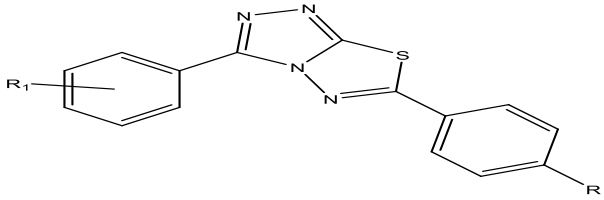
R = NH_2, OCH_3, Br, OH, NO_2, CH_3

II. ***Asma, Kalluraya, B et al in 2018*** investigates the synthesis, antimicrobial, antioxidant, and molecular docking of bis-1,2,4-triazolo[3,4-b]-1,3,4-thiadiazoles derived from aryl sydnones. Pyrazole derivatives exhibit various biological activities, including antibacterial, antiviral, anticancer, anti-inflammatory, antidiabetic, anti-depressant, antioxidant, antitubercular, and antihypertensive properties.



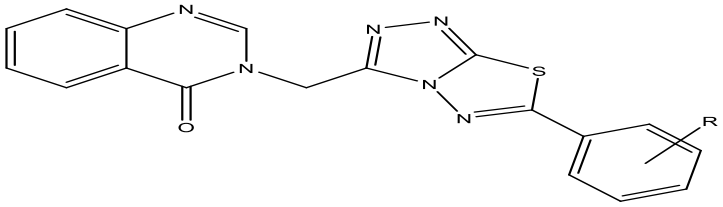
R = H, CH_3, OCH_3 R_1= CH_3, C_2H_5

III. ***Lin Lu et al in 2017*** investigates the synthesis and biological activities of twelve novel triazolothiadiazole derivatives, synthesized from 4-amino-5-substituted-4H-1,2,4-triazole-3-thiols with aromatic carboxylic acids. The compounds were tested against Escherichia coli, Staphylococcus aureus, Pyricularia oryzae, and Rhizoctniasolani using the disc diffusion method, with compounds 2e and 2k showing excellent antibacterial and antifungal activities.



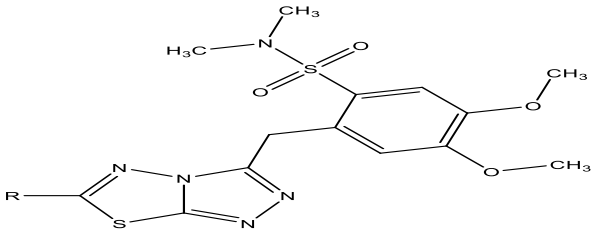
R_1 = 2-Cl, 2-F, 4-Cl, 4-F R = H, NO_2, $(CH_3)_3$

IV. ***Lv, X et al in 2017*** investigates the synthesis and antimicrobial properties of new quinazolin-4(3H)-one derivatives (6a-6y) with a 1,2,4-triazolo[3,4-b][1,3,4]thiadiazole moiety. Results show compounds 6h, 6k, and 6land6y have better EC50 values against phytopathogenic bacterium Xanthomonas oryzae than commercial bactericide Bismerthiazol.

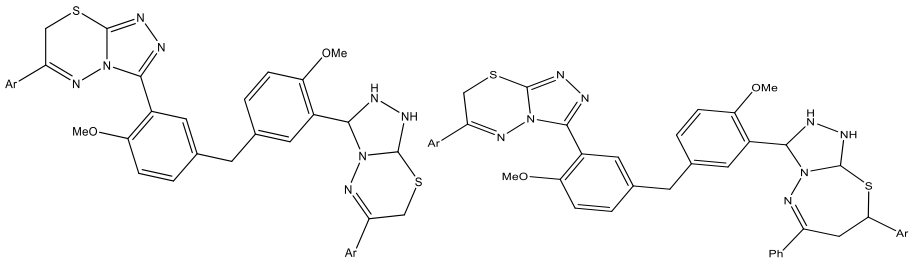


R = H, Cl, F, NO_2, NH_2, OH, OCH_3

V. ***Charitos, G et al. in 2016*** have developed new antitumor agents, specifically 3,6-disubstituted 1,2,4-triazolo-[3,4-b]-1,3,4-thiadiazole derivatives, which showed substantial cytostatic and cytotoxic antineoplastic activity in vitro and low acute toxicities in vivo. In silico screening identified protein targets like apoptotic protease-activating factor 1 and tyrosine-protein kinase HCK.

