A Review on Pyridine–Sulphonamide Derivatives synthetic Approaches and Antimicrobial and Antimycobacterial Potential

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Abstract:

Drug-resistant diseases are increasing and need new and effective treatments. Drug discovery in medicinal chemistry has succeeded in combining a pyridine ring with a sulphonamide functionality. The pyridine ring interacts with biological targets. The sulphonamide group stabilizes, solubilizes and penetrates cells. They make a wide range of biologically active molecules. This review deals with recent synthetic methodologies, structural features and biological evaluations of simple and fused ring pyridine-sulphonyl amide derivatives. Emphasis is placed on the activity against Gram-positive and Gram-negative bacteria, pathogenic fungi, and Mycobacterium tuberculosis. This review covers recent synthetic methods, structural features, and biological evaluations of simple and fused-ring pyridine-sulphonamide derivatives. Their activity against harmful Gram-positive and Gram-negative bacteria, pathogenic fungi, and Mycobacterium tuberculosis is emphasized. The reviewed derivatives demonstrated promising antimicrobial activities, highlighting the potential of pyridine–sulphonamide hybrids as lead structures for further drug development.

1. Introduction:

Heterocyclic compounds constitute a major class of organic molecules in medicinal chemistry owing to their structural diversity and wide range of biological activities. (1) Heterocyclic scaffolds containing nitrogen, oxygen, or sulphur are found in numerous natural products, including nucleic acids, vitamins, alkaloids, and antibiotics, and are also integral components of many clinically important pharmaceutical agents. (2) Their ability to provide diverse electronic, steric, and hydrogen-bonding properties makes them valuable frameworks for designing and optimising biologically active molecules. (3)

Pyridine is a well-known nitrogen-containing heterocyclic scaffold in medicinal chemistry and is considered an important six-membered aromatic heterocycle. The nitrogen atom of the pyridine ring is more basic since it has a lone pair of electrons. This characteristic enables it to coordinate metal ions and to interact with biological species. (4) Furthermore, the pyridine scaffold are many more diverse substituents, thereby enabling the systematic modulating of the physicochemical and pharmacological properties of the resulting Moreover, the pyridine scaffold represents a convenient platform for the integration of different substituents, allowing a systematic fine-tuning of the physicochemical and pharmacological characteristics of the compounds thus obtained. The characteristics of pyridine have resulted in its widespread usage. (5)

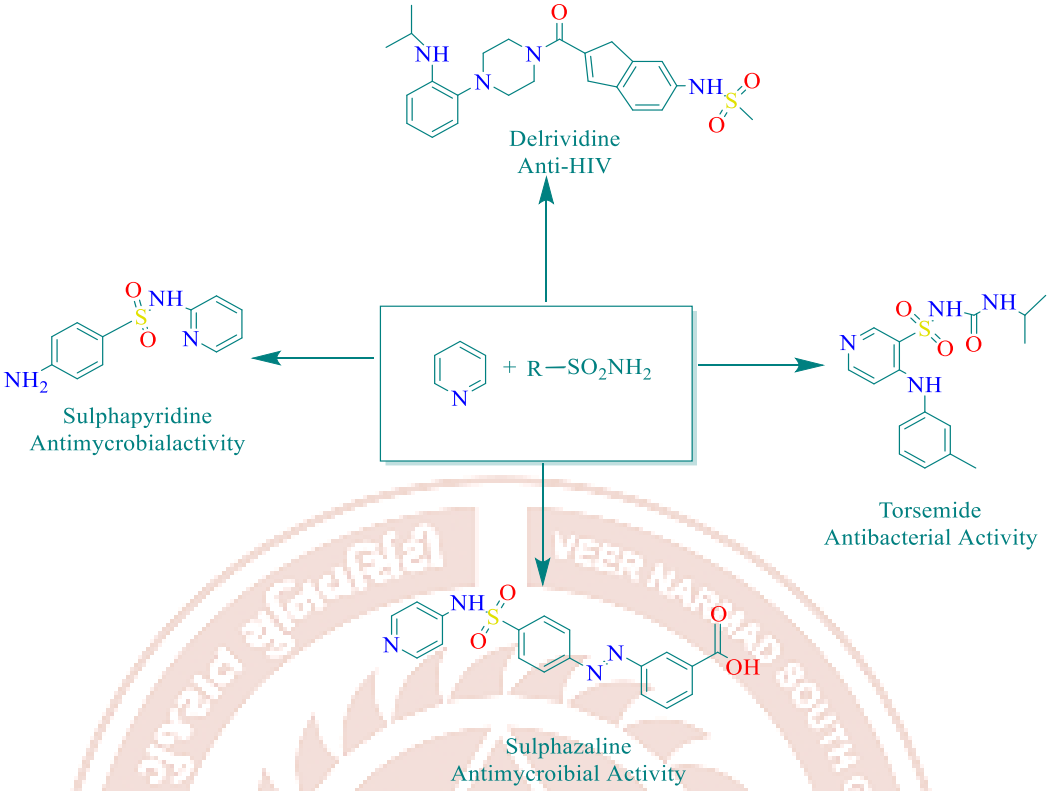
Sulphonamides are an interesting class of compounds which have been identified as important in medicinal chemistry. The sulphonamide functional group can take part in

hydrogen-bonding interactions and can have a major influence on the polarity, acidity, solubility and molecular recognition properties of a molecule. (6) Moreover, the modification of the sulphonamide nitrogen and the aromatic or heteroaromatic ring can affect lipophilicity, membrane permeability and biological activity. (7) Compounds bearing sulphonamide groups have found importance as scaffolds in the synthesis of antibacterial, antifungal, anti-inflammatory, anticancer and many other medicinal drugs. (8)

The combination of a pyridine core with a sulphonamide fragment is a promising approach to the design of structurally diverse and potentially bioactive compounds. The heteroaromatic nitrogen and the sulphonamide functional group may work in concert to provide enhanced or synergistic interactions with biological targets. (9) Besides, the change of the substitution pattern of the pyridine ring and the sulphonamide nitrogen provides an opportunity to investigate structure-activity relationships and enhance relevant physicochemical properties. Therefore, pyridine-based sulphonamides have gained considerable interest as potential antibacterial and antifungal agents. (10)

The increasing issue of antimicrobial resistance has led to an urgent need for the discovery of new and more effective antibacterial and antifungal medicines with beneficial pharmacological characteristics. (11) The synthesis of structurally modified heterocyclic compounds, particularly those bearing pharmacologically active functional groups, continues to be a major strategy in the development of new therapeutic agents. (12)

This review summarized of synthetic approaches, structural features, and biological activities of pyridine–sulphonamide derivatives were designed and synthesised, and their structures were characterised by appropriate spectroscopic and analytical techniques. The synthesised compounds were subsequently subjected to biological activity testing. The aim of this work was to investigate the pyridine sulphonamide scaffold as a source of new bioactive molecules and to study the effect of structural modification on their biological properties. (13)



