Power System Technology
ISSN:1000-3673

Received: 16-01-2024 Revised: 12-02-2024 Accepted: 07-03-2024

Exploring the Antibacterial Potential of Gabapentin Sulfonamide Analogues: Synthesis and Characterization

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ABSTRACT

Gabapentin Sulfonamide (2-(1-((4-methylphenylsulfonamido) methyl) cyclohexyl acetic acid) **(3F)** and their novel derivatives were synthesized. Gabapentin **(1F)** reacted with other reactant 4-methyl benzenesulphonyl chloride ($C_7H_7ClO_2S$) **(2F)** in the presence of 10% Na_2CO_3 to synthesize the 2-(1-((4-methylphenylsulfonamido) methyl) cyclohexyl acetic acid **(3F).** This product **(3F)** was applied more for the preparation of derivatives of Gabapentin sulfonamide upon reaction with a series of organic alkyl/aralkyl halides by the application of base LiH and solvent DMF. Synthesized compounds were checked for their antibacterial activity by using various strains of bacteria including *Escherichia Coli*, *Streptococcus faecalis*, *S. typhi*, *Staphylococcus aureus* and *Pseudomonas aeruginosa* which showed excellent inhibited activity. Among the bacterial species, the compounds **5Fb** and **5Fc** have outstanding antibacterial activity for *Pseudomomas aeruginosa (-) ATCC 14502* with zone of inhibition comparable with control drug (MIC 12.18). All the compounds were moderately to low active against the *S. typhi*. Structures of all the derivatives was confirmed by using UV- visible, IR, ^{1}H-NMR and mass spectrometry.

Keywords: (2-(1-((4-methylphenylsulfonamido) methyl) cyclohexyl, Gabapentin, 4-methyl Benzene Sulfonylchloride, antibacterial activity.

Power System Technology
ISSN:1000-3673

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1. INTRODUCTION

Domagk first identified Prontosil's azo dye's that have antibacterial capabilities leading to the creation of sulfa medicines in 1935[1]. In the early 30s the drugs of sulfonamides were discovered which work as antibacterial drugs and that was very fascinating time for chemotherapeutic agents. The synthesis of folic acid in bacteria is catalyzed by an enzyme Dihydropteroate synthase (DHPS). Sulfonamides show their effective activity by the incorporating para amino benzoic acid (PABA) which will act on the enzyme (DHPS) which will not work effectively to catalyzes the pathways for synthesis of folic acid in bacteria. In this way this sulfonamide will stop the growth of bacteria and so have bacteriostatic activity[2]. The molecules consist of $–SO_2NH-$ functional group are known as sulfonamides[3]. This group is present in different biologically active compounds where it is responsible for anti-microbial activity[4]. Sulphonamide due to the presence of free amino group can be used for the synthesis of sulphonamide derivatives. This group can easily be changed by the derivatization[5]. Sulfonamides which are antibiotic are derived from the sulfanilamide and they have attached substituent to N_1 position and aromatic amine at position of N_4[6]. The synthesis of folic acid in bacteria is blocked due to presence of sulphonamide group which results to reduce or treat infections caused by bacteria[7]. Various derivatives of sulphonamide are used as anti-oxidants. Sulphonamide are extensively used as anti-cancer, anti-obesity, anti-inflammatory, and anti-thyroid. Sulphonamide is also used as an HIV protease inhibitor[8]. Sulphonamide compounds have various applications in pharmaceutics due to their due to their antiviral[9], anti-inflammatory, and anticancer activity[10]. Their antifungal activity also studied and investigated against Fausarium solani, Candida glabrata, Aspergillus flavus[5]. The presence of amino group in sulfone group at position 4 will cause sulfonamide to be antagonized by PABA. The decreased activity of sulfonamide occurs if its benzene ring is replaced by some other ring systems[11]. Widely used sulfa medicines that possess sulfa groups include Sulfisoxazole[12], Sulfamethoxazole[13], and Sulfadiazine[14]. Sulphonamide that is absorbed readily and also shows rapid elimination, most often introduced into the body systematically[15]. Human neuropathic pain can be effectively managed with the anticonvulsant medication Gabapentin[16]. Co(II) complexes have been found to have antioxidant, antifungal, and antibacterial properties. In addition, gabapentin and Co(II) metal ions had antifungal and antibacterial properties[17]. Gabapentin is a second-generation neuroleptic medication licenced by the Food and Drug Administration (FDA), with dorothy effects and a structure similar to gamma-aminobutyric acid. Gabapentin has been shown to be helpful in treating a variety of neuropathic problems, such as painful neuropathy caused by diabetes, cancer neuropathy, trigeminal neuropathy[18], and bipolar disorders[19]. Gram positive bacteria were found to be more susceptible to the antibacterial effects of hydrazide-hydrazone scaffolds generated from gabapentin than Gram negative bacteria and also exhibit antioxidant activity[20]. Since no work has been performed to carry out synthesis of gabapentin sulphonamide derivatives so due to pharmaceutic significance of sulphonamide compounds, we have executed a scheme for the manufacturing, antibacterial activity for different bacteria species including gram +ve bacteria as well as gram negative and

