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Recent Advances in Development of Sulfonamide Derivatives and Their Pharmacological Effects- A Review

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Abstract First drugs which were largely used for chemotherapeutically and preventive use were the sulfonamides. Sulfonamides have a wide range of pharmacological activities such as against rheumatoid arthritis, anti-hypertensive, anti-epileptic, anti-bacterial, anti-protozoal, anti-fungal, non-peptidic vasopressin receptor antagonists, anti-inflammatory, and translation initiation inhibitors. These sulfonamides have a variety of synthetic reactions to work with. This review comprises of recent advances related to synthesis and pharmacological effects of sulfonamides especially in concern to anti-epileptic and anti-microbial agents.

Keywords: *sulfonamide, anti-epileptic, anti-microbial*

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1. Introduction

Sulfonamide is the basis of several groups of drugs. The original antibacterial sulfonamides are synthetic antimicrobial agents that contain the sulfonamide group. Some sulfonamides are also devoid of antibacterial activity, e.g., the anticonvulsant sultiame. The sulfonylureas and thiazide diuretics are newer drug groups based on the antibacterial sulfonamides.

Epilepsy is usually defined as a tendency to recurrent seizures. The word "epilepsy" is derived from Latin and Greek words for "seizure" or "to seize upon". This implies that epilepsy is an ancient disorder; indeed, in all civilizations it can be traced as far back as medical records exist.

- Epileptic drug targets-
- Voltage-gated sodium channels
- Voltage-gated calcium channels
- Inhibitory neurotransmission
- Excitatory neurotransmission

Mechanisms of action of existing agents-

- Blockade of voltage-gated sodium channels
- Blockade of Voltage-gated calcium channels
- Activation of the ionotropic GABA A receptor
- Alteration of GABA turnover
- Blockade of the NMDA subtype of glutamate receptor
- Inhibition of carbonic anhydrase

Antimicrobial agents are the drugs, chemicals, or other substances that kill or slow the growth of microbes. They include antibacterial drugs, antiviral agents, anti-fungal agents [1].

Some known anti-microbial agents-

- Sulfadiazine
- Trimethoprim
- Ciprofloxacin
- Pencillins
- Doxycycline
- Chloramphenicol
- Streptomycin
- Erythromycin
- Clindamycin
- Clindamycin
- Linezolid
- Colistin
- Nitrofurantoin
- Metronidazole
- Isoniazid

2. Developments to Sulfonamides Having Anticonvulsant Activity

In the year 2002 a series of aromatic/heterocyclic sulfonamides incorporating valproyl moieties were prepared by B. Masereel et. al. to design antiepileptic compounds possessing in their structure two moieties known to induce such a pharmacological activity: valproic acid, one of the most widely used antiepileptic drugs, and the sulfonamide residue included in acetazolamide and topiramate, two carbonic anhydrase inhibitors with antiepileptic properties. Some of these derivatives showed very high inhibitory potency against three carbonic anhydrase (CA) isozymes, such as CA I, CA II, and CA IV, involved in important physiological processes.

Topiramate, a recently developed antiepileptic drug possessing a sulfamate moiety, also shares this property, although earlier literature data reported this compound to be a weak-moderate CA I, II, and IV inhibitor. The valproyl derivative of acetazolamide (5-valproylamido-1,3,4-thiadiazole-2-sulfonamide) was one of the best hCA I and hCA II inhibitor in the series and exhibited very strong anticonvulsant properties in an MES test in mice. It was observed that some lipophilic derivatives, such as 5-benzoylamido-, 5-toluenesulfonylamido-, 5-adamantylcarboxamido-, and 5-pivaloylamido-1,3,4-thiadiazole-2-sulfonamide, show promising in vivo anticonvulsant properties and that these compounds may be considered as interesting leads for developing anticonvulsant or selective cerebrovasodilator drugs [2].

In the same year a pharmacophoric pattern of sulfonamide was presented by I. A. Barrios et. al., which concerns compounds structurally related to tropiramate with anti-convulsant activity against the maximal electroshock seizure (MES test). The pharmacophore is characterized by a polar sulfonamide group and lipophilic moiety that should comply with structural and conformational requirements in addition to the electronic one, whose descriptors are analyzed in order to discern the associated requirements. It has been derived from a conformational study, based on a quantum- chemical calculations, followed by a similarity analysis that include structures synthesized and tested in our lab, together with drugs that are already in clinical use. They depicted that third negatively charged atom in the negative end of the polar portion decreases the anti-MES activity [3].