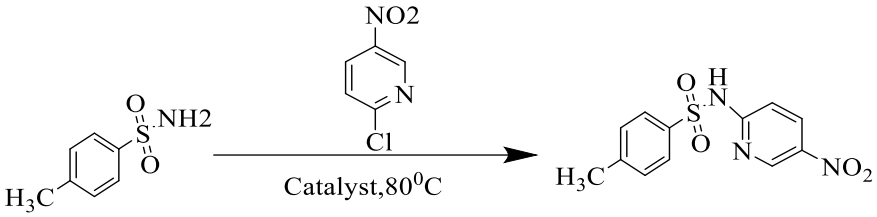
Currently in use Pyridine containing Sulpha drugs (Fig .1)

2. Synthesis, Biological Activities, and Structure–Activity Relationship

2.1 Antibacterial Activity

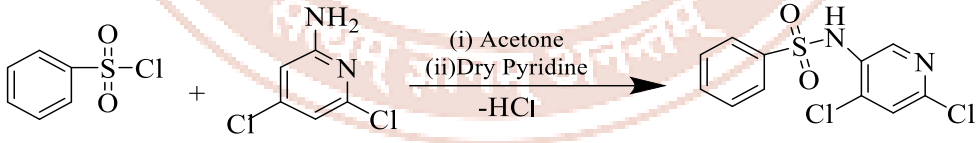
2.1.1 4-methyl-N-(5-nitropyridin-2-yl)benzene sulphonamide

Ochu et al. reported 4-methyl-N-(5-nitropyridin-2-yl)benzene sulphonamide as a sulphonamide derivative having a pyridine moiety with significant a broad-spectrum activities. The synthesis was carried out first by preparing 4-methylbenzenesulphonamide from 4-methylbenzenesulphonyl chloride and then introducing the pyridine part by nickel-catalysed Buchwald–Hartwig coupling of the sulphonamide with 2-chloro-5-nitropyridine. The structure was characterised by FT-IR, ^{1}H NMR, ^{13}C NMR, and mass spectroscopy. The compound showed broad-spectrum antimicrobial activity against B. subtilis, S. aureus, P. aeruginosa, E. coli, C. albicans, and A. niger with MIC values of 1.6, 1.4, 1.7, 2.6, 0.6, and 0.9 mg/mL, respectively. The broad spectrum activity of this compound is mainly due to the nitro (-NO2) group at C-5 position of pyridine ring which is a strongly electron withdrawing group, increasing target interactions and its most active antibacterial and antifungal compound of series as a lead compound for further optimization. (14)



2.1.2 N-(2,6-dichloropyridin-4-yl) benzene sulphonamide

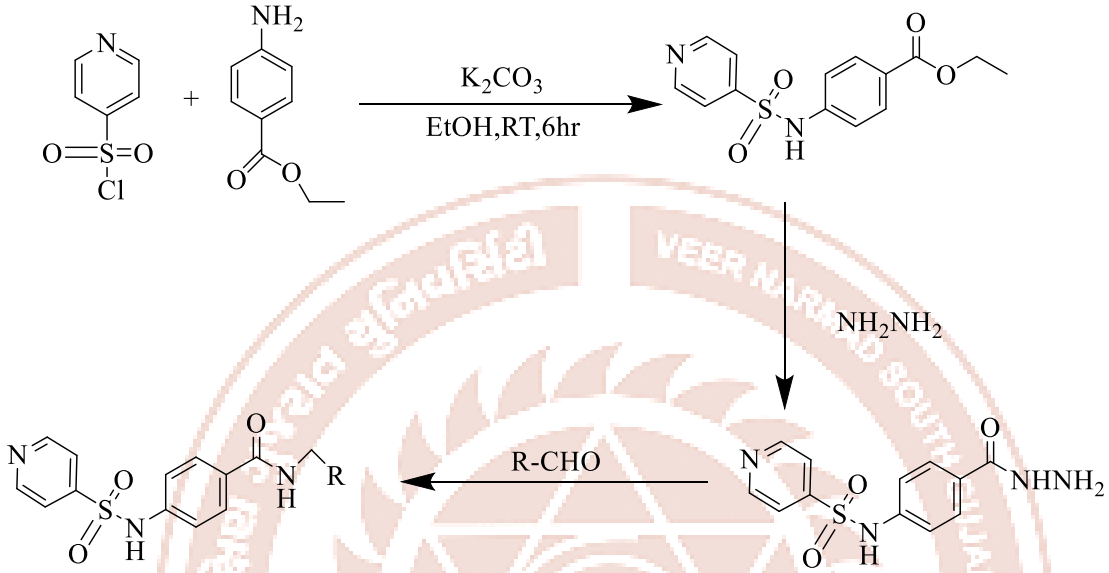
Igwe et.al reported sulphonamide derivative N-(2,6-dichloropyridin-4-yl)benzene sulphonamide possessing pyridine moiety which demonstrated significant antibacterial and antifungal activities. The compound was obtained by N-sulphonylation of 2,6-dichloropyridin-4-amine with benzene sulphonyl chloride in acetone in the presence of pyridine as base to give the corresponding N-heteroaryl sulphonamide. The FTIR, 1H NMR and 13C NMR spectroscopy was used to characterize the synthesized compound and confirmed the successful formation of the sulphonamide linkage and integrity of the heteroaromatic system. The compound was screened for activity against Bacillus cereus, Sarcina lutea, Pseudomonas aeruginosa, Escherichia coli, Salmonella typhi, Klebsiella pneumoniae, and the fungal strains Candida albicans and Aspergillus niger. Significant zones of inhibition of 27-28 mm were observed against B. cereus and S. lutea, respectively and 23-24 mm against P.eruginosa and K. pneumoniae. MIC values ranged from 0.0794 to 0.1950 mg/mL, with the highest potency against A. niger (0.0794 mg/mL). In SAR terms, the substitution of two lipophilic and electron withdrawing chlorine atoms at the C-2 and C-6 positions of the 4-aminopyridine nucleus greatly enhances the cellular permeability and target interactions, confirming the strong pharmacophoric potential of the di chloro pyridyl sulphonamide scaffolds as lead antimicrobial agents. (15)



2.1.3 (E)-N-(4-(2-(4-methoxy benzylidene)hydrazine carbonyl)phenyl)pyridine-4-sulphonamide

Shrivastava et al. reported a series of pyridine-4-sulphonamide Schiff bases such as (E)-N-(4-(2-(4-methoxybenzylidene)hydrazinecarbonyl)phenyl)pyridine-4-sulphonamide as potential antimicrobial agents. The compounds were prepared by condensation of the intermediate ethyl 4-(N-methylpyridine-4-sulphonamido)phenyl hydrazide with substituted aromatic aldehydes to give the characteristic azomethine (–C=N–) linkage. The structure of the target compound containing 4-methoxybenzylidene substituent was confirmed by FTIR, 1H NMR, 13C NMR, mass spectrometry and elemental analysis. The synthesized Schiff bases were screened for antimicrobial activity against

Staphylococcus aureus, Bacillus subtilis, Escherichia coli, Pseudomonas aeruginosa, Candida albicans and Aspergillus niger. Methoxy- and nitro-substituted derivatives outperformed bacteria against fungal strains. From an SAR perspective, the electron-donating methoxy group increases electron delocalization over the hydrazone–azomethine linker, improving membrane interaction and bioactivity. Consequently, the pyridine-sulphonamide Schiff base framework was identified as a viable and tunable pharmacophore for ongoing antimicrobial drug development [16].