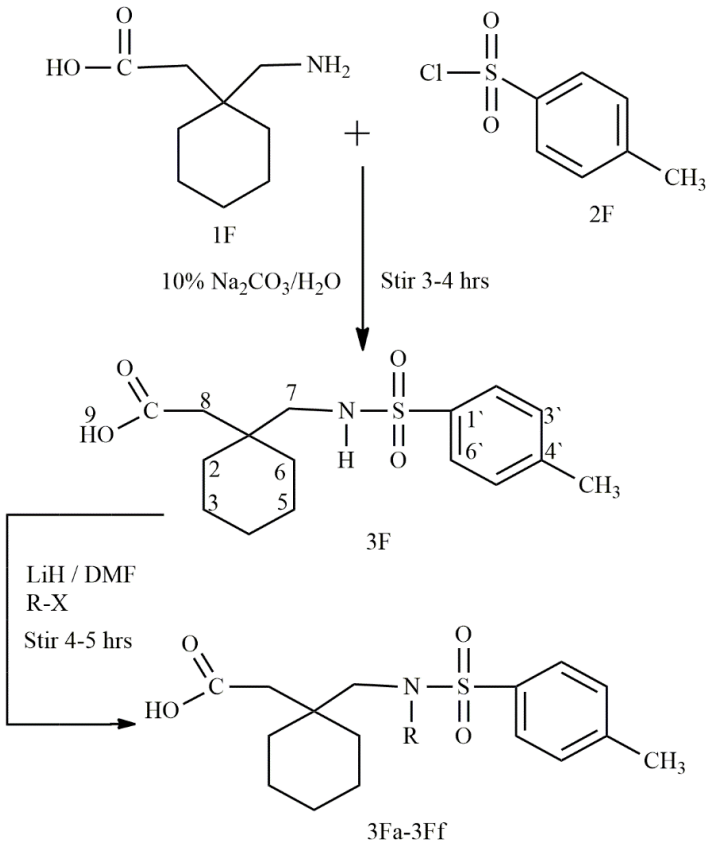
Power System Technology
ISSN:1000-3673
Received: 16-01-2024 Revised: 12-02-2024 Accepted: 07-03-2024

structure of all derivatives was evaluated using IR spectroscopy, mass spectrometry and ^{1}H-NMR spectroscopy.

2. EXPERIMENTAL

2.1. General

All the chemical used 2-(1-(aminomethyl) cyclohexyl) acetic acid (gabapentin), 4-methyl benzene sulfonylchloride were purchased from Sigma Aldrich. TLC was employed to check the pureness for prepared compounds and this technique was applied to measure the work advancement by use



Scheme-1: Outline scheme for the synthesis of parent compound 2-(1-((4-methylphenylsulfonamido) methyl) cyclohexyl acetic acid (3F) and its derivatives (3Fa to 3Ff)

of methanol(MeOH) and n-hexane as solvents with varying concentration. Ceric sulphate solution was used for better visualization to observe TLC plates under light of UV at 254 nm. Determination of Melting points (M.P) of all the manufactured compounds were done by using Gallenkamp. The IR spectrum is obtained in KBr pellet by using Thermo scientific NICOLET IS10 spectrophotometer. The ^{1}H-NMR spectra was taken at 400MHz using CDCl3 as solvent.