A. Marc et. al. prepared a series of aromatic/heterocyclic sulfonamides in the year 2004 incorporating adamantyl moieties by reaction of aromatic/heterocyclic aminosulfonamides with the acyl chlorides derived from adamantyl-1-carboxylic acid and 1-adamantyl-acetic acid. Related derivatives were obtained from the above-mentioned aminosulfonamides with adamantyl isocyanate and adamantyl iso-thiocyanate, respectively. Some of these derivatives showed good inhibitory potency against two human CA isozymes involved in important physiological processes, CA I, and CA II, of the same order of magnitude as the clinically used drugs acetazolamide and methazolamide. The lipophilicity of the best CA inhibitors was determined and expressed as their experimental log k' IAM and theoretical ClogP value. Their lipophilicity was propitious with the crossing of the blood-brain barrier. The anticonvulsant activity of some of the best CA inhibitors reported here has been evaluated in a MES test in mice. After intra-peritoneal injection (30 mg kg^{-1}), their two compounds exhibited a high protection against electrically induced convulsions(>90%). Their ED 50 was 3.5 and 2.6 mg kg^{-1} [4]. They prepared their series of compounds with the given reaction scheme-

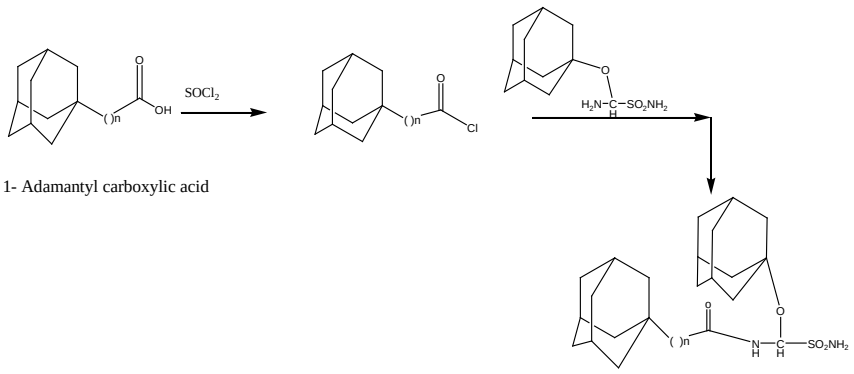


Figure 1. Scheme given by A. Marc for the synthesis of aromatic/heterocyclic sulfonamides

In the year 2004, Chazalette et. al. prepared a series of aromatic sulfonamides incorporating indane moieties starting from commercially available 1- and 2-indanamine, and their activity as inhibitors of two carbonic anhydrase isozymes, hCA I and II was studied. The new sulfonamides incorporating acetamido, 4-chloro-benzoyl, valproyl, tetra-, and pentafluorobenzoyl moieties acted as very potent inhibitors of the slow red blood cell isozyme hCA I (K(i)s in the range of 1.6-8.5 nM), which usually has a lower affinity for such inhibitors, as compared to isozyme II. Some derivatives also showed excellent hCA II inhibitory properties (Ki in the range of 2.3-12 nM), but the anticonvulsant activity of these sulfonamides was rather low as compared to that of other sulfonamide/sulfamate CA inhibitors, such as methazolamide. Furthermore, the 2-amino/acetamido-indane-5-sulfonic acids prepared during this work also showed interesting CA inhibitory properties, with inhibition constants in the range of 43-89 nM against the two isozymes, being among the most potent sulfonic acid CA inhibitors reported so far [5].

