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REVIEW ARTICLE

Exploring the Efficacy of Sulphonamide in Novel Therapeutic Approaches: New Hope

Neha Varshney[1], Reema Sinha[1*], Pankaj Kumar[2], Anuj K. Singh[2]

ABSTRACT

Sulphonamides are widely used in medicine for their antibacterial, antifungal, antiviral, antitumor, anti-inflammatory, and carbonic anhydrase-inhibiting properties. They can block protein and nucleic acid production in bacteria. Adding aromatic heterocycles like benzotriazole and benzimidazole to sulphonamides can enhance their antibacterial potency. Fluoro- and chloro-substituted benzyl groups have also been added to improve pharmacological properties. Sulphonamides can react with and ketones to form Schiff bases, which have antimicrobial and antimycotic properties. It has applications as an antimicrobial agent, hypoglycemic agent, diuretic, and more. The therapeutic actions of sulphonamides involve inhibiting enzymes like carbonic anhydrases, cyclooxygenases, and dihydropteroate synthetase. This allows them to have antimicrobial, anti-inflammatory, aldehydes, antiprotozoal and other effects. Sulphonamides like acetazolamide, celecoxib, zonisamide, and benzolamide have wide clinical applications as diuretics, anticancer agents, antiepileptics, anti-inflammatories, and more. Research is ongoing into synthesizing new sulphonamide derivatives with improved efficacy, potency, and safety profiles for treating various diseases.

Keywords: Antifungal, Sulphonamide, Potency, Efficacy, Antimicrobial.

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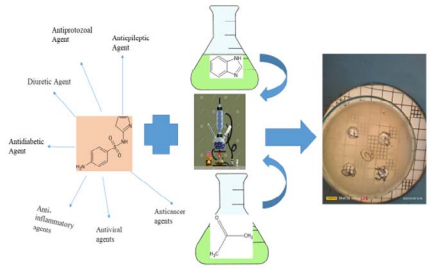

Graphical Abstract

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INTRODUCTION

The prevention and treatment of bacterial infections in biological systems has long been the focus of sulfonamides, artificial antifolic agents. Recently, their wide range of pharmacological actions - including those that are antibacterial, antifungal, antiviral, antitumor, anti-inflammatory, and carbonic anhydrase inhibitors - have brought them great favor in biology and medicine.

Sulphonamide

Sulfonamides, which are aminobenzoic acid's counterparts, may compete with it to block the production of proteins and nucleic acids, which would subsequently stop the spread of different microbes. Moreover, because sulfonamide molecules can coordinate phenylamino and sulfonyl amino groups to integrate the characteristics of various fragments, they have drawn considerable attention in supramolecular chemistry research.[1-3]

Silver-sulfadiazine in particular has been used extensively in burn therapy, outperforming Silver nitrate or the free ligand. Many sulfonamides containing aromatic heterocycles, such as pyridazine, isoxazole, thiazole, and pyrimidine, have been created and utilized successfully in clinical settings up to this point. Examples of these include sulfadiazine, sulfachlorpyridazine, sulfathiazole, and sulfisoxazole, all of which have excellent antibacterial properties. This has led to significant efforts being made to synthesize and develop entirely new structural sulfonamide derivatives that have minimal toxicity, great action, and a broad spectrum.[4,5] Adding aromatic heterocycles to target compounds, such as benzotriazole and benzimidazole, as well as benzene-fused azoles like tetrazole, thiazole, and imidazole, can significantly increase their antibacterial properties. In comparison to precursor sulfonamide, 1,2,3-triazole sulfonamide WXL-1, which contains a 2,4-difluorobenzyl group, exhibited about 32-fold more potency against *Pseudomonas aeruginosa* and *Shigella dysenteriae*.[6,7] The 2-methyl-5-nitroimidazole fragment bearing sulfonamide ZHZ–1 exhibited nearly the same anti-P. aeruginosa efficacy as chloromycin (MIC = 16 μg/mL). Subsequent investigation revealed that this compound could efficiently intercalate into the DNA