Power System Technology
ISSN:1000-3673

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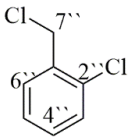
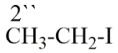
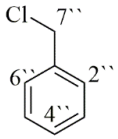
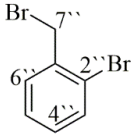
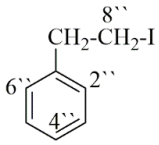
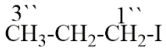
R-x=Different alkyl halide for synthesis of parent 2-(1-((4-methylphenylsulfinamido) methyl) cyclohexyl acetic acid sulfonamide derivatives

Compd. No.	R-X	Compd. No.	R-X
(3Fa)		(3Fd)	
(3Fb)		(3Fe)	
(3Fc)		(3Ff)	

2.2.General method for the preparation of 2-(1-((4-methylphenylsulfinamido) methyl) cyclohexyl acetic acid (3F)

1.0 g (0.00584 mol) of 2-(1-(aminomethyl)cyclohexyl) acetic acid weighed and taken in flask. And then other reagent 4-methylbenzene-1-sulfonyl Chloride (0.00584 mol) also taken in the same flask. The pH (9-10) of the system was maintained by the mixing of 10% aqueous soln. of the sodium carbonate (Na_2CO_3) at room temperature. And then stirring of reaction system was carried out for 3 to 4 hrs. TLC plate was used to check the progress of proceeding reaction. The precipitates were then filtered to collect the product and washed with distilled water/ether to get the parent compound **(3F)** on drying. The synthesis of parent compound 3F shown in scheme 1.

2.2.1. 2-(1-((4-methylphenylsulfonamido)methyl)cyclohexyl)acetic acid (3F)

M.F; $C_{16}H_{23}NO_4S$,M.wt: 325.42 $gmol^{-1}$, yield 75%, m.p 239, IR Stretching (KBR, V_{max}/cm): 3350 (O-H), 1715 (C=O), 3400 (N-H), 1100 (C-N), 1357 (S=O), 1475 (C=C); ^1H NMR (400 MHz, CDCl3, ppm): δ 1.56, 1.31 (m, *J* = 16.38, 4H, H-2 & H-6), 1.53,1.43 (m, *J* = 12.92, 4H, H-3 & H-5), 1.49, 1.47 (m, *J*= 11.87, 2H, H-4), 3.08 (s, 2H, H-7), 2.15 (s, 2H, H-8), 11 (s, 1H, H-9), 7.74 (d, *J* = 8.04, 2H, H-2` & H-6`), 7.40 (d, *J* = 8.04, 2H, H-3` & H-5 EI-MS: m/z 327.40

Power System Technology
ISSN:1000-3673
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$[M+2]^+$, 325.42 $[M]^+$, 141.19 $[M-C_8H_{10}NSO_2]^+$, 155.22 $[M-C_9H_{16}NO_2]^+$, 233.32 $[M-C_7H_7]^+$, 91.13 $[M-C_9H_{16}NO_4S]^+$

2.3 General process for the synthesis of derivatives of N-alkyl/aralkyl substituted (3Fa to 3Ff)

After making solution of compound (**3F**), 0.5g (0.00154 mol) of this compound weighed and added in the flask of 100 ml. The solvent added in the mixture was DMF (5ml). To proceed the reaction a strong base LiH (0.003 g) was introduced in the flask. Then the different aralkyl/aryl/alkyl halides (0.00154 mol) as shown in table 1 were added in the same flask containing the reaction media. After this the mixture was stirred for almost 4-5hrs to carry out reaction suitably. The forwarding of the reaction was examined by the use of TLC plates with different solvents of varying concentration. Then the precipitates produced in this reaction filtered. After filtration the collected product washed with water and dry to get synthesized compounds. Scheme 1 shows the general synthesis steps.

2.3.1. 2-(1-((N-(2-chlorobenzyl)-4-methylphenylsulfonamido)methyl)cyclohexyl)acetic acid (3Fa):

Molecular Formula $C_{23}H_{28}ClNO_4S$, Molecular Weight 449.02 $gmol^{-1}$, yield 77%, m.p 344, IR Stretching (KBR, V_{max}/cm): 3348 (O-H), 1712 (C=O), 1080 (N-C), 1352 (S=O), 1473 (C=C); ^1H NMR (400 MHz, CDCl3, ppm): δ 1.54,1.33 (m, *J* = 16.39, 4H, H-2 & H-6), 1.50, 1.41 (m, *J*= 12.90, 4H, H-3 & H-5), 1.46, 1.48 (m, *J*=11.87, 2H, H-4), 3.07 (s, 2H, H-7), 2.1 (s, 2H, H-8), 9.01 (s, 1H, H-9), 7.73 (d, *J* = 8.04, 2H, H-2` & H-6`), 7.40 (d, *J* = 8.04, 2H, H-3` & H-5`), 4.42 (s, 1H, H-1``), 7.45 (t, *J* = 8.10, 1H, H-3``), 7.31 (m, *J* = 8.10, 1H, H-4``), 7.19 (t, *J* = 8.06, 1H, H-5``), 7.35 (d, *J* = 8.06, 1H, H-6``), 4.56 (s, 2H, H-7``) ; EI-MS: m/z 451.01 $[M+2]^+$, 449.02 $[M]^+$, 308 $[M-C_8H_{13}O_2]^+$, 155.19 $[M-C_{16}H_{21}ClNO_2]^+$, 91.09 $[M-C_{16}H_{21}ClNO_4S]^+$