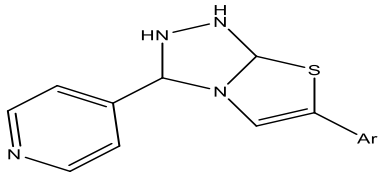


VI. ***Srinivas, A in 2016*** study investigates the synthesis and antimicrobial properties of bis[4-methoxy-3-(6-aryl-7H-[1,2,4]triazolo[3,4-b]] and bis[(triazolo[3,4-b]thiadiazepin-3-yl)phenyl]metha (5a–e and 6a–e) compounds. It tests their antibacterial and antifungal properties against bacteria and fungi. The compounds showed potent activity, indicating potential for further development. The synthesis of bis(4-methoxy-3-(6,8-diphenyl)-7,8-dihydro[[1,3,4 thiadiazepin-3-yl)phenyl] methanes (6a) was successful, yielding 72%.



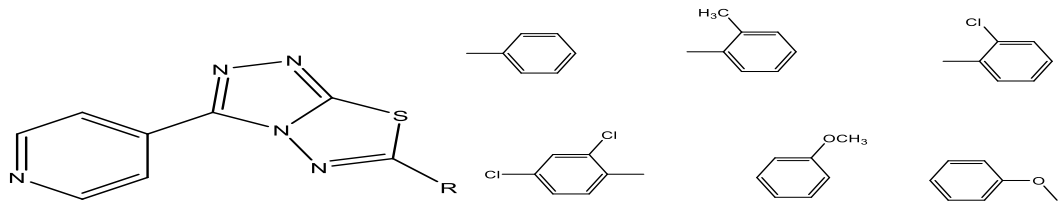
C_6H_5, 4-MeO-C_6H_4, 4-OH-C_6H_3

VII. ***Khan, I et al in 2014*** synthesized conjugated heterocycles using cyclocondensation reactions, characterized by various methods. Most compounds showed good to excellent activity against acetylcholinesterase, with Compound5d showing IC50 values of 0.77-0.08mM. These compounds were tested for anticancer activity against lung carcinoma, kidney fibroblast, and leishmanias.

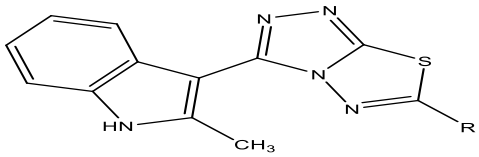


Ar = 2-F-4-Cl-C_6H_3, 3-Cl-4-F-C_6H_3, 2-CH_3-3-FURYL

VIII. ***Gilani, S. J et al in 2011*** investigates the development of antimicrobials that inhibit bacteria's growth and multiplication, making them effective in treating infectious diseases. Researchers synthesized hybrid compounds combining isoniazid and heterocyclic ring systems, revealing moderate antimicrobial activity against all tested pathogenic bacterial and fungal strains. The compounds' purity was confirmed through TLC and elemental analysis.

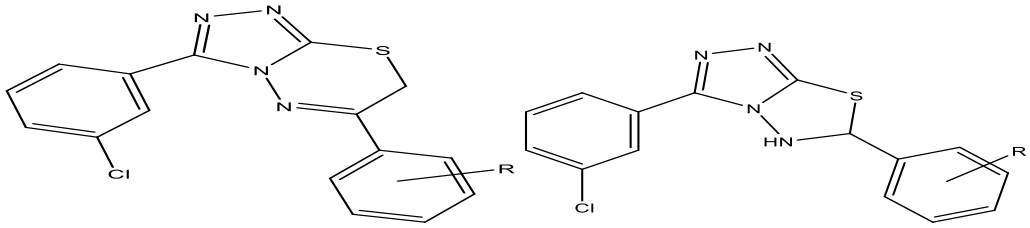


IX. ***Gomha, S. M., & Riyadh, S. M et al in 2011*** investigates the synthesis of novel compounds, specifically 3-(2-methyl-1H-indol-3-yl)-6-aryl-triazolo[5a,b], which are potent antioxidants, anticancer agents, antifungal, and antibacterial agents. Researchers used microwave irradiation to create new compounds with indole moieties, attracting interest for their antioxidant and anticancer properties.