of the calf thymus to form compound-DNA complexes, which may inhibit DNA replication to exert their potent antimicrobial activities. Given these stimulating characteristics, the methylene moiety – a bioisostere of amino group – was added to the sulfonamide fragment on the synthesis of sulfonamide azoles, with the intention of examining the impact on antimicrobial activity.[8] Since the benzimidazole ring is a fused heterocycle of benzene and imidazole, it shares structural similarities with purine. As a result, its derivatives can compete with purine to prevent the creation of proteins and nucleic acids inside bacterial cell walls, which can either kill or stunt the growth of bacterial strains. In order to enhance the pharmacological characteristics of the target molecules by speeding up drug transit and absorption in vivo, fluoro- and chloro-substituted benzyl groups were also added.[9-11] Any primary amine can react under certain circumstances with an aldehyde or ketone to generate Schiff bases. A Schiff base is an aldehyde or ketone's nitrogen counterpart in which the carbonyl group (CO) has been swapped out for an imine or azomethine group.[11]

The goal is to discover new chemical compounds with more effective and coherent antimicrobial activity because the percentage of life-threatening infections is rising.

Sulphathiazole

Sulfathiazole (Figure.1) is a short-acting sulfonamide. It is also known by the names solfatiazolo, sulphathiatole, sulfonazolum, norsulfazolum, and sulf anilamidothiazolum. It is N~-thiazol-2-ylsulphanilamide chemically. Other chemical names are: N1-2=thiazolylsulfanilamide, 4-amino-N-2=th iazolyl benzenesul f onamide , 2-sulf an~lamidothiazole , 24 sulf anilylam1no)- t hia zole,2-(paminobenzenesulf onamido) th iazol. The synthesis of sulphathiazole has been done by the mentioned scheme (Figure 2). It also occurs as sulfathiazole sodium (soluble sulf athiazole).[12,13]

Schiff Base

Ashraf *et al*., has reported Schiff bases are condensation products of primary amines with carbonyl compounds. These compounds share the azomethine group, which has the generic formula RHC=N-R1, where R and R1 are heterocyclic, cycloalkyl, alkyl, or aryl groups that can be replaced in different ways. These substances are also referred to as azomethines, imines, or anils. Numerous investigations demonstrated the significant chemical and biological significance of a single pair of electrons in a sp2 hybridized orbital of the nitrogen atom belonging to the azomethine group. Due to the unique characteristic of the C=N group, Schiff bases are often

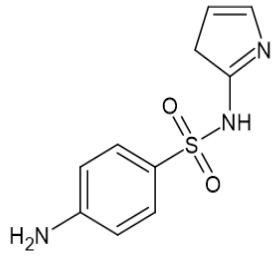

Figure1: Sulphathaizole

good chelating agents due to their synthetic flexibility and ease of synthesis, particularly when a functional group like -OH or -SH is present near the azomethine group to create a five or six-membered ring with the metal ion.[14] Salicylaldehyde schiff bases have also been shown to have antimicrobial or antimycotic properties as well as to regulate plant growth. Additionally, Schiff bases exhibit certain analytical uses. The -N=CH- (imine) group, which distinguishes Schiff Bases, is important for understanding the mechanisms underlying the transamination and racemization reactions in biological systems. Schiff bases are effective against many different types of pathogens, *including Staphylococcus aureus, Escherichia coli, and Candida albicans*.[14,15]

Synthesis of Sulphathiazole

Chemistry of sulphonamide

Sulfonamides are amphoteric chemical compounds that are regarded as weak organic acids with pKa values between 4.79 and 8.56. They can be produced by reacting a sulfonyl chloride with ammonia or amine derivatives. Sulfonamides have a low solubility in water; however, their solubility may be enhanced by raising the medium's pH. Their sodium salts dissolve in water with ease. Sulfacetamide is used to treat eye infections and has a neutral pH.