2.3.2. 2-(1-((N-benzyl-4-methylphenylsulfonamido)methyl)cyclohexyl)acetic acid (3Fb):

Molecular Formula $C_{23}H_{29}NO_4S$, Molecular Weight 415.57 $gmol^{-1}$, yield 72%, m.p 257, IR Stretching (KBR, Vmax/cm): 3345 (O-H), 1710 (C=O), 1078 (N-C), 1351 (S=O), 1470 (C=C); ^1H NMR (400 MHz, CDCl3, ppm): δ 1.55,1.30 (m, *J* = 16.37, 4H, H-2 & H-6), 1.52, 1.40 (m, *J* = 12.92, 4H, H-3 & H-5), 1.48, 1.46 (m, *J* = 11.86, 2H, H-4), 3.08 (s, 2H, H-7), 2.15 (s, 2H, H-8), 10 (s, 1H, H-9), 7.72 (d, *J* = 8.05, 2H, H-2` & H-6`), 7.41 (d, *J* = 8.01, 2H, H-3` & H-5`), 7.3 (d, *J* = 8.07, 2H ,H-2``& H-3``), 7.23 (m, *J* = 7.72, 1H, H-4``), 7.28 (t, *J* = 7.86, 1H, H-5``), 7.20 (d, *J* = 7.87, 1H, H-6``), 4.59 (s, 2H, H-7``), EI-MS: m/z 417.49 $[M+2]^+$, 415.57 $[M]^+$, 274 $[M-C_8H_{13}O_2]^+$, 155.20 $[M-C_{16}H_{22}NO_2]^+$, 91.08 $[M-C_{16}H_{22}NO_4S]^+$

2.3.3. 2-(1-((4-methyl-N-phenethylphenylsulfonamido)methyl)cyclohexyl)acetic acid (3Fc):

Molecular Formula $C_{24}H_{31}NO_4S$, Molecular Weight: 429.60 $gmol^{-1}$, yield 80%, m.p 263, IR Stretching (KBR, Vmax/cm): 3347 (O-H), 1713 (C=O), 1081 (N-C), 1353 (S=O), 1472 (C=C); ^1H NMR (400 MHz, CDCl3, ppm): δ 1.52,1.29 (m, *J* = 16.38, 4H, H-2 & H-6), 1.54, 1.43 (m, *J* = 12.91, 4H, H-3 & H-5), 1.49, 1.47 (m, *J* = 11.85, 2H, H-4), 3.09 (s, 2H, H-7), 2.14 (s, 2H, H-8

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ISSN:1000-3673
Received: 16-01-2024 Revised: 12-02-2024 Accepted: 07-03-2024

), 11 (s, 1H, H-9), 7.70 (d, *J* = 8.04, 2H, H-2` & H-6`), 7.40 (d, *J* = 8.04, 2H, H-3` & H-5`), 7.1 (d, *J* = 7.83, 2H, H-2``& H-6``), 7.24 (t, *J* = 7.82, 2H, H-3``& H-5``), 7.18 (m, *J* = 7.73, 1H, H-4``), 2.96 (d, *J* = 6.99, 2H, H-7``), 3.5 (d, *J* = 6.99, 2H, H-8``), EI-MS: m/z 431.58 $[M+2]^+$, 429.60 $[M]^+$, 338.02 $[M-C_7H_7]^+$, 155.22 $[M-C_{17}H_{24}NO_2]^+$, 288.01 $[M-C_8H_{13}O_2]^+$, 91.01 $[M-C_{17}H_{24}NO_4S]^+$

2.3.4. 2-(1-((N-ethyl-4-methylphenylsulfonamido)methyl)cyclohexyl)acetic acid (3Fd):