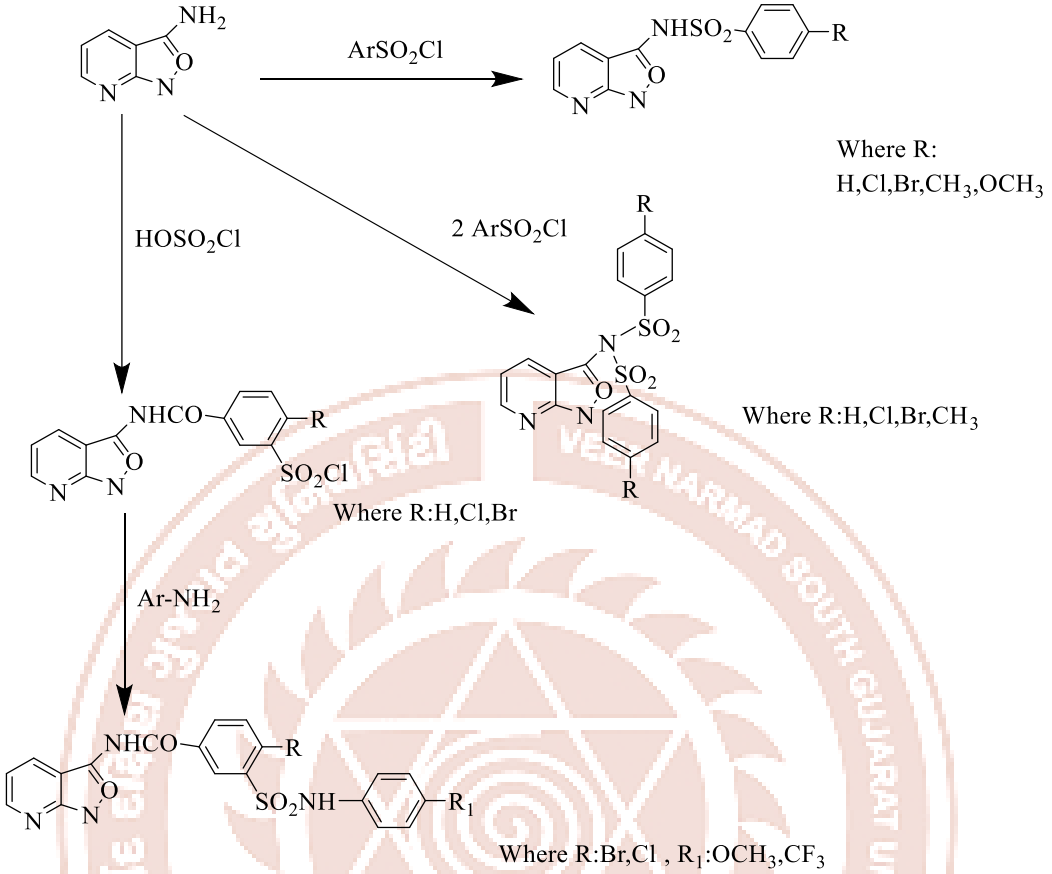


Where R: phenyl-78% ,Cl-phenyl-72%, OH-phenyl-75%, CH_3-phenyl-74.8%, NO_2-phenyl-73%,Br-phenyl-72.62%,CH_3O-phenyl-74.45%, $(CH_3)_2N$-phenyl-73%,Thiophene-76%, Furan-76%

2.1.4 N-Isoxazolo[5,4-b]pyridin-3-yl-4-methylbenzenesulphonamide

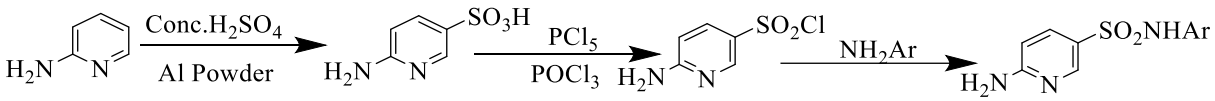
Poręba et al. described N-(isoxazolo[5,4-b]pyridin-3-yl)-4-methylbenzenesulphonamide, a pyridine-containing sulphonamide derivative, as an antibacterial and antiproliferative agent. The compound was prepared via sulphonylation of 3-aminoisoxazolo[5,4-b]pyridine with 4-methylbenzenesulphonyl chloride to produce the matching sulphonamide hybrid. We had a both traditional heating and microwave-assisted methods, the latter of which reduces reaction time and increases the yield dramatically. Antibacterial screening of N-(isoxazolo[5,4-b]pyridin-3-yl)-4-methylbenzenesulphonamide against Escherichia coli and Pseudomonas aeruginosa gave significant inhibition zones of 22 mm and 32 mm, respectively, at concentration of 500 µg/disc with minimum inhibitory concentration (MIC) of 44 µg/mL against P. aeruginosa. The derivative also shown relatively poor antiproliferative activity against MCF-7 breast cancer cell line (IC50 = 161.08 µg/mL after 72 h). From the structure–activity relationship (SAR) point of view, the annulation of the pyridine ring with an isoxazole heterocycle imparts the required structural rigidity and optimised lipophilicity to enable the specific interaction with bacterial cell wall with high

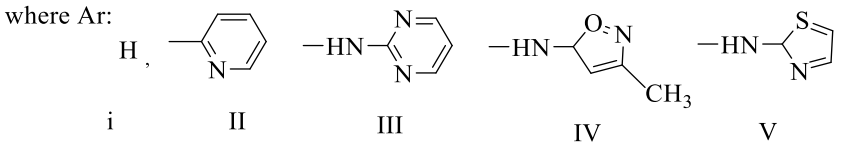
selectivity over mammalian cells and confirms this fused scaffold as an emerging platform for the development of antibacterial leads. (17)