While the nitrogen of SO_2NH_2 is denoted as N1, the nitrogen of the amino group at para position is designated as N4, many systemic sulfa medications were acquired by substituting at the N1 position, whereas GIT-acting sulfa medications were obtained by substituting at the N4 position. Thousands of intriguing compounds are created by these two substitutions at the N1 and N4 positions, and some of them have clinical importance.[16,17]

Therapeutic Action of Sulphonamide

Hypoglycemic agent

Te following (figure 3) schematically illustrates 2245 RP's method of action in beta cells. 2254 RP reduces the potassium conductance of the beta-cell membrane by blocking ATP-sensitive K + channels. This results in depolarization and the activation of voltage-dependent

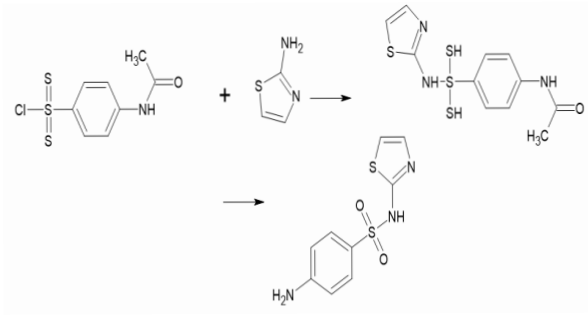

Figure 2: Synthesis of sulphathiazole

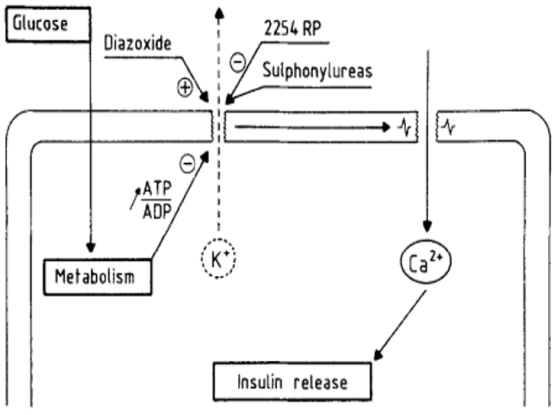

Figure 3: Method of action in beta cells

Ca 2 § channels. The subsequent Ca2+ influx increases the amount of free Ca2+ in the cytoplasm, activating an effector system that ultimately causes the exocytosis of insulin granules. This series of occurrences is comparable to that set off by first- or second-generation sulphonylureas. Pharmacological therapies claiming to influence beta-cell activity find ATP-sensitive K+ channels to be an exceptionally sensitive target, owing to their pivotal involvement in regulating the membrane potential of beta cells. All of the hypoglycemic medications that are now prescribed to treat Type 2 diabetes patients' inadequate insulin release work against this target. Novel compounds that may quickly and transiently block ATP-sensitive K+ channels, whether or not they are sulphonamides, would undoubtedly expand our treatment options. But as our knowledge of beta-cell physiology and pathology has grown, it is now necessary to search for medications that work at different places.[18,19,20] It would be foolish to purposefully limit our therapeutic options to substances targeting the same one target for the next fifty years. to have atleast three different isozymes, COX1 through COX3, have been identified to date. Cyclooxygenases (COXs) catalyze the committed step in the conversion of arachidonic acid to prostaglandins (PGs) and thromboxane.[20, 21]

Diuretic activity

Historically, the primary goal of using diuretics in medicine was to alter the ionic content and volume of bodily fluids.[22-24] Therefore, their use – alone or in conjunction with particular treatment protocols – is very advantageous for the management of edema in general as well as for the treatment of patients with hypertension and those afflicted by cardiovascular illnesses.[25] The first sulfonamide-based diuretic to be introduced into the clinic for systemic administration was acetazolamide, which has been in widespread use since 1956. The first generation sulfonamidic diuretics have physiological effects on the kidneys that are typical of them. These effects include a rapid increase in urine volume that turned from being slightly acidic (about 6) to basic (approximately 8).[26,27] The primary side effect of the urine pH shift is metabolic acidosis, which is caused by the retention of tritatable acid and ammonia. Furthermore, the bicarbonate ion excretion – which has sodium and potassium as counterions – is enhanced when the kidneys' CAs are inhibited, reaching values up to 120 times higher than normal ones. Due to the activation of CA-independent re-absorption mechanisms, the removal of significant amounts of sodium bicarbonate is a self-limiting process.[27,28,29] Furthermore, because fewer proton ions are accessible when the kidneys' CAs are inhibited, this has a significant impact on the Na-H antiporters that are expressed at the baso-lateral membrane of the nephrons. The overall result is an increase in sodium bicarbonate excretion in the nephronic cells' interstitial area, which creates an osmotic potential and causes the organism to lose water. The primary cause of the diuretic action is the suppression of the CAs expressed in the nephron's proximal tube segment. As was already indicated, the primary adverse impact linked to the inhibition of the renal CAs is metabolic acidosis. Kidney stone formation and encephalopathy are other complications that have been noted; in both cases, their occurrence is rather low and they will only manifest in patients with a compromised clinical picture he general consequences resulting from the indiscriminate inhibition of the CA isoforms expressed in the other organs and tissues include fatigue, general malaise, weight loss, and gastrointestinal irritations. KI values of the first-generation sulfonamide-based diuretics, which amply demonstrate their efficacy as human CAs' inhibitors. Benzolamide marked a significant advancement in mitigating the adverse consequences caused by the indiscriminate inhibition of human CA isoforms. This molecule's in vitro kinetic profile is comparable to that of the first-generation diuretics previously mentioned, but it exhibits a ten-fold increase in bicarbonate excretion and, Notably, a selective accumulation of renal tissue was noted, and there is a ten-