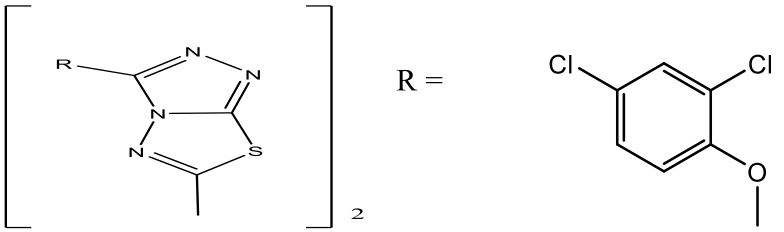
R = C_6H_5, 4-CH_3-C_6H_4

X. ***Purohit, D. H et al in 2010*** studied the synthesis and antimicrobial activity of new 1,3,4-Thiadiazoles and 1,3,4-Thiadiazines with 1,2,4-triazolo nucleus. These compounds, known for their potent antimicrobial, anticonvulsant, antiidepressant, antihypertensive, antitumorial, and anti-inflammatory properties, were synthesized using dry DMF

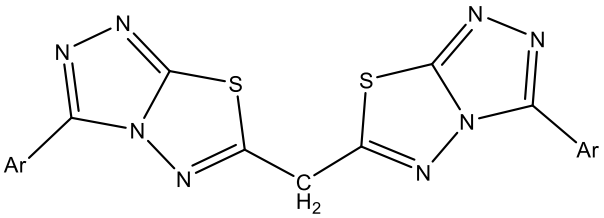


R = C_6H_5, 4-OCH_3-C_6H_4, 2,4-$(CH_3)_2$-C_6H_3, 2-OH-C_6H_4, 3-NO_2-C_6H_4

XI. ***Shehry, M. F. E et al in 2010*** investigates the use of 1,2,4-triazoles with a (2,4-dichlorophenoxy) moiety as chemical therapeutic agents. The compounds were prepared using a condensation method and analyzed using spectral, IR, and 1H NMR data. They showed promising toxicity against Biomphalariaalexandrinas snails.



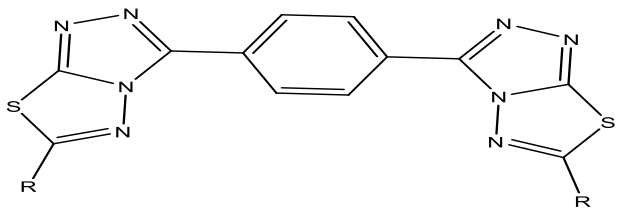
XII. ***Li, D. J., & Fub, H. Q in 2007*** have synthesized fifteen new compounds, including l,7-bis[(3-aryl)-1,2,4-triazolo[3,4-0]-[l,3,4]thiaheptanes], which were tested for their antibacterial properties against E. coli, S. aureus, and B. subtilis using the cup-plate method. The study offers insights into potential applications in cancer treatment, fungicidal activities, and anticancer properties.



Ar = Ph, 2-Cl-Ph, 3-Cl-Ph, 2-CH_3-Ph, 4-CH_3-Ph, 3-Br-Ph, 4-OCH_3-Ph

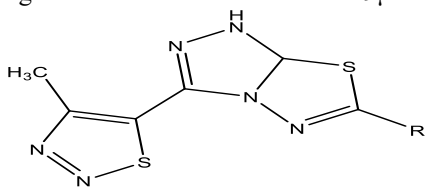
XIII. ***Palekar, V. S et al in 2009*** study explores the synthesis and antibacterial properties of bis-1,2,4-triazolo[3,4-b]-1,3,4-thiadiazoles and bis-4-thiazolidinone derivatives from terephthalic dihydrazide, a thermoplastic polyester used in textile

apparel, photographic films, and soft drink bottles. The five-membered heterocyclic compounds showed good antibacterial activity against all strains, while compounds 2b showed higher activity against E. coli and B. cereus.