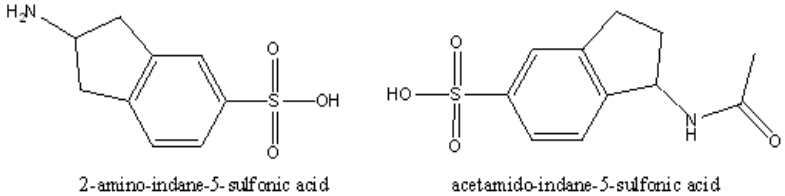
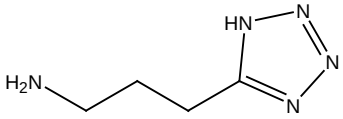


Figure 2. Sulfonic acid derivatives as anticonvulsant agents

In the year 2005 a series of potential substrates of aminobutyric acid aminotransferase (GABA-AT) with lipophilic bioisosteres of the carboxylic acid group were synthesized and tested by Hai Yuan and Richard B. Silverman. Most of the synthesized compounds showed substrate activities with GABA-AT; 1H-tetrazole-5-

propanamine was the best of those tested. The potential time-dependent inhibitor of GABA-AT, 1H-tetrazole-5-(a-vinyl-propanamine), was designed based on the structures of antiepilepsy drug vigabatrin (4-amino-hex-5-enoic acid. One of the synthesized compounds showed time-dependent inhibition of GABA-AT, but its potency is lower than that of vigabatrin. Methylation of the tetrazole group resulted in loss of time-dependent activity, suggesting that the tetrazole ring, the carboxylate bioisostere, exists in its deprotonated form in the enzyme active site [6].



1H-tetrazole-5-propanamine

Figure 3. Substrates of aminobutyric acid aminotransferase

Besides this, in the year 2006 Gregory Krauss has discussed about the hypersensitivity syndrome (HSS) as the reactions which are one of the most feared idiosyncratic drug reactions and are most common with ex-posure to antiepileptic drugs (AEDs), sulfonamides, non-steroidal antiinflammatory drugs, corticosteroids, and allopurinol. HSS is associated with chemotoxic and T-cell–mediated inflammatory injuries in barrier tissue systems that contain cytochrome oxidases (e.g., skin, mucosa, liver, and lungs) and can be seen as a derangement in the defense system against xenobiotics—bioactive foreign molecules. The mechanisms for anticonvulsant HSS are incompletely understood but involve genetic susceptibility, with accumulation of AEDs and oxidized metabolites causing major histocompatibility complex (MHC) and non–MHC–dependent clonal activation of T cells and subsequent cytokine/chemokine production in T cells, keratinocytes, and other target cells. This review discusses the classification and possible mechanisms for anticonvulsant HSS [7].

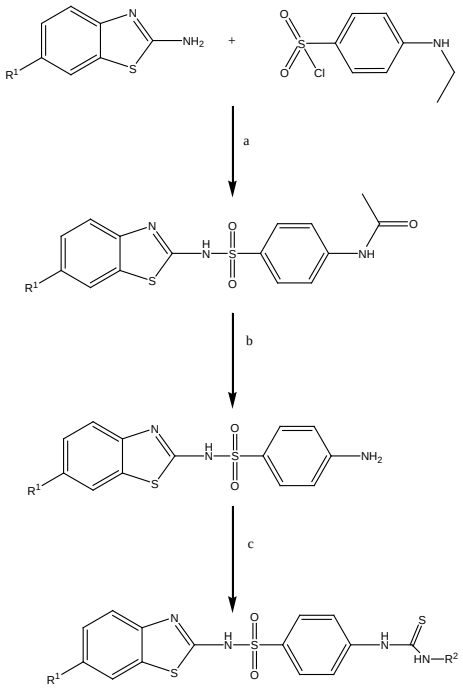


Figure 4. Scheme for the preparation of benzothiazole derivatives of sulfonamide given by Nadeem Siddiqui in 2007. (a)pyridine/Ac_2O; (b)CH_3COOH (80%) boiling 6 h; (c) NCS, EtOH/reflux, 2 h. R^1- F, Cl, OCH_3. R^2- CH_3, C_2H_5

In the year 2007 Nadeem Siddiqui has synthesized a series of sulphonamide derivatives in good yield and evaluated for their possible anticonvulsant activity and neurotoxic study. The structures of the synthesized compounds were confirmed on the basis of their spectral data and elemental analysis. Majority of the compounds were active in MES and scPTZ tests. All the compounds were less toxic than the standard drug phenytoin.