fold increase in the excretion of bicarbonate, indicating a diuretic impact Benzolamide 's pharmacokinetic characteristics, however, were unsatisfactory, preventing further development for clinical application. In the clinic, first-generation diuretics are nevertheless often used despite their lack of organ selectivity. More significantly, the lead molecule that initiated the creation of the second-generation sulfonamide-based diuretics was the prototype acetazolamide(figure 4). With the exception of furosemide , the kinetic data pertaining to second-generation diuretics made it abundantly evident that these drugs are less potent inhibitors of the CA I/II isoforms than those in the preceding series. Conversely, they demonstrated good potencies for each of the other isoforms.[26,29,30]

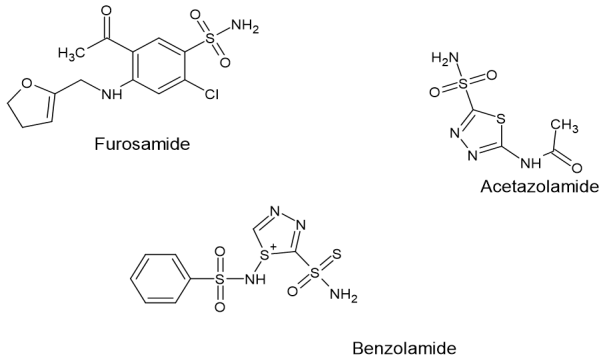

Figure 4: Diuretic drugs containing sulphonamide group

Antiepileptic activity

Zonisamide (figure 5) is an AED that is unrelated to other AEDs and is chemically categorized as a sulphonamide. Zonisamide, 1,2-benzisoxazole-3-methanesulfonamide, is the active component. It doesn't have the ureide structure that the majority of AEDs on the market have.

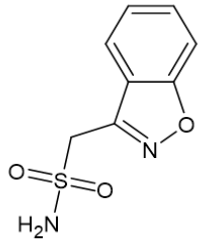

Figure 5: Zonasamide

Although the exact processes underlying zonisamide's antiepileptic activity are unknown, they most likely involve:

- Sodium channel blockage
- T-type calcium channel blockage
- suppression of glutamatergic excitatory transmission
- Effect of scavenging free radicals.

In cultivated neuroblastoma cells of human origin, the effects of zonisamide on voltage-dependent T-type calcium current have been done. Without altering its inactivation kinetics or voltage dependency effect, zonisamide decreased concentration-dependent voltage-dependent T-type calcium current (IC). One potential mechanism behind epileptiform cellular bursting is the suppression of an essential part of the inward current by zonisamide, which blocks T-type calcium channels. therefore preventing the seizure activity from spreading.

Rats anesthetized with urethane were used to study the effects of zonisamide on Ca^2 and K induced hippocampus extracellular glutamate release using an in vivo microdialysis glutamate biosensor. By preventing excitatory glutamatergic transmission, zonisamide may lessen epileptiform occurrences, according to the findings.