2.1.5 N-(Pyridin-2-yl)-6-aminopyridine-3-sulphonamide

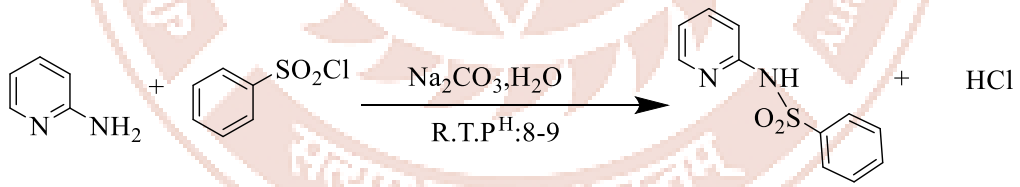
Singh et al. reported a new pyrido sulphonamide derivative N-(pyridin-2-yl)-6-aminopyridine-3-sulphonamide with good antibacterial activity. The synthesis was carried out by converting 2-aminopyridine to 6-aminopyridine-3-sulphonic acid, then the corresponding sulphonyl chloride, and finally reacting with a substituted amine to give the sulphonamide. The synthesized compound was characterized by IR, mass and 1H NMR spectroscopy. The antibacterial activity of N-(Pyridin-2-yl)-6-aminopyridine-3-sulphonamide was evaluated against Staphylococcus aureus, Escherichia coli, Bacillus subtilis and Pseudomonas aeruginosa by cup plate method. At 150 µg/mL, it produced inhibition zones of 20, 18, 26, and 30 mm, respectively. No activity was observed against Candida albicans. The results suggested that the incorporation of a heteroaromatic pyridine ring in the sulphonamide scaffold can improve antibacterial activity. (18)





2.1.6 N-(pyridin-2-yl)benzene sulphonamide

Ijeomah et.al reported the synthesis and antibacterial evaluation against N-(pyridin-2-yl)benzene sulphonamide. The compound was prepared by the reaction of benzene sulphonyl chloride with 2-aminopyridine in aqueous alkaline solution, using sodium carbonate. The UV-Vis, FTIR, 1H NMR and 13C NMR spectroscopy confirmed the successful sulphonamide linkage and synthesis of the molecule. Antibacterial activity was determined by agar-well diffusion method against the bacteria Staphylococcus aureus, Salmonella typhi and Escherichia coli with inhibition zones diameters of 21, 18 and 26 mm respectively. The inhibition zone against E. coli was 26 mm which was significantly higher than that of ciprofloxacin (16 mm) under the same experimental conditions. SAR analysis shows that directly attaching the sulphonamide moiety to the C-2 position of the simple pyridine ring maintains steric compactness and optimal target interaction, validating this scaffold as a useful structural template for developing potent antibacterial agents. (19)

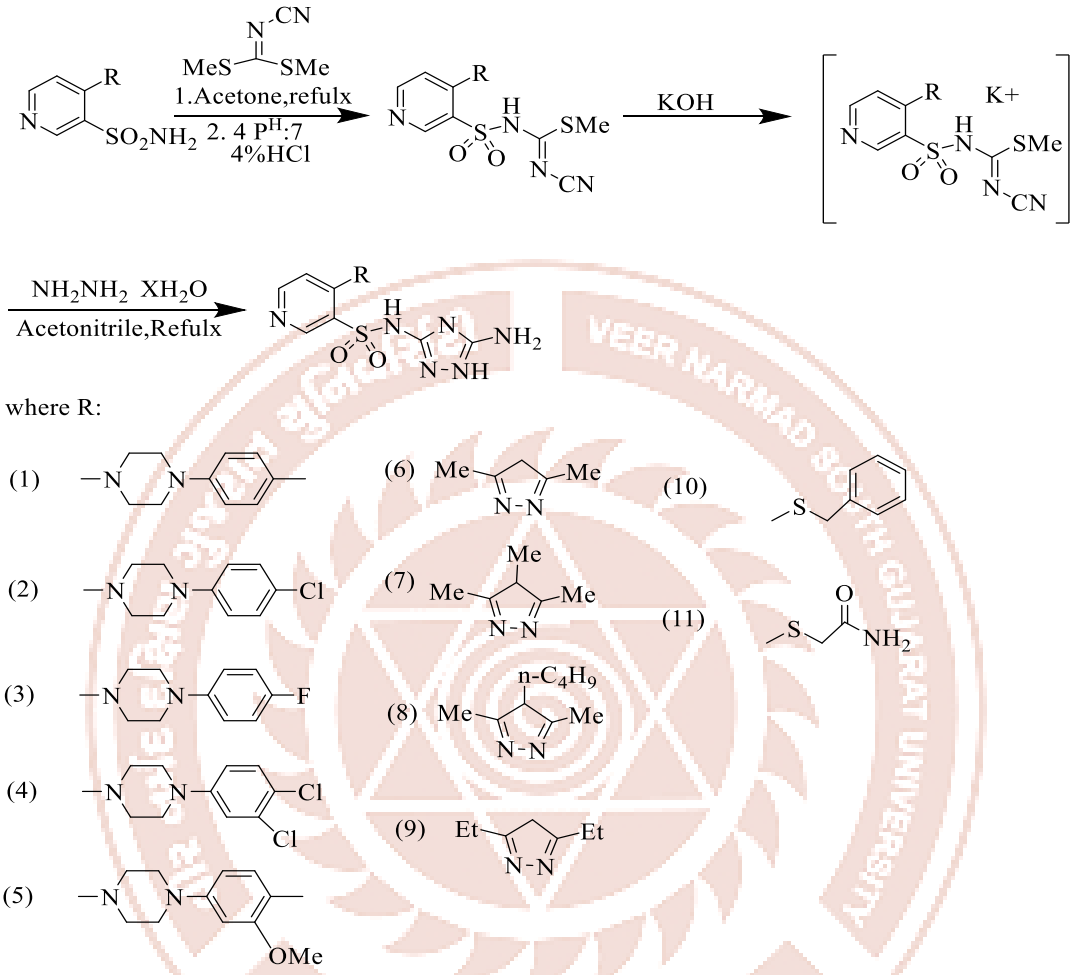


2.2 Antifungal Activity

2.2.1 4-(4-Phenylpiperazin-1-yl)-N-(5-amino-1H-1,2,4-triazol-3-yl)pyridine-3-sulphonamide.

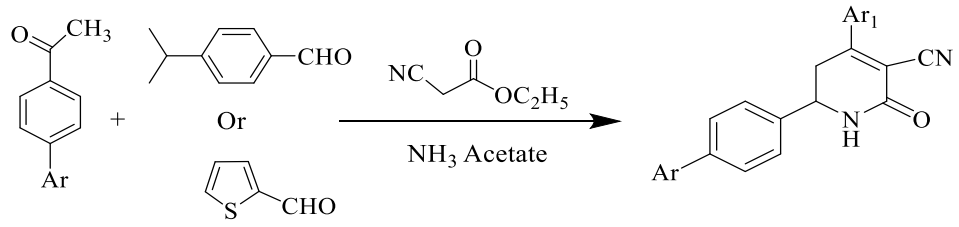
Szafrański et al. reported 4-(4-phenylpiperazin-1-yl)-N-(5-amino-1H-1,2,4-triazol-3-yl)pyridine-3-sulphonamide, a pyridine-3-sulphonamide derivative with promising antifungal activity. The compound was prepared through a multistep synthesis starting from 4-chloropyridine-3-sulphonamide, followed by the introduction of the substituted piperazine group and the conversion of the sulphonamide functionality to the corresponding 1,2,4-triazole derivative using hydrazine hydrate. 4-(4-Phenylpiperazin-1-yl)-N-(5-amino-1H-1,2,4-triazol-3-yl)pyridine-3-sulphonamide showed good activity against Candida albicans with MIC values

ranging from ≤6.2 to 100 µg/mL, and it also showed satisfactory activiagainst Rhodotorula mucilaginosa. Molecular docking against CYP51 had a binding energy of -9.9 kcal/mol, better than that of fluconazole (-8.1 kcal/mol). 4-(4-Phenylpiperazin-1-yl)-N-(5-amino-1H-1,2,4-triazol-3-yl)pyridine-3-sulphonamide. (20)



2.2.2 N-(4-(5-Cyano-6-(β-D-galactopyranosyloxy) -4-(thien-2-yl)-1,6-dihydropyridin-2-yl) phenyl)-4-methylbenzenesulphonamide.