He describes that it is quite apparent that there are at least four parameters for the activity of anticonvulsant drugs, that is, (i) a lipophilic domain, (ii) a distal hydrophobic center whose size affects the pharmacokinetic property, (iii) SO_2NH-group acts as a hydrogen donor, and (iv) a two-electron donor (–C=N–) system is also present. Hydrophobic size appears to govern the MES or scPTZ activity [8].

A series of aromatic/heterocyclic sulfonamides incorporating 2,3:4,5-bis-O-(isopropylidene)-β-D-fructopyranosyl-thioureido moieties has been synthesized and assayed by Jean-Yves Winum in 2007 for the inhibition of seven human isoforms of the zinc enzyme carbonic anhydrase. The new derivatives behaved as weak hCA I inhibitors, were efficient hCA II inhibitors, and slightly inhibited isoforms hCA IV and hCA VA. Only the sulfanilamide derivative showed efficient and selective inhibition of hCA IV. These derivatives also showed excellent hCA VII inhibitory activity, being less efficient as inhibitors of the transmembrane isoforms hCA IX and hCA XIV. Two of the new compounds showed anticonvulsant action in a maximal electroshock seizure test in mice, with the fluorosulfanilamide derivative being a more efficient anticonvulsant than the antiepileptic drug topiramate [9].

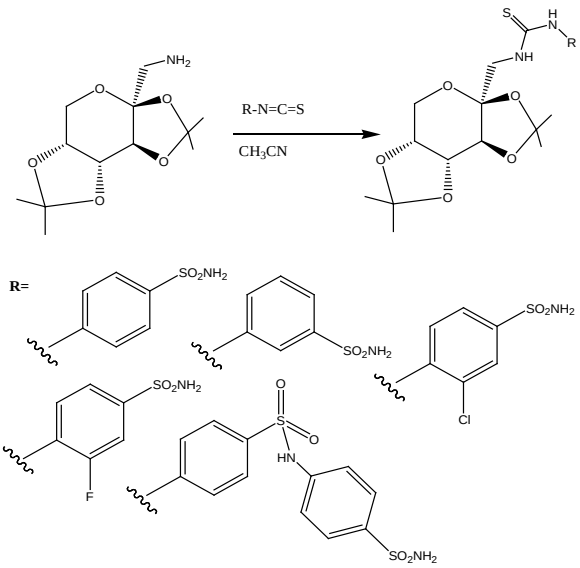


Figure 5. Scheme for the preparation of thioureido derivatives of sulfonamide

In 2009, Rosaria Gitto synthesized a series of 1-aryl-6,7-dimethoxy-3,4-dihydroisoquinoline-2(1H)-sulfonamides. The new compounds incorporate the main features of the above-mentioned anticonvulsants and a sulfonamide function capable to inhibit the enzyme carbonic anhydrase (CA, EC 4.2.1.1), which represents an attractive target in epilepsy. Pharmacological effects were evaluated in vivo against audiogenic seizures in DBA/2 mice and in vitro against several CA isoforms. Some of

the new molecules showed anticonvulsant properties better than topiramate, but weak inhibitory activity and low selectivity in enzymatic assay [10].

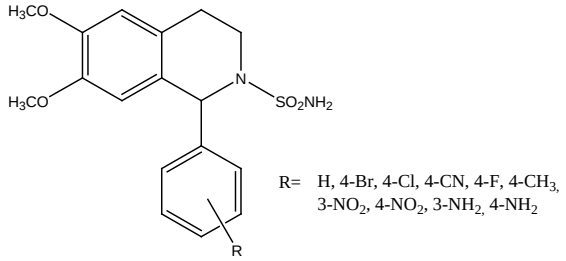


Figure 6. 1-aryl-6,7-dimethoxy-3,4-dihydroisoquinoline-2(1H)-sulfonamides and derivatives

In 2009 De Simone et. al. examine the full inhibition profile against all mammalian carbonic anhydrases of the above antiepileptic drugs together with two investigational, structurally related sulfonamides, one of which is and the other is not an anticonvulsant. No clear-cut data allow them to propose which are the carbonic anhydrases involved in these processes, but strong carbonic anhydrase II, VII, IX, and XII inhibition, correlated with sufficiently high liposolubility may lead to effective anticonvulsants of this pharmacological class [11].