Electron spin resonance was used to analyze zonisamide's ability to scavenge free radicals. Zonisamide scavenged hydroxyl and nitric oxide radicals in a dose-dependent manner in the micromolar range. This shows that stabilizing neuronal membranes and shielding neurons from damage by free radicals may be part of zonisamide's antiepileptic action mechanism.[31,32,33]

Anticancer activity

There are two more series of antimitotic sulphonamides. The first series, HMN-154 (figure 6) (A-benzenesulfonamide), HMN-176 (B: an active metabolite of A), and HMN-214 (C : a prodrug of B), is patented by Nippon Shinyaku and H Hidaka. HMN-154 is the result of changing the para-hydroxyanilino group in E7010's(inhibition of tubulin polymerization)structure to a pyridylvinyl group. It was demonstrated by flow cytometric analysis that HMN-154 stops the advancement of the cell cycle in the M phase. It hasn't been documented, nevertheless, that the substance, like E7010, binds to the colchicine site to directly inhibit tubulin polymerization. Conference reports from 1998 state that one of HMN-154 185.86's direct cellular targets is the B-subunit of the transcriptional activator NF-Y. The expression of the genes for cdc2, cyclin A, cdc25c, and mdr-1 is significantly influenced by NF-Y, and the B-subunit is responsible for the DNA binding of the entire NY-F complex. To lower the mRNA levels, HMN-154 inhibited the promoter activity of several genes. suggesting that the substance might impair the expression of the NY-F-associated gene, at least in part, to display antitumor effect. HMN-176 shown activity against a range of cancer cell lines in growth inhibition studies conducted in vitro, with IC50 values spanning from 0.097 to 0.17 μM [87]. HMN-214 showed good antitumor effectiveness against a number of rodent tumors (colon 26, P388, L1210, etc.) and human tumor xenografts (WiDr

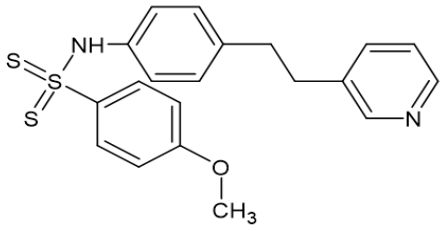

Figure 6: HMN-154

colon, COLO205 colon, A549 non-small cell lung, PC-3 prostate, etc.) when given orally at doses of 10-100 mg/kg on diverse schedules. In the US, HMN-214 is presently undergoing phase I clinical studies.[34,35]

The other class of antimitotic sulphonamides, which are primarily derivatives of pentafluoroben zenesulphonamide, were patented by Tularik. The best chemical in this series, T138067, was discovered to bind covalently to β-tubulin at the Cys239 residue in the colchicine site, inhibiting tubulin polymerization . The cytotoxicity was at least 2-log lower when the fluorine atom para was substituted with either chlorine or bromine to the sulphonamide group. The antiproliferative activity vanished entirely when a hydrogen atom took the place of the fluorine atom at the identical location. These findings are consistent with the hypothesis that Cys239 of B-tubulin nucleophilically substitutes aromatic amino acids at the para position. With IC50 values ranging from 0.011-0.165 μM, T138067 was demonstrated to be equally active against a number of multi-drug resistant (MDR) sub-lines and their mother cancer cell lines. After intraperitoneal injection (i.p.) of T138067 (40 mg/kg), paclitaxel (30 mg/kg), and vinblastine (1 mg/kg) three times a week, comparable anti-tumour efficacies were noted for each medication in the CCRF-CEM lymphoblastic leukaemia xenograft model. Although T138067 showed the same level of effectiveness against the MDR sub-line xenografts, the other two medications showed around 50% less efficacy against the identical MDR tumors. This suggests that T138067 may be useful in treating MDR-phenotype human cancers.[36,37,38] The US-based Phase I clinical studies of this medication were started in March 1998 and are presently ongoing, using several oral drug delivery dosage regimens. Phase II trials for patients with hepatocel lular cancer are anticipated to start this year. It appears that further research on the second-generation analog T900607 is still happening 191.92).[38,39]