Chemical Formula $C_{18}H_{27}NO_4S$ Molecular Weight 353.50 $gmol^{-1}$, yield 77%, m.p 271, IR Stretching (KBR, Vmax/cm): 3340 (O-H), 1711 (C=O), 1076 (N-C Stretching),1351 (S=O), 1470 (C=C); ^1H NMR (400 MHz, CDCl3, ppm): δ 1.56,1.31 (m, *J*= 16.38, 4H, H-2 & H-6), 1.53,1.41 (m, *J*= 12.90, 4H, H-3 & H-5), 1.48,1.46 (m, *J* = 11.86, 2H, H-4), 3.08 (s, 2H, H-7), 2.16 (s, 2H, H-8), 10.99 (s, 1H, H-9), 7.74 (d, *J* = 8.03, 2H, H-2` & H-6`), 7.41 (d, *J* = 8.04, 2H, H-3` & H-5`), 3.39 (q, *J* = 7.02, 2H, H-1``), 1.14 (t, *J* = 7.02, 3H, H-2``); EI-MS: m/z 455 $[M+2]^+$, 453 $[M]^+$, 338.01 $[M-CH_3]^+$, 155.22 $[M-C_{11}H_{20}NO_2]^+$, 212.50 $[M-C_8H_{13}O_2]^+$, 91.01 $[M-C_{11}H_{20}NO_4S]^+$

2.3.5. 2-(1-((N-(2-bromobenzyl)-4-methylphenylsulfonamido)methyl)cyclohexyl)acetic acid (3Fe):

Molecular Formula $C_{23}H_{28}BrNO_4S$, Molecular Weight 494.47 $gmol^{-1}$, yield 86%, m.p 2 IR Stretching (KBR, Vmax/cm): 3348 (O-H), 1720 (C=O),1079 (N-C),1352 (S=O),1472 (C=C); ^1H NMR (400 MHz, CDCl3, ppm): δ 1.54,129 (m, *J* = 16.38, 4H, H-2 & H-6), 1.50,1.43 (m, *J* = 12.92, 4H, H-3 & H-5), 1.49,1.47 (m, *J* = 11.87, 2H, H-4), 3.09 (s, 2H, H-7), 2.17 (s, 2H, H-8), 11 (s, 1H, H-9), 7.76 (d, *J* = 8.03, 2H, H-2` & H-6`), 7.40 (d, *J* = 8.02, 2H, H-3` & H-5`),7.47 (t, *J* = 8.05, 1H, H-3``), 7.28 (m, *J* = 8.06, 1H, H-4``), 6.92 (t, *J* = 8.14, 1H, H-5``), 7.31 (d, *J* = 8.14, 1H, H-6``), 4.61 (s, 2H, H-7``); EI-MS: m/z 496.45 $[M+2]^+$, 494.47 $[M]^+$, 353.46 $[M-C_8H_{13}O_2]^+$, 155.21 $[M-C_{16}H_{21}NO_2]^+$,91.13 $[M-C_{16}H_{21}BrNO_4S]^+$

2.3.6. 2-(1-((4-methyl-N-propylphenylsulfonamido)methyl)cyclohexyl)acetic acid (3Ff):

Molecular Formula $C_{19}H_{29}NO_4S$, molecular weight 367.53 $gmol^{-1}$, yield 83%, m.p 283, IR Stretching (KBR, Vmax/cm): 3344 (O-H), 1712 (C=O),1076 (N-C),1350 (S=O),1470 (C=C); ^1H NMR (400 MHz, CDCl3, ppm): δ 1.57,1.31 (m, *J* = 16.37, 4H, H-2 & H-6), 1.54,1.45 (m, *J* = 12.90, 4H, H-3 & H-5), 1.50,1.49 (m, *J* = 11.86, 2H, H-4), 3.08 (s, 2H, H-7), 2.12 (s, 2H, H-8), 11.01 (s, 1H, H-9), 7.78 (d, *J* = 8.07, 2H, H-2` & H-6`), 7.41 (d, *J* = 8.01, 2H, H-3` & H-5`), 3.31 (t, *J* = 7.07, 2H, H-1``), 1.15 (m, *J* = 7.09, 2H, H-2``), 0.09 (t, *J* = 7.10, 3H, H-3``); EI-MS: m/z 369.51 $[M+2]^+$, 367.53 $[M]^+$, 338 $[M-C_2H_5]^+$, 155.19 $[M-C_{12}H_{22}NO_2]^+$, 226.53 $[M-C_8H_{13}O_2]^+$, 91.12 $[M-C_{12}H_{22}NO_4S]^+$