In the year 2010 Naama Hen et. al. proposed a novel class of aromatic amides composed of phenylacetic acid or branched aliphatic carboxylic acids, with five to nine carbons in their carboxylic moiety, and aminobenzenesulfonamide were synthesized and evaluated in the anticonvulsant rat-maximal electroshock (MES) and subcutaneous metrazol seizure (scMet) tests. Fourteen of the synthesized amides had an anticonvulsant ED_{50} of <50 mg/kg in the rat-MES test. The amides 2-methyl-N-(4-sulfamoylphenyl)butyramide, 2-ethyl-N-(4-sulfamoylphenyl)butyramide, and 3,3-dimethyl-N-(4-sulfamoylphenyl)butyramide were the most potent compounds possessing MES-ED_{50} values of 7.6, 9.9, and 9.4 mg/kg and remarkable protective index values of 65.7, 50.5, and 53.2, respectively. These potent sulfanylamides caused neural tube defects only at doses markedly exceeding their effective dose [12].

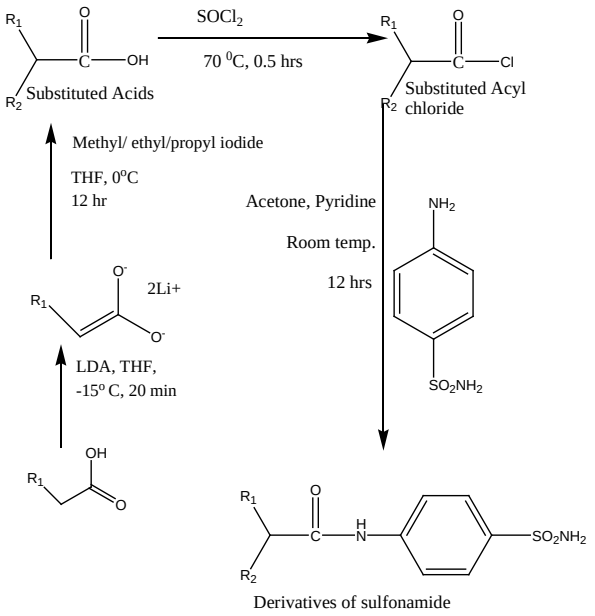


Figure 7. Synthesis of branched chain aliphatic carboxylic acids and amide derivatives

A series of 4-thiazolidinones bearing a sulfonamide group (4a-w) were prepared by Nadeem siddiqui et. al. in 2010 by cyclizing various 5-bromo-2-methoxy-N'-[(1E)-arylmethylene/arylethylidene] benzenesulfonohydrazides. All the compounds were characterized by IR, (1)H NMR, and elemental analysis. The compounds were tested for their anticonvulsant activity utilizing MES and scPTZ animal models. The majority of the compounds exhibited significant activity against both animal models; however, few compounds displayed promising activity and could be considered as leads for further investigations [13].

Manuel Koller et. al. in the year 2011 synthesized quinazoline-2,4-diones with a sulfonamide group attached to the N(3) ring atom constitute a novel class of competitive AMPA receptor antagonists. One of the synthesized compounds show nanomolar receptor affinity, whereas other examples of the series display oral anticonvulsant activity in animal models [14].