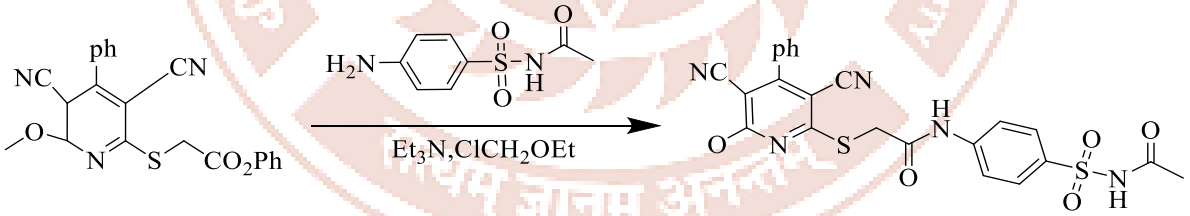
Moustafa et al. reported N-(4-(5-cyano-6-(β-D-galactopyranosyloxy)-4-(thien-2-yl)-1,6-dihydropyridin-2-yl)phenyl)-4-methylbenzenesulphonamide (a pyridone-sulphonamide glycoside with substantial antibacterial action). The synthesis consisted of glycosylation of a suitable 2-pyridonesulfonamide precursor with a protected galactopyranosyl bromide and subsequent deacetylation to get the free glycoside. N-(4-(5-Cyano-6-(b-D-galactopyranosyloxy)-4-(thien-2-yl)-1,6-dihydropyridin-2-yl)p-methylbenzenesulphonamide against S. aureus, S. epidermidis, E. coli, K. pneumoniae, and P. aeruginosa with zone of inhibition 21, 20, 16, 20, and 17 mm correspondingly at a dose of 300 µg. In addition, the compound shown has antifungal efficacy against C. albicans and A. niger with zones of inhibition of 20 mm and 21 mm, respectively. (21)



Ar = p-CH_3-C_6H_4-SO_2NH-;Ar_1 = p.$(CH_3)_2CH$-C_6H_4
Ar =p-CH_3-C_6H_4-SO_2NH-; Ar_1= thien-2-yl

2.2.3 N-[4-(N-Acetylsulfamoyl)phenyl]-2-[(3,5-dicyano-6-ethoxy-4-phenylpyridin-2yl)thio]acetamide.

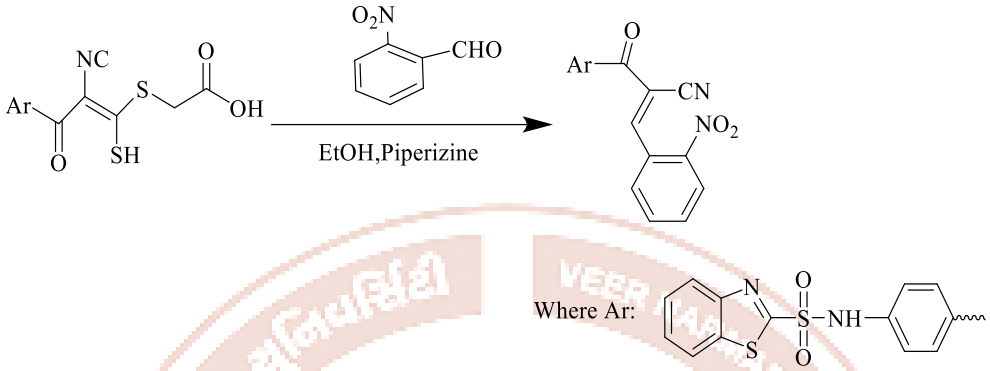
El-Sayed et al. reported that the pyridine-based sulphonamide derivative N-[4-(N-acetyl sulfamoyl) phenyl]-2-[(3,5-dicyano-6-ethoxy-4-phenylpyridin-2-yl)thio] acetamide exhibited significant antimicrobial activity. This compound was obtained from 2-[(3,5-dicyano-6-ethoxy-4-phenylpyridin-2-yl)thio]acetic acid by the reaction with the sulpha-drug sulpha acetamide in the presence of triethyl orthoformate and triethylamine. N-[4-(N-Acetylsulfamoyl)phenyl]-2-[(3,5-dicyano-6-ethoxy-4-phenylpyridin-2yl) thio] acetamide was active against S. aureus, B. cereus, E. coli, and P. aeruginosa with inhibition zones of 32, 33, 34, and 34 mm, respectively, at 300 µg/mL. Moreover, it exhibited antifungal activity against A. flavus and A. niger with inhibition zones of 32 and 24 mm, respectively. The authors reported that the antimicrobial activity was increased by the attachment of sulfa-drug moieties to the pyridine system (22).



2.2.4 N-(4-(2-Cyano-3-(2-nitrophenyl)acryloyl)phenyl)thiazolo[5,4-b]pyridine-2-sulphon -amide

Alenazi reported N-(4-(2-cyano-3-(2-nitrophenyl)acryloyl)phenyl)thiazolo[5,4-b]pyridine-2-sulphonamide as a novel pyridine-sulphonamide derivative with promising antimicrobial activity. The compound was synthesized by condensation of the cyanoacetyl sulphonamide intermediate 3 with 2-nitrobenzaldehyde in ethanol in the presence of piperidine, producing the corresponding cyano cinnamamide derivative. N-(4-(2-Cyano-3-(2-nitrophenyl)acryloyl)phenyl)thiazolo[5,4-b]pyridine-2-sulphonamide exhibited strong activity against Staphylococcus aureus, Escherichia coli and Candida albicans. It showed an MIC of

3.125 µg/mL against S. aureus, 6.25 µg/mL against E. coli, and 3.125 µg/mL against C. albicans, with inhibition zones reaching 46 mm against C. albicans. The authors identified N-(4-(2-Cyano-3-(2-nitrophenyl)acryloyl)phenyl)thiazolo[5,4-b]pyridine-2-sulphonamide as one of the most promising derivatives because of its low MIC, broad-spectrum activity and favourable interaction with the DHFR target. (23)