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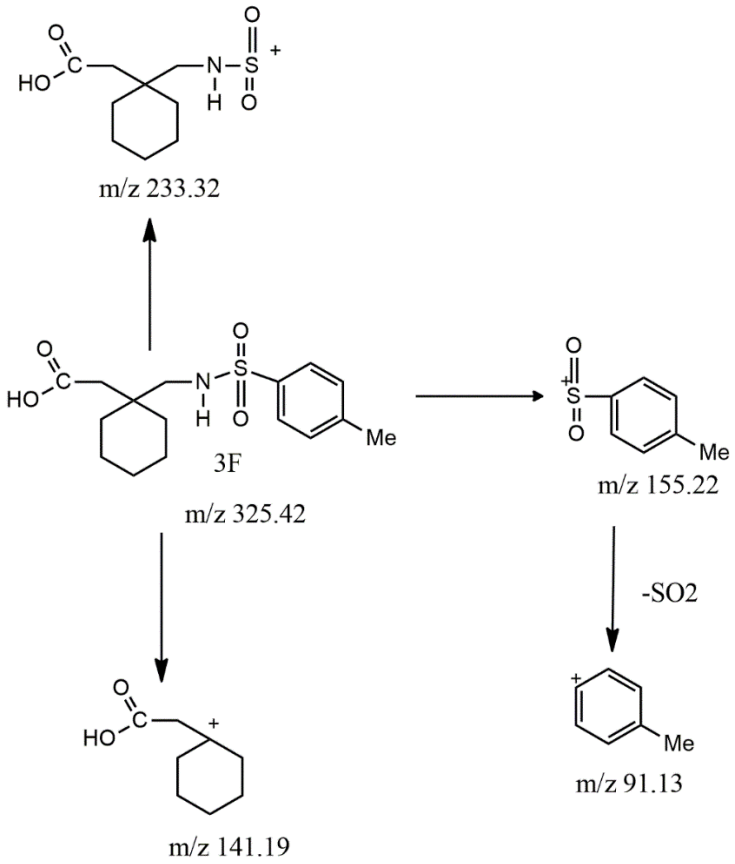

Figure 1. Mass spectrometry Fragments of parent compound(3F)

2.4 Antibacterial Assay

By using the broth dilution method in accordance with the CLSI 2012 standard methodology, the MIC for the test solutions was obtained. The cultures were serially diluted until they reached a density of 2X 10^4 cells per ml. Haemocytometer was used to count the number of cells.100 µL of cell culture were injected into 2 milliliters of MHA broth that was poured into tubes. Each tube was then filled with 100 µL of various concentrations of antibiotic (4.25, 8.5, 17.0, 34.0, and 68 mg/ml). Every experiment was conducted in conjunction with growth control. For 48 hours, anaerobic jars were used to incubate every test tube. The determination of optical density at 600nm was carried out by following the incubation period. MIC was determined as the lowest extract concentration that prevented 20% of the test microorganisms from growing. The MIC was described as the quantity or concentration at which color changed the least. Bacterial inhibition percentage % was calculated by applying following equation:

%age of inhibition: (Control OD − (Sample OD/Control OD)) × 100.

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Table 2.
Anti-bacterial activity values of Minimum Inhibitory Concentration (MIC)