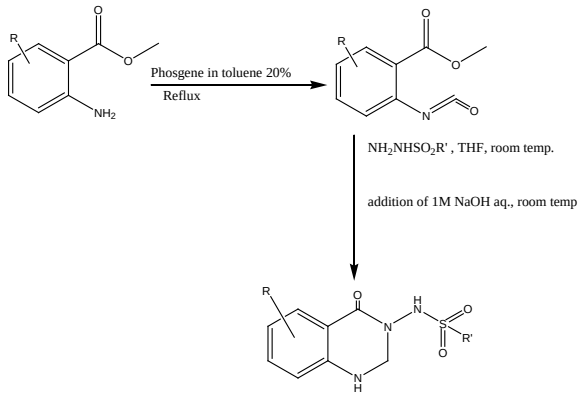


Figure 8. General access to the quinazolinedione sulfonamides

3D-QSAR methods, CoMFA region focusing (CoMFA-RF) and CoMSIA along with docking studies were carried out by Jahan B. Ghasemi et. al. in the year 2011 for investigating 32 carbonic anhydrase I inhibitors. These inhibitors have been studied for the development of antiglaucoma, antitumor, antiobesity or anticonvulsant drugs. Docking analysis by GOLD provide conformations which have been realigned in CoMFA and CoMSIA models. Training set for the CoMFA–RF and CoMSIA models using 24 docked conformations gives q^2_{Loo} values of 0.615 and 0.637 and r^2_{nv} values of 0.701 and 0.713, respectively. The results of CoMFA-RF and CoMSIA with and without docked conformations were compared. The ability of prediction and robustness of the models were evaluated by test set, cross validation (leave-one-out and leave-ten-out), bootstrapping, and progressive scrambling approaches. The all-orientation search (AOS) was used to achieve the best orientation to minimize the effect of initial orientation of the structures. The docking results confirmed CoMFA and CoMSIA contour maps [15].

Ajeet et. al. in the year 2012 suggested that novel sulfonamide derivatives are potent anticonvulsant agents on the basis of the pharmacophoric pattern of well known anticonvulsants agents of different classes. For the stated purpose they used docking as virtual screening method and it is also the basis for pharmacophoric pattern determination. They used the AutoDock software as virtual screening tool. On the basis of pharmacophoric pattern they suggested the new anticonvulsant agents.

These agents were then screened on the basis of docking procedures and further in-silico evaluation of novel agents has been performed. The docking analysis has revealed that the novel agent 2-hydroxy-2-[(4-sulfamoyl-phenylcarbamoyl)-methyl]-succinic acid (CS) shows binding with voltage gated sodium channel, GABA aminotransferase and also with voltage gated calcium channel but after comparing the number of hydrogen bonds and binding affinity, CS is supposed to be bind perfectly with GABA aminotransferase with 7 hydrogen bonds and -6.8 Kcal/mol of binding energy. The other novel agents, 6-(4-Sulfamoyl-phenylcarbamoyl)-nicotinic acid (DPS), 2-Amino-3-hydroxy-N-(4-sulfamoyl-phenyl)-propionamide (SRS) and 2,3-dihydroxy-N-(4-sulfamoyl-phenyl)-succinamic acid (TS) do not shows any binding with GABA aminotransferase while they shows binding with voltage gated sodium and calcium channels [16].

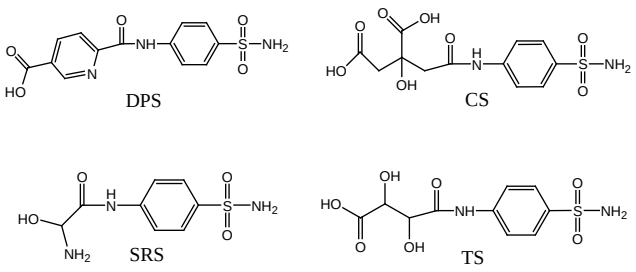


Figure 9. Novel acid derivatives of sulfonamide designed by Ajeet et. al. in 2012.

In the year 2013 Ajeet et. al. has correlated the inhibition constant of sulfonamide derivative with the fragment complexity, molecular weight and ALogP descriptors for studying the Quantitative Structure Activity Relationship (QSAR) and suggested that correlation may be an adequate predictive model which can help to provide guidance in designing and subsequently yielding greatly specific compounds that may have reduced side effects and improved pharmacological activities. They used Multiple Linear Regression (MLR) for developing QSAR model. For the validation of the developed QSAR model, statistical analysis such as cross validation test (LOO-CV and LFO-CV), quality factor, fischers test, root mean square deviation (RMSD), standard deviation, variance, Y-randomization test etc.; have been performed and all the tests validated this QSAR model with fraction of variance r^2 = 0.8103, LOO-CV q^2 = 0.8080 and LFO-CV q_f^2 = 0.8018 [17]. The suggested model is given as follows-

$$\begin{aligned}\log Ki &= 1.501718\ (0.6738898)\\ &-0.3703334\ (0.1807285)(\text{AlogP})\\ &-0.0253653\ (0.0076488)(\text{FC})\\ &+0.0012944\ (0.0034213)(\text{Mol.Wt.})\end{aligned}$$