Antiprotozoal activity

Folates are necessary for various cellular processes as well as the manufacture of thymidine monophosphate. Because the metabolism of folate in bacteria is different from that in mammalian cells, DHFR inhibitors (proguanil, pyrimethamine, trimethoprim) and DHPS inhibitors (sulfadiazine, sulfamethoxazole) are important antibacterial medicines.[40,41] De novo folate synthesis occurs in bacteria using small molecular weight precursors such as p-aminobenzoic acid. Instead of creating new folates from scratch, mammalian cells preserve the higher molecular weight folates. Sulphonamides and sui phones, which are analogues of p-aminobenzoic acid, prevent the manufacture of bacterial dihydropteroates, which in turn prevents the synthesis of thymidylate in mammals but not in bacteriaRapid absorption and distribution of sulfadiazine and sulfamethoxazole occur throughout the body, including in the CSF, where levels range from 10 to 80% of serum levels. T'12 values are approximately 10h. Acetylation of sulphonamides in the liver renders them inactive; the drug's parent and acetylated forms are eliminated through the urine. Moreover, DHFR inhibitors are quickly and entirely absorbed, distributing to the CSF. Trimethoprim's enhanced therapeutic index in early trials led to its selection as an antibacterial drug over a number of other DHFR inhibitors (Bushby & Hitchings 1968). Trimethoprim and several sulphonamide dosages were used to find the ideal sulphonamide to trimethoprim ratio (20:1) for antibacterial activity . Because both medications have similar t'12 values, an oral regimen of sulfamethoxazole and trimethoprim in a 5:1 ratio (cotrimoxazole) produces ideal relative serum concentrations (20:1) and maintains this ratio after coadministration of the drugs. Sulphonamides prevent several protozoa from synthesizing folates de novo, including P. carinii and Toxoplasma gondii (Kovacs et al. 1989). Furthermore, pyrimethamine, a DHFR inhibitor, has an approximately tenfold higher activity against the toxoplasma enzyme compared to the mammalian enzyme (Kovacs et al. 1987). Lastly, Toxoplasma gondii exhibits inadequate folate production during transit (Kovacs et al. 1988). Therefore, it makes biological sense to treat toxoplasmosis with pyrimethamine + sulphonamides (sulfadiazine) with folinic acid rescue. Sulphonamides hinder P. carinii's de novo production of folates. According to Allegra et al. (1987), P. carinii DHFR is "" 100 times more sensitive to trimethoprim than the mammalian enzyme, and cotrimoxazole is currently the recommended treatment for this infection. However, this set combination might not provide the best agent ratio to treat P. carinii infections because it was created to provide the best agent ratio for antibacterial action.[42,43]

Anti-inflammatory activity

The first step in the conversion of arachidonic acid to prostaglandins (PGs) and thromboxane is catalyzed by cyclooxygenases (COXs), of which at least three different isozymes have been identified to date: COX1 through

COX3. The constitutive version of COX1, as opposed to the inducible form, was thought to be primarily linked to inflammatory disorders, while the PGs' positive effects were attributed to COX1. This resulted in the discovery of coxibs (compounds that exhibit preferential inhibition of COX2 over COX1) in the 1990s; these included a number of medications that were approved prior to 2000, including rofecoxib, celecoxib, and valdecoxib.in given figure 7 The latter two (compounds Celecoxib and Valdecoxib respectively) are main sulfonamides, while the first is a methylsulfone. Celecoxib was still being used in clinical settings, despite the initial reasoning behind the development of this class of nonsteroidal anti-inflammatory agents appearing to have been flawed by a number of intentional and inadvertent facts from the pharmaceutical companies (Merck & Co. and Pharmacia-Pfizer joint venture), among them unreported side effects that ultimately resulted in the withdrawal of two of these drugs. It should be noted that among the three original medications in this class, this one was the least COX2- selective. As previously indicated in the review's early paragraphs, it was subsequently demonstrated that the principal sulfonamide COX2-"selective" inhibitors are also significant, oftentimes low nanomolar CAIs. Due to the sulfonamide coxibs' unpredictable fortunes, development in the area slowed until recently, when apricoxib —an additional molecule of this type—was authorized for clinical use. It should be noted that the chemical structures of apricoxib and celecoxib and valdecoxib are strikingly similar. In two inflammatory breast cancer cell lines, it has been demonstrated to have equipotency to celecoxib in suppressing PG E2 production. Based on these COX2 inhibitory actions, Tragara Pharmaceuticals patented this drug as useful for the treatment of malignancies, tumors, and tumor-associated diseases. Though this hasn't been studied yet, the material is obviously a CA inhibitor as well as a major sulfonamide, and as such, it probably has a strong effect on the tumor-associated isoforms of CA IX and XII . Therefore, it's possible that this sulfonammide's antitumor action mechanism is more intricate than its creators initially believed.[44,45]