2.2.5 N-{4-[N-(4-methylpyrimidin-2-yl)sulphamoyl]phenyl}-2-{[4-(pyridin-4-ylamino) thiazol-2-yl]amino}acetamide

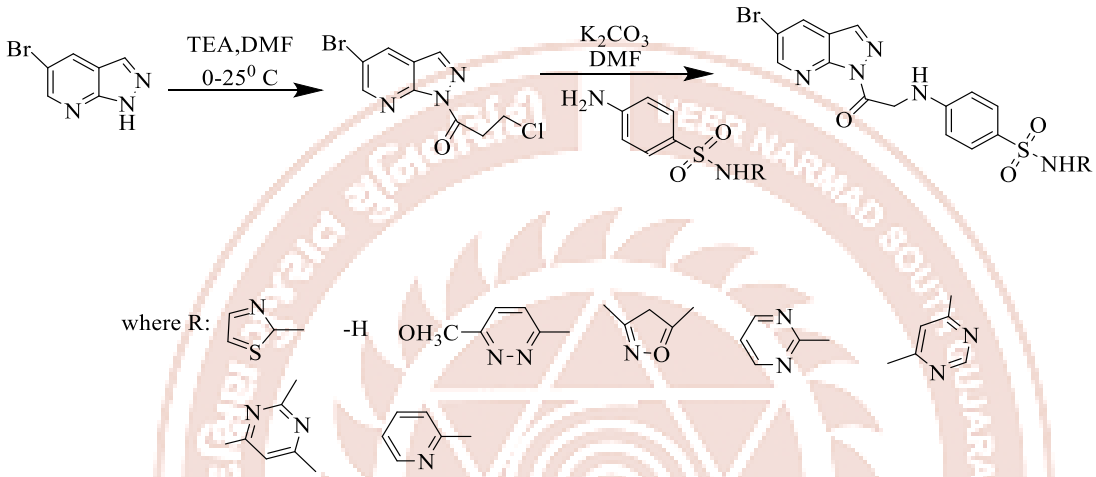
Raoof and Al-Azzawi et al. reported N-{4-[N-(4-methylpyrimidin-2-yl)sulphamoyl]phenyl}-2-{[4-(pyridin-4-ylamino)thiazol-2-yl]amino}acetamide as a novel pyridine–thiazole–sulphonamide hybrid. The synthesis involved preparation of 4-(pyridin-4-yl)-1,3-thiazol-2-amine, followed by chloro acetylation of sulphamerazine and coupling of the resulting intermediate with the thiazole derivative to produce the final hybrid. The structure was confirmed by IR, 1H NMR, 13C NMR, and elemental analysis. N-{4-[N-(4-methylpyrimidin-2-yl) sulphamoyl]phenyl}-2-{[4-(pyridin-4-ylamino)thiazol-2-yl]amino} acetamide showed strong antimicrobial activity, with inhibition zones of 34 mm against S. aureus, 31 mm against S. pneumoniae, 34 mm against E. faecalis, 30 mm against P. aeruginosa, and 20 mm against C. albicans. The compound demonstrated improved activity compared with sulphamerazine, highlighting the potential of pyridine–thiazole incorporation for developing enhanced sulphonamide antimicrobial agents .(24)

2.3 Antimycobacterial Activity

2.3.1 4-((2-(5-Bromo-1H-pyrazolo[3,4-b]pyridin-1-yl)-2-oxoethyl)amino)-N-(various substitutions)benzene sulphonamides

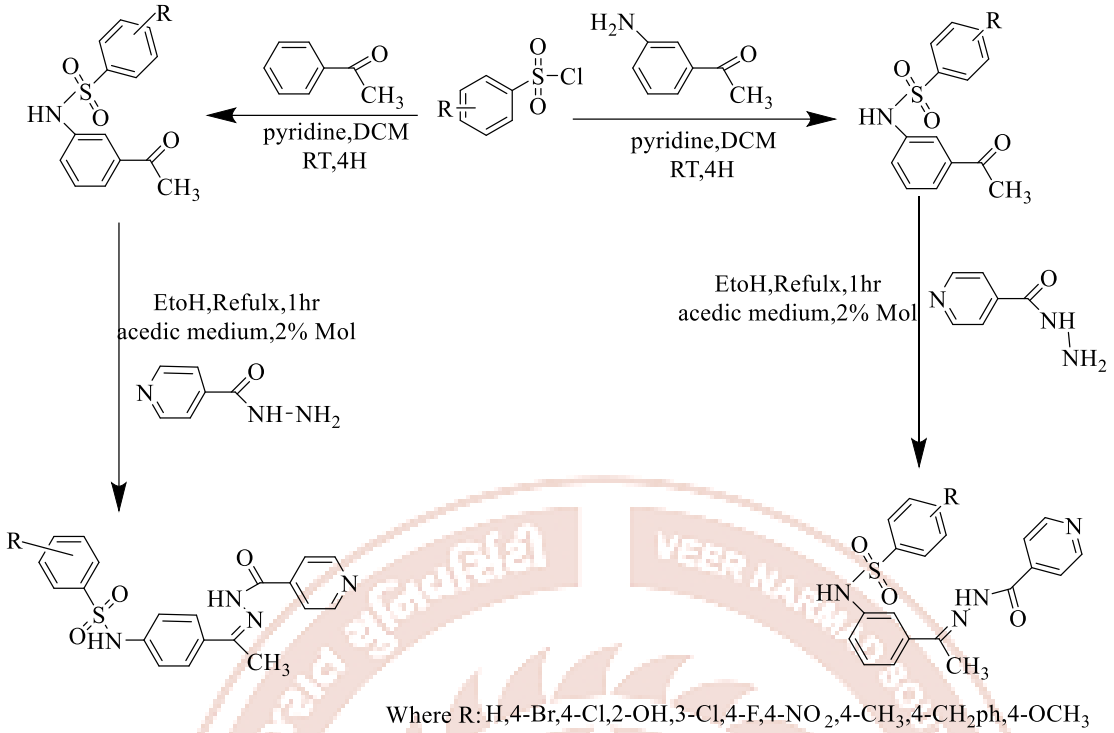
Variya et al. described a series of benzene sulphonamide substituted pyrazolo[3,4-b]pyridine (as potential antibacterial and anti-tubercular agents. The compounds were synthesized by first preparing a 5-bromo-1H-pyrazolo[3,4-b] pyridine derived chloro ethanone intermediate, which was then coupled to diverse sulphonamide bearing drugs. The synthesized derivatives were characterized by FT-IR, 1H NMR, 13C NMR, ESI-MS and elemental

analysis. 4-((2-(5-Bromo-1H-pyrazolo[3,4-b]pyridin-1 yl)-2-oxoethyl)amino)-N-(5-methylisoxazol-3-yl) benzene sulphonamide, 4-((2-(5-Bromo-1H-pyrazolo[3,4-b]pyridin-1 yl)-2-oxoethyl)amino)-N-(4-methylpyrimidin-2 yl)benzene sulphonamide and 4-((2-(5-Bromo-1H-pyrazolo[3,4-b]pyridin-1-yl)-2-oxoethyl)amino)-N-(6-methoxypyridazin-3-yl) benzene sulphonamide exhibited excellent inhibition against Mycobacterium tuberculosis H37Rv. Their anti-tubercular MIC values were 25, 6.25 and 6.25 µg/mL, respectively, as compared to 0.20 µg/mL for isoniazid. These results indicate pyrazolop yridine-sulphonamide derivatives as potential scaffolds for further anti-tubercular drug development. (26)