Christophe Salome et. al. in 2010 has worked and established the structure-activity relationship (SAR) for the N-benzyl group in the clinical antiepileptic agent (R)-lacosamide [(R)-N-benzyl 2-acetamido-3-methoxypropionamide, (R)-3]. They prepared 43 compounds and then evaluated at the National Institute of Neurological Disorders and Stroke Anticonvulsant Screening Program for seizure protection in the maximal electroshock (MES) and subcutaneous Metrazol models. On comparing activities for two series of substituted aryl regioisomers they found that 40-modified derivatives had the highest activity. It was stated that structural latitude existed at the 40-site. The SAR indicated that non-bulky 40-substituted (R)-3 derivatives exhibited superb activity, independent of their electronic properties. It was also concluded that MES test of several compounds were comparable with or exceeded that of (R)-3 and surpassed the activities observed for the traditional antiepileptic agents phenytoin, phenobarbital, and valproate [18].

3. Developments to sulfonamides Having Activities other than Anticonvulsant

According to Uday Kalidhar et. al. Benzimidazoles and sulfonamides play an important role in medical field with so many pharmacological activities such as antimicrobial, antiviral, antidiabetic and anticancer activity. They said that potency of these clinically useful drugs in treatment of microbial infections and other activities encouraged them to development some more potent and significant compounds. They found Benzimidazoles remarkably effective and extensively biochemical and pharmacological studies have confirmed these molecules effective against various strains of microorganisms [1].

In 2011, Naama Hen et. al. had synthesized Aromatic amides comprising branched aliphatic carboxylic acids and 4-aminobenzenesulfonamide and them evaluated for their inhibition of carbonic anhydrase (CA) isoforms. Of the most anticonvulsant-active compounds, only few were potent inhibitors of CAs VII and XIV. Their structural studies suggest that differences in the active sites' hydrophobicity modulate the affinity of the inhibitors [19].

They obtained these compounds by coupling of 4-aminobenzenesulfonamides or 4-alkylamino-benzenesulfonamides (alkyl = methyl or ethyl) with phenylacetic acid or branched aliphatic carboxylic acids. Naama Hen et. al. studied hydrophobicity differences in the CA isoforms, it clearly showed that small differences in hydrophobic residues in the CA active sites modulate the affinity of the inhibitors with various aliphatic chains. But in the series of 4-aminobenzenesulfonamide derivatives, Naama Hen et. al. emerged with little correlation between anticonvulsant (MES) activity and inhibition of CA I, II, VII, or XIV. They also consider that most AEDs including the CAIs AAZ, TPM, and ZNS have multiple mechanisms of action, there are many unknown issues regarding the correlation between CAs' inhibition and AEDs' activity, and therefore, resolving them is not so straightforward (because of too many CA isoforms) [19].

The binding of zonisamide to purified, recombinant monoamine oxidases (MAOs) has been investigated by Claudia Binda et. al. in 2011. They found it a competitive inhibitor of human MAO B, of rat MAO B and of zebrafish MAO. No inhibition is observed with purified human or rat MAO A. They found that 1.8 A° structure of the MAO B complex demonstrated its binding within the substrate cavity [20].

In 2012 a series of new sulfonamide derivatives of tryptamine as N-(2-(1H-indol-3-yl)ethyl)-substituted-sulfonamides were synthesized by simple substitution of

sulfonyl chlorides containing pharmacologically active functionalities with tryptamine in presence of triethylamine by T. Narasaiah et. al. Structures of all the newly synthesized compounds were characterized by them with IR, ^{1}H, ^{13}C NMR, mass and elemental analysis. They evaluated antimicrobial activity of the compounds and minimum inhibitory concentrations were also determined by them at two different concentrations (100, 200 µg/mL) and found fluorinated and nitrogenated sulfonamides active. T. Narasaiah et. al. also said that few of the titled compounds also exhibited potential antibacterial and antifungal activities [21].

Nassir N. Al-Mohammed et. al. has synthesized novel substituted sulfonamide compounds in the year 2013 and their structures were confirmed by ^{1}H-NMR, ^{13}C-NMR, FT-IR, and mass spectroscopy. They screened the compounds for antibacterial activities against standard strains of 6 Gram positive and 4 Gram negative bacteria using the micro broth dilution assay. They stated that most of the compounds studied showed promising activities against both types of bacteria [22].