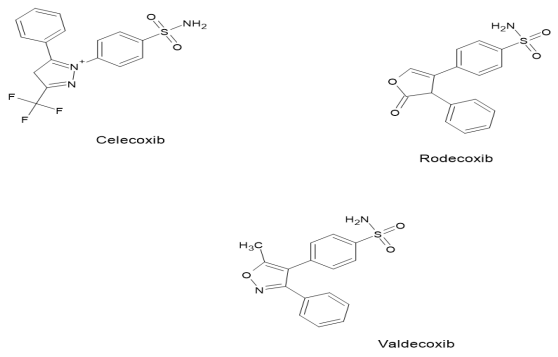

Figure 7: Anti -inflammatory drugs containing sulphonamide group

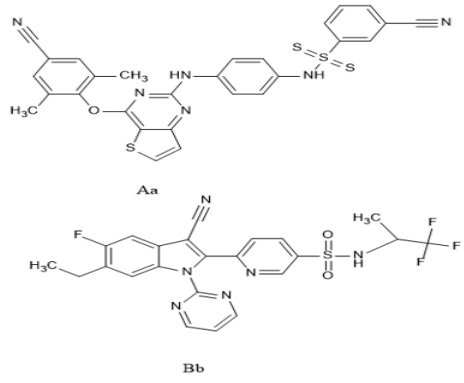

Figure 8:(a) Antiviral compounds containing sulphonamide group

Antiviral activity

Kang etal. designed and synthesized thiophene-pyrimidine analogues and evaluated their activity against a panel of mutant HIV-1 strain sn MT-4 cells, it was discovered that all of the analogs exhibited decent to exceptional effectiveness against wild-type HIV-1. With EC50 values of 0.428 and 0.675 μM, respectively, compound Aa demonstrated the highest potency against the single mutants Y181C and Y188L, surpassing even the efficacy of the reference drug AZT. The development of thiophene pyrimidine-based NNRTIs with stronger efficacy against HIV strains carrying RT mutations is anticipated to benefit from these findings. Zhang et al. investigated pyridine- sulfonamides as a powerful inhibitor (8a) of NS4B in Hepatitis C virus (HCV). Compound Bb exhibited exceptional efficacy against the HCV 1b replicon, demonstrating an EC50 of 2 nM and a selectivity index more than 5000 in relation to cellular GAPDH.[46]

Compound Bb is a promising candidate for a future therapeutic development program due to its overall characteristics.

Using the half-leaf approach discovered by Yang et al., a number of thiadiazole containing sulfonamide analogues have also shown promise antiviral efficacy against tobacco mosaic virus. Comparing compounds A (42%) and B (42%) to the reference medication Ningnanmycin (54%), promising TMV inhibition was observed. The sulfonamide moiety's SAR structural alteration has a significant effect on the compounds' antiviral activity. A new family of chalcone-containing purines and benzenesulfonamide hybrids was developed by Hu et al., who then investigated the compounds' antiviral capabilities against TMV and CMV. With an EC50 value of 51.65 μg/mL, compound C was reported to exhibit exceptional activity against TMV, outperforming ribavirin (150.45 μg/mL). According to