2.3.2 isoniazid-hydrazone-aryl sulphonamide hybrids

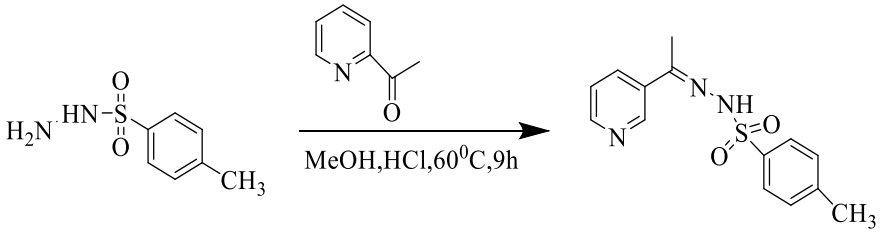
Kadima et al. reported potential antimycobacterial agents of a number of isoniazid-hydrazone-aryl sulphonamide hybrids containing a pyridine ring and a sulphonamide pharmacophore. The compounds were designed by the molecular docking studies against the active site of InhA and then synthesized by N-sulphonylation of substituted aminoacetophenones followed by condensation with isoniazid in ethanol in presence of acetic acid. The synthesized hybrids demonstrated considerably improved activity than their sulphonamide precursors. All the substituted derivatives were active against M. tuberculosis with MIC values of 0.156 µg/mL while some of the other derivatives were found to be active with MIC values of 0.313 µg/mL. These results illustrate the potential of the combination of the pyridine-containing isoniazid pharmacophore with an aryl sulphonamide moiety for the development of new anti-tubercular agents. (27)



Where R: H,4-Br,4-Cl,2-OH,3-Cl,4-F,4-NO_2,4-CH_3,4-CH_2ph,4-OCH_3

2.3.3 4-Methyl-N′-(1-(pyridin-2-yl) ethylidene)benzene sulphono hydrazide

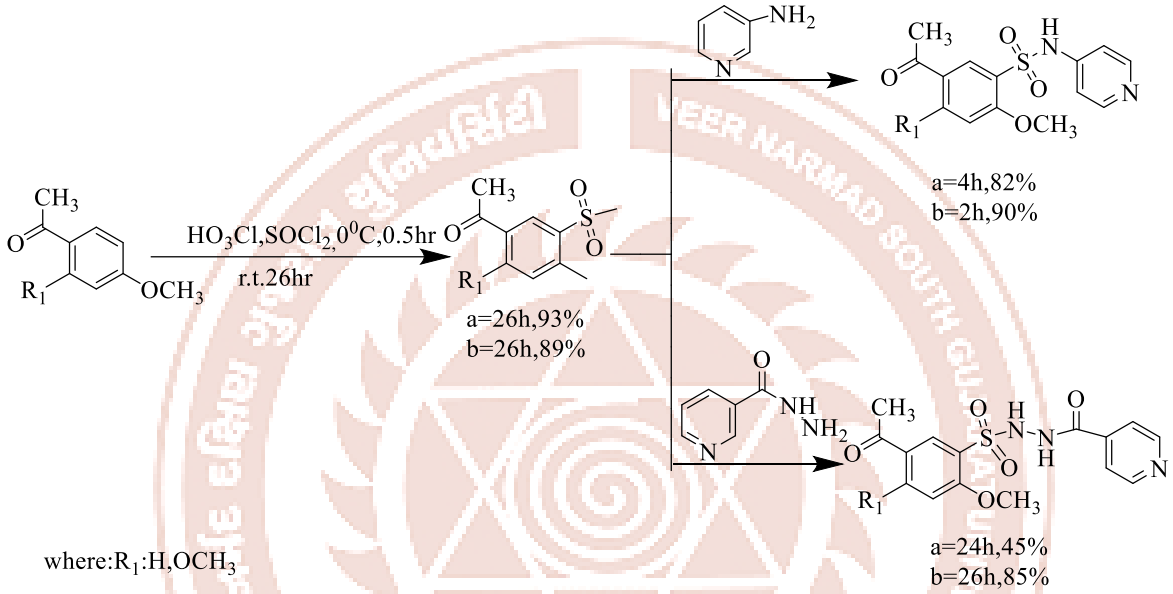
Al-Warhi et al. synthesized pyridine-based sulphonylhydrazone 4-methyl-N′-(1-(pyridin-2-yl)ethylidene)benzene sulphonohydrazide and described it as a promising anti-mycobacterial compound targeting InhA. The compound was prepared by condensation of 2-acetylpyridine with p-toluenesulphonylhydrazide in acidic conditions in methanol to give the corresponding pyridine containing sulfonylhydrazone. Among the synthesized derivatives, . 4-Methyl-N′-(1-(pyridin-2-yl) ethylidene)benzene sulphono hydrazide exhibited the most potent activity against Mycobacterium tuberculosis with MIC of 8 µg/mL; its MIC against M. abscessus was >125 µg/mL. The compound also reduced intracellular mycobacterial viability in human macrophages and displayed antibiofilm activity. Furthermore, compound 7 exhibited the inhibitory activity against InhA with IC50 value of 0.91 ± 0.03 µM, which further confirms the possible utilization of pyridine sulphonamide as the scaffold for further antituberculosis development. (28)



2.3.4 Pyridine-containing chalcone–sulphonamide hybrid

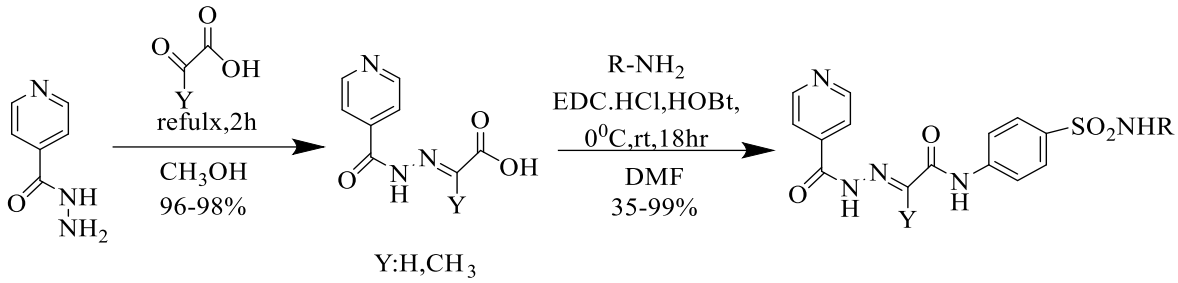
Castaño et al. reported .Pyridine-containing chalcone–sulphonamide hybrid, an isoniazid-derived pyridine-containing chalcone–sulphonamide hybrid, as promising

antitubercular compound. The pyridine sulphonamide precursor was prepared from appropriate benzenesulphonyl chloride and isoniazid and then reacted through Claisen-Schmidt condensation with an aromatic aldehyde to provide the chalcone-sulphonamide framework. Compound 20e exhibited promising activity against Mycobacterium tuberculosis H37Rv (MIC = 9.0 µM) and against M. bovis BCG (MIC = 9.0 µM). It also displayed promising activity against the LAM9 strain of M. tuberculosis with a MIC of 8.97 µM. The compound was bacteriostatic but its low Vero-cell IC_{50} (0.26 ± 0.69 µM) afforded a low selectivity index suggesting the necessity for further optimization. (29)