In the year 2014, Aneta Kołaczek et. al. said that synthesis of sulfonamide derivatives has been reported in many ways. They assumed that these classes of compounds are considered as "scalffolds" in medicinal chemistry to drug development with different biological activities. In concern to organic chemistry, these compounds have a functional application in the industry in some products of health, food colorants and others, therefore it is necessary to continue with research projects that help to synthesize new compounds with sulfonamide group [23].

Substituted N-acetyl-4-amino-benzenesulfonamide derivatives were designed by Ajeet et. al. in 2014 using ChemDraw Ultra 7.0 and energy minimization of derivatives was achieved with Chem3D Pro of ChemOffice suit, keeping in view the structural requirements of pharmacophore. Their proposed synthesis along with in-silico study (docking analysis) in favor of antimicrobial activity has been shown in this work with the possible mechanism of reaction. Docking studies were carried out to study the binding properties of drugs with molecular targets with the help of AutoDock Vina (Python-Prescription 0.8). Titled compounds exhibited good binding properties with molecular target pseudomonas aeruginosa exotoxin A in Lamarckian genetic algorithm based flexible docking studies [24].

A series of substituted 4-amino-benzenesulfonamides / N-acetyl-4-amino-benzenesulfonamide were designed & synthesized keeping in view the structural requirements of pharmacophore and were evaluated for *in-silico* antimicrobial activity by Ajeet et. al. in the year 2014. For establishing the structure, spectral characterization like FT-IR, 1H NMR, GC-MS and elemental analysis (CHNS) has been performed by them. The antimicrobial activity of the titled compounds was assessed using *in-silico* studies (QSAR screening and Docking). They said that it was carried out for the prediction of pharmacokinetic properties and to study the binding properties of drugs with molecular targets. They also concluded that titled compounds exhibited good binding properties with molecular target. They stated that molecular target responsible for the antimicrobial activity of substituted 4-amino-benzenesulfonamides / N-acetyl-4-amino-benzenesulfonamides may be pseudomonas aeruginosa exotoxin A [25].

In the context of studying the treatment of cancer Sapna Rani et. al. has found the significant effects of the derivatives of the sulfonamides, this promotes them to design novel derivatives by the means of in-silico resources with anticancer effects. They performed this study with the help of Chemdraw Ultra 7.0, AutoDock Vina (Python Prescription 0.8), and PaDEL software. Their results revealed that ligand-protein interaction affinity of all designed molecules ranges from -6.8 Kcal/mol to -8.6 Kcal/mol which is approximately comparable to pre-existing human topoisomerase II inhibitor i.e. etoposide (CID: 36462, ligand-protein interaction affinity is -9.7 Kcal/mol) [26].

Ajeet et. al. in the year 2014 stated that the purpose of work was to design derivatives of Quinazolinedione sulfonamide as anti-bacetrial agents with the help of computing software and docking procedures. They said that Quinazolinediones are fluoroquinolone-like inhibitors of bacterial gyrase and sulfonamides have highest powerful antibacterial activity, so, a hybrid of these two agents has been designed by them. This work has been performed with the help of Chemdraw Ultra 7.0, AutoDock Vina. For the studies Bacillus subtilis lipase A, E-coli primosomal protein and heterodimeric hexaprenyl diphosphate synthase has been taken by Ajeet et. al. Their results reveal that the protein-ligand interaction energy of one of derivatives was -5.9 Kcal/mol which is much closer to standard drug (CID no. 4539) as -6.2 Kcal/mol when the derivatives were treated with Bacillus subtilis lipase A. But they found exciting results when treating the derivatives with E-coli primosomal protein, and heterodimeric hexaprenyl diphosphate synthase [27].

4. Conclusion

In summary, it could be concluded that the sulfonamides have too many possibilities to be synthesize and it has a number of possible pharmacological activities especially when we thought about the anti-convulsants and anti-microbial. These compounds have unlimited possibilities in industries too, therefore related researches should be carried out much more to synthesize novel derivatives of sulfonamide with varying pharmacological activities.

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