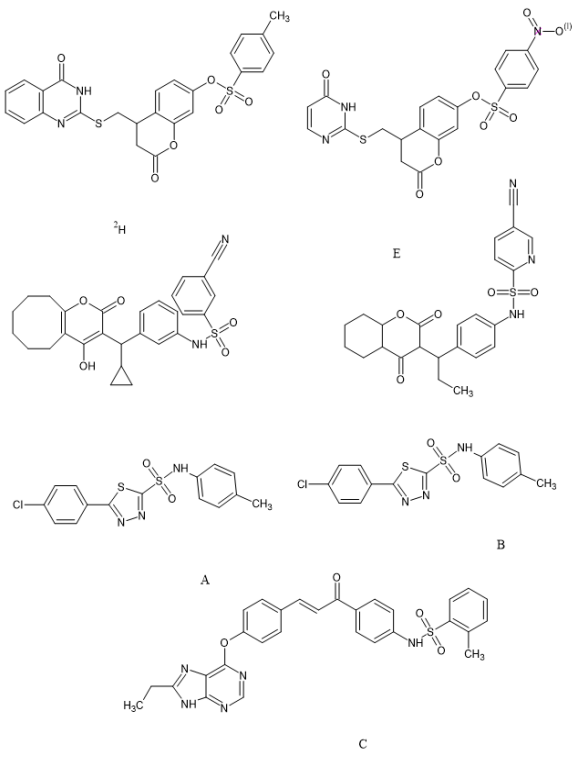

Figure 8: (b) Antiviral compounds containing sulphonamide and heterocyclic group

the SAR analysis, the addition of EDGs at the aromatic ring 2-position of benzenesulfonamide and the low steric hindrance group enhanced the antiviral capabilities. These results suggested that chalcone derivatives should be investigated further and used as models for novel antiviral drugs . Strong antiviral activity (Ki = 0.8 nM, IC50 = 1.5 μM) was observed for compound D. With a t1/2 = 6 h, the oral bioavailability of this drug varied from 42% in rats to 77% in dogs . Compound E, which had a substantially lower ED50 value of 0.95 μM, was shown to have strong antiviral activity in cell culture and great binding affinity for the HIV protease (Ki values in the 0.05 nM) once the 5,6-double bond in the pyrone ring was saturated. Finally, Hwu et al. have continued to discover a new class of powerful coumarin-benzimidazole hybrids with strong anti-HCV action (8b). Two of these, compound F (EC50 = 10.2 μM) and compound G (EC50 = 13 μM), showed outstanding antiviral efficacy against the chikungunya virus (CHIKV). According to the SAR, the key to the double conjugated uracilecoumarins' anti-CHIKV efficacy was their elongation into triply conjugated uracilecoumarinearenes by the usage of the -SO2 linker. The selectivity indexes of bezouracil derivatives F were higher than those of uracil G or thymine.[47,48]

CONCLUSION

Sulfonamides, as a class of synthetic antimicrobial agents, have demonstrated a wide range of pharmacological activities, including antibacterial, antifungal, antiviral, antitumor, anti-inflammatory, and carbonic anhydrase inhibitory effects. Their versatility and potential for further development make them an essential area of research in medicinal chemistry.

Through structural modifications, such as the incorporation of aromatic heterocycles, fluorinated or chlorinated benzyl groups, and the formation of Schiff bases, sulfonamides have shown improved potency, selectivity, and pharmacokinetic properties. Numerous sulfonamide derivatives have been synthesized for their therapeutic potential, leading to the development of clinically approved drugs for various indications, including diuretics (acetazolamide, benzolamide), anti-inflammatory agents (celecoxib, valdecoxib), antiepileptics (zonisamide), and anticancer agents (HMN-214, T138067).

Furthermore, sulfonamides have demonstrated promising antiprotozoal and antiviral activities, making them potential candidates for the treatment of neglected tropical diseases and emerging viral infections. It is crucial to address the potential adverse effects associated with sulfonamides, such as metabolic acidosis, renal toxicity, and hypersensitivity reactions, through careful structural design and rigorous preclinical and clinical evaluations.

So,this may concluded that the sulfonamide class of compounds like sulphathiazole continues to be a fertile ground for medicinal chemistry research, offering opportunities for the development of new therapeutic agents targeting a wide range of diseases and conditions. Many sulphonamide drug can be used for repurposing the synthesis of novel sulfonamide-based antibacterial agents, with the creation of innovative modifications using compounds already in existence, can be used for drug repurposing.

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