Compounds	*Escherichla coli (-)* ATCC 10536		*Pseudomonas aeruginosa (-)* ATCC 14502		*Streptococcus faecalis (+)* ATCC 10541		*Staphylococcus aureus (+) PS* ATCC 6538 p		*S. typhi(-)*	
	%) Inhibition	MIC	%) Inhibition	MIC	%) Inhibition	MIC	%) Inhibition	MIC	%) Inhibition	MIC
3F	76.65 ±1.99	11.2 ± 2.10	81.1± 41.80	13.55± 2.35	68.01± 1.67	13.50± 3.05	64.25± 3.05	13.40±5.2	64.60± 2.57	16.15± 1.16
3Fa	69.93 ±2.90	9.28 ± 1.45	71.16 ±1.30	14.36± 1.67	50.61± 3.72	17.53± 3.45	63.86±2.69	21.40± 2.0	73.45± 5.15	20.14± 2.0
3Fb	67.40 ±1.69	>500	70.11± 2.25	12.11± 1.70	60.01± 1.32	15.13± 2.12	58.30±2.14	18.95±4.45	53.01± 2.0	19.01± 2.91
3Fc	67.35 ±2.1	17.1 ± 1.86	64.90± 1.30	12.14± 3.07	53.17± 3.60	14.68 ±5.62	53.01± 1.91	14.20± 2.81	70.55 ±5.45	19.03± 4.35
3Fd	67.37 ±1.73	10.41± 1.27	52.21± 2.15	16.01± 1.10	60.74± 0.78	54.10 ±2.06	66.77± 2.09	15.55± 5.55	65.65± 5.30	15.37± 4.95
3Fe	65.57 ±1.53	8.93 ± 2.95	50.10± 1.95	20.66± 3.00	45.45± 1.47	55.64± 3.50	52.18±1.0	67.55± 5.76	40.60± 3.30	11.45± 5.89
3Ff	51.84 ±3.0	>500	50.55± 2.10	11.03± 4.13	60.36± 2.44	66.67± 3.60	39.18 2.23	46.79±3.23	75.60± 0.45	11.89± 4.0
Ciprofloxacin	80.14 ±2.0	0.625±2.31	80.14± 2.11	0.625± 1.84	80.24± 2.01	91.14± 0.02	1.26±0.11	1.25 ±1.10	8.14±2.10	1.25±2.01

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Received: 16-01-2024 Revised: 12-02-2024 Accepted: 07-03-2024

3. RESULTS AND DISCUSSION

2-(1-((4-methylphenylsulfonamido) methyl) cyclohexyl acetic acid (3F) was synthesized by the reaction of 2-(1-(aminomethyl) cyclohexyl) acetic acid with 4-methylbenzene-1-sulfonyl Chloride. Derivatives of parent compound (3F) were also synthesized by the reaction of different alky/aralkyl groups in the presence of base LiH as activating group. All the established compounds were tested for their antibacterial function against *Escherichla coli (-) ATCC 10536, Pseudomonas aeruginosa (-) ATCC 14502, Streptococcus faecalis (+) ATCC 10541, Staphylococcus aureus (+) PS ATCC 6538 p and S. typhi (-)* by using ciprofloxacin as reference antibacterial drug by following the guidelines of CLSI. Among the bacterial species, the compounds **3Fb** and **3Fc** have outstanding antibacterial activity for *Pseudomonas aeruginosa* ***(-)*** ATCC 14502 with zone of inhibition comparable with control drug (MIC 12.18). Compounds **3Fa** (MIC 9.28), and **3Fe** (MIC 8.93), exhibited excellent activities against *E. coli* analogous with zone of inhibition as by reference ciprofloxacin, while **3Fb** and **3Ff** manifest no activity (MIC > 500). The residual compounds were adequate active against the stated strain. All the compounds were moderately to low active against the *S. typhi.* Compounds **3Fb** (MIC18.95±4.45), **3Fd** (MIC 15.55), and **3Fa** (MIC 21.40) exhibited moderate activity, while **3Fe** showed reduced activity against the *S. aureus*. The MIC concentration values and zone of inhibitions are presented in Table-2. Various spectroscopic methods (^{1}H-NMR, IR, and EI-MS) were utilized to confirm the molecular framework of all prepared compounds. The distinguished peak in EI-MS showed at m/z 325.42 was the peak of molecular ion. While the other two peaks at m/z 155.22 and 91.13 shows methyl benzene sulfonyl and methyl benzene presence in the parent (3F) compound. EI-MS fragments of parent compound shown in figure 1. The existence of different bands was ensured by IR spectrum investigation. In IR spectrum (O-H) group stretching occurred at 3350 cm^{-1} and (C=O) stretching shows at 1715 cm^{-1}. Similarly, other peaks at 3400 cm^{-1}, 1357 $cm^{-}1$, 1100 cm^{-1}, & 1475 cm^{-1} showed the stretching frequency of different functional groups (N-H), (S=O), (C-N), and (C=C) respectively. ^{1}H-NMR spectra showed signals at δ(ppm) 7.74 (d, *J* = 8.04, 2H, H-2`& H-6`) and 7.40 (d, *J* = 8.04, 2H, H-3` & H-5`) downfield shift due to electron-withdrawing effect of sulfonyl group attached with benzene. The presence of cyclohexane ring in Gabapentin compound was confirmed by the signal that showed at δ1.56, 1.31 (m, *J* = 16.38, 4H, H-2 & H-6), 1.53,1.43 (m, *J* = 12.92, 4H, H-3 and H-5). The other signals at 3.08 (s, 2H, H-7), 2.15 (s, 2H, H-8) confirmed the presence of $–CH_2$ groups attached to nitrogen and acetyl group of sulfonamides. So, the name of compound (3F) given was 2-(1-((4-methylphenylsulfonamido) methyl) cyclohexyl acetic acid.