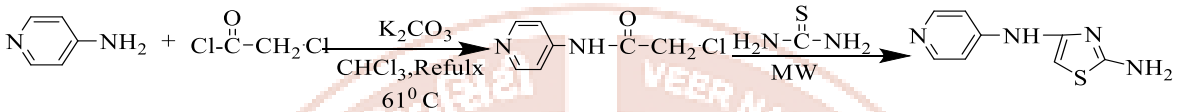


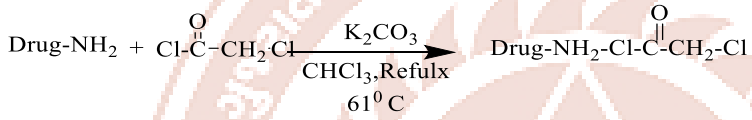
2.3.5 Isoniazid–sulphamethoxazole hybrid

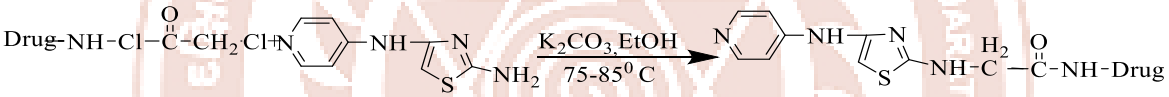
Pflégr et al. have reported a series of isoniazid-based pyridine–sulphonamide hybrids designed to combine the antimycobacterial activity of isoniazid with that of the sulphonamides. The key hydrazone acid intermediate was prepared from the reaction of isoniazid with an oxocarboxylic acid and subsequent carbodiimide mediated amide coupling with sulphonamide derivatives. Among synthesized compounds, sulpha methoxazole derivative showed the highest activity against Mycobacterium tuberculosis H37Rv with MIC of 0.5–1 µM similar to the reference isoniazid. It also exhibited moderate activity against M. kansasii with MIC values of 16–32 µM whereas the activity against M. avium was weak. The study revealed that the combination of two antimicrobial pharmacophores in one molecular scaffold may improve the antimycobacterial activity. (30)



Where R:H,5-Me-isoxazole-3-yl , Thiazol-2-yl,6-MeO-pyridazin-3-yl , Pyrimidin-2-yl, 4,6-Di Me-pyrimidin-2-yl, 5-MeO-pyrimidin-2-yl



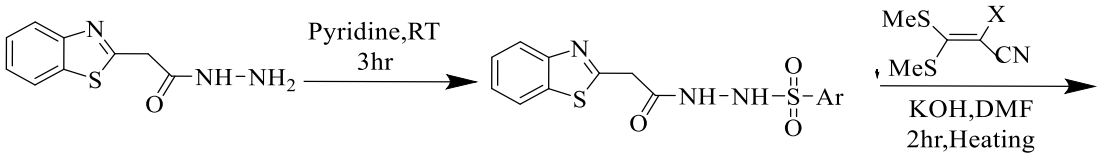


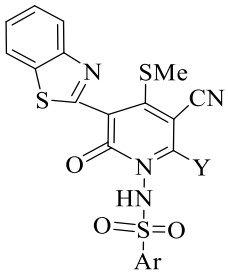


Where Drug—NH_2:sulphamethazine, sulphamerazine, sulphamethoxazole.

2.3.6 N-(6-amino-3-(benzo[d]thiazol-2-yl)-5-cyano-4-(methylthio)-2-oxopyridin-1(2H)-yl)benzenesulphonamide

Azzam et al. reported N-(6-amino-3-(benzo[d]thiazol-2-yl)-5-cyano-4-(methylthio)-2-oxopyridin-1(2H)-yl)benzenesulphonamide as an N-sulphonamide 2-pyridone derivative having a benzothiazole moiety. The compound was synthesized by reaction of an N′-(2-(benzo[d]thiazol-2-yl)acetyl)aryl sulphonohydrazide precursor with a ketene dithioacetal derivative and subsequent cyclization to form the 2-pyridone ring. FT-IR, 1H NMR, 13C NMR and elemental analysis confirmed the structure of N-(6-amino-3-(benzo[d]thiazol-2-yl)-5-cyano-4-(methylthio)-2-oxopyridin-1(2H)-yl)benzenesulphonamide Characteristic signals for NH/NH_2, cyano, carbonyl and sulphonamide groups were observed. The compound N-(6-amino-3-(benzo[d]thiazol-2-yl)-5-cyano-4-(methylthio)-2-oxopyridin-1(2H)-yl)benzene sulphonamide showed good antibacterial activity against E. coli with inhibition zone of 26.0 ± 0.5 mm and MIC value of 62.5 µg/mL. It also showed activity against C. albicans with an inhibition zone of 21.0 ± 1.0 mm and MIC of 62.5 µg/Ml. (25)





Where Ar:C_6H_5, 4-CH_3-C_6H_4
X:CN,COOEt
Y:NH_2,OH

3. Conclusion:

Pyridine–sulphonamide derivatives are promising heterocyclic compounds for antimicrobial drug discovery, exhibiting antibacterial, antifungal and antimycobacterial activities. Their antimicrobial potency is strongly influenced by the substitution pattern, molecular architecture and physicochemical properties. Structural modifications, including aryl groups, fused heterocycles, hydrazone linkages and other pharmacophores, have produced several promising lead compounds. However, differences in microbial strains and assay conditions limit direct comparison of reported results, and good in vitro activity does not guarantee therapeutic efficacy. Future studies should focus on structure–activity relationships, mechanisms of action, cytotoxicity, pharmacokinetic optimization and in vivo evaluation. Standardized biological testing and computational studies may further support the development of pyridine–sulphonamide hybrids as clinically relevant antimicrobial agents.

4. Credit author statement

Dipali Maisuriya Validation, Formal analysis, Data curation, Writing - original draft, Investigation; Bhadreshkumar N. Parmar: Conceptualization, review & editing; Mahima A, Rathod; review & editing; Amitkumar C. Purohit: Conceptualization, Resources, review, & editing, Supervision. Declaration of competing interest There are no potential conflicts of interest reported by the authors.

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