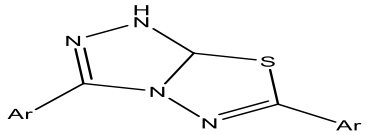
2-Cl-C_6H_4, 4-NO_2-C_6H_4

XIV. ***Fan, Z et al in 2010*** investigates the synthesis, crystal structure, and biological activity of 4-Methyl-1,2,3-thiadiazole-containing 1,2,4-triazolo[3,4-b][1,3,4]-thiadiazoles. Heterocyclic compounds are essential in agrochemicals. The study synthesized 6-substituted 3-(4-methyl-1,2,3-thiadiazolyl)[1,2] using bioactive substructure combinations. The crystal structure of 3-(4-Methyl-1,2,3-thiadiazolyl)-6-(4-methylphenyl) was determined using X-ray diffraction crystallography. The study found growth inhibition against fungi, with median effective concentrations ranging from 7.28μmol/L against Pellicullariasasakii to 42.49μmol/L against Alternaria solani



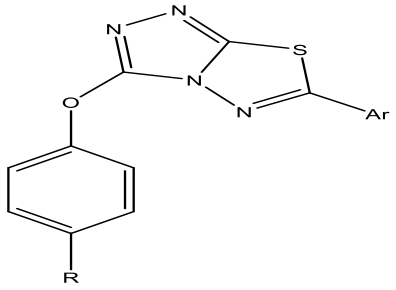
R = $C(CH_3)_3$, 2-Furyl, 4-pyridyl, N-methyl-5-ethyl-3-pyrazolyl

XV. ***Mathew, V et al in 2006*** study aims to create new therapeutic and antimicrobial agents by synthesizing heterocyclic compounds with four five-membered rings, specifically dioxymethylene A7-A18. The process involves a nucleophilic substitution reaction between dimethyl 5-yl-isophthalate and 1,2-dibromomethan, with sodium carbonate as a catalyst. The resulting compound A3-A6 is prepared by refluxing A2 with various 4-substitutedphenyl isothiocyanates in ethanol.



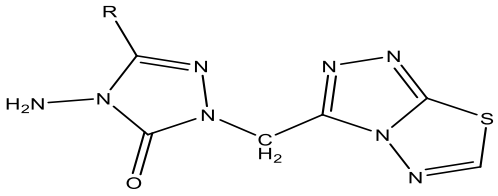
Ar = 4-OCH_3-Ph, CH_3-Ph, Cl-Ph

XVI. ***Karabasanagouda, T et al in 2007*** study investigates the synthesis and antimicrobial properties of three novel 1,2,4-triazolo[3,4-b]-1,3,4-thiadiazoles and 1,2,4-triazolo[3,4-b]-1,3,4-thiadiazines, created from 4-thioalkyl phenols through a multi-step reaction sequence. Compounds 1aebreacted with ethyl chloroacetate, 2aeb were oxidized to [4-(methyl sulphonyl) phenoxy] acetate, and 2aeb were treated with carbon disulphide and methanolic potassium hydroxide to yield corresponding potassium dithiocarbazates.



R = SCH_3, SC_2H_5, SO_2, CH_3 Ar = C_6H_5, 2-Cl-C_6H_4, 4-CH_3-C_6H_4, 4-OCH_3-C_6H_4, 4-NH_2-C_6H_4

XVII. ***Demirbaş, N et al in 2005*** study investigates the synthesis and antimicrobial properties of new quinazolin-4(3H)-one derivatives (6a-6y) with a 1,2,4-triazolo[3,4-b][1,3,4]thiadiazole moiety. Results show compounds 6h, 6k, and 6land6y have better EC50 values against phytopathogenic bacterium Xanthomonas oryzae than commercial bactericide Bismerthiazol.



CH_3, $CH_2C_6H_5$, $CH_2C_6H_4Cl$, C_6H_5

CONCLUSION

In conclusion, the exploration of various moieties such as azetidinone, benzothiazole, naphthalene, thiadiazole, triazole, and triazolothiadiazole has emerged as a vital avenue in the development of new antibacterial medications. Each of these structural frameworks offers unique pharmacological properties and the potential for chemical modifications that can enhance their therapeutic efficacy. As antibiotic resistance continues to pose a significant global health challenge, understanding the structure-activity relationships of these compounds is crucial for optimizing their effectiveness against resistant bacterial strains. Continued research in this area holds promise for the discovery of novel antibacterial agents that can address the urgent need for effective treatments in the face of evolving microbial threats.

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