4. CONCLUSION

The synthesis of new derivatives (3Fa to 3Ff) of compound (3F) and their anti-bacterial activity with biological activity being studied in this article. The preparation methods were simple and all the compound were obtained in excellent yields. Antibacterial activity of compound 3Fb and 3Fc showed outstanding results. The parent compound (3F) and their derivatives (3Fa to 3Ff) would

Power System Technology
ISSN:1000-3673
Received: 16-01-2024 Revised: 12-02-2024 Accepted: 07-03-2024

be used as best pharmacological agents for various clinical sectors that may help in the formation of novel medicines.

Data Availability

The data that support the findings of this study are available from the corresponding author upon reasonable request.

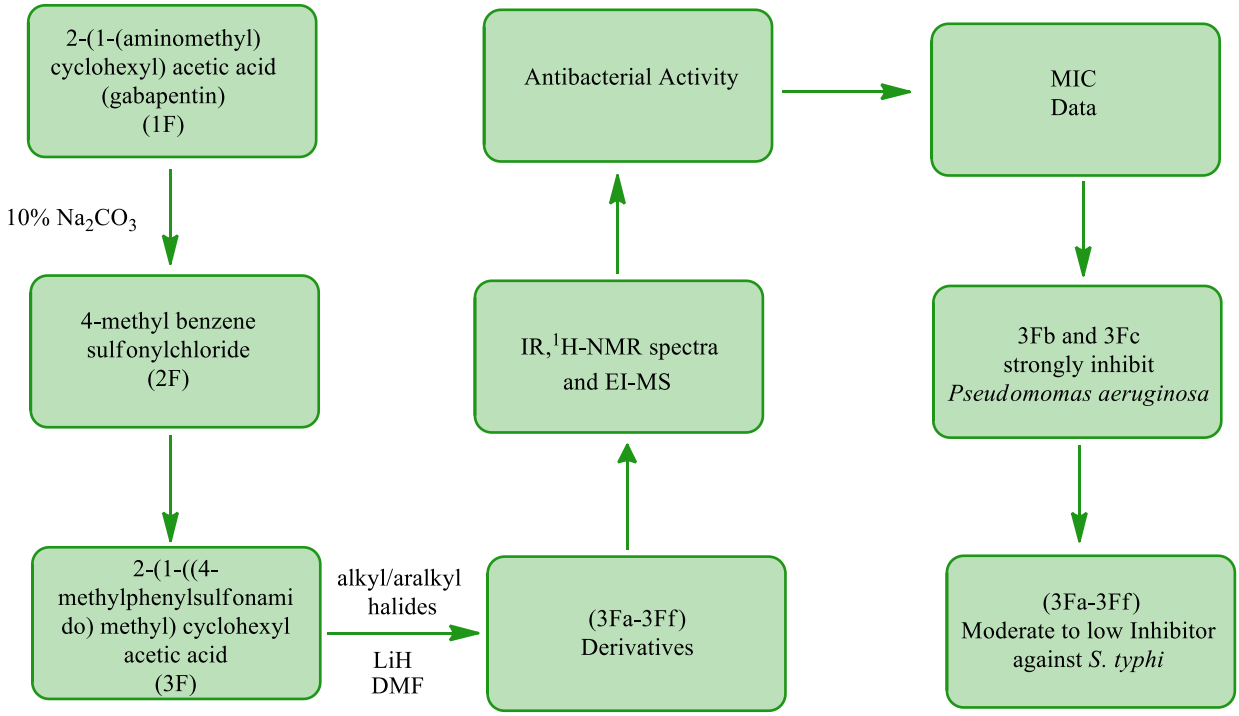
FUNDING DETAILS

This study did not get any financial provision.

CONFLICTS OF INTEREST

No authors have reported any competing interest.

Graphical Abstract



Graphical Representation of Abstract

Power System Technology
ISSN:1000-3673

Received: 16-01-2024 Revised: 12-02-2024 Accepted: 07-03-2024

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