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Synthesis, Characterization and Biological Evaluation of Novel Sulfonamides Containing N-((1-Alkyl-5-(Substituted Phenyl)-1*H*-Benzo[D]Imidazol-2-Yl) Methyl) Substituted Aryl/Alkyl Sulfonamide Derivatives

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ABSTRACT

A series of novel N-((1-alkyl-5-(substituted phenyl)-1H-benzo[d]imidazol-2-yl) methyl) substituted aryl/alkyl sulfonamide derivatives were synthesized for evaluation of their antimicrobial activity. The newly synthesized compounds were characterized by spectroscopic studies such as 1H NMR, Mass spectroscopy. All the synthesized compounds were screened for their in vitro antimicrobial activity. Some of the compounds showed good biological activity.

Keywords: Antimicrobial activity, 1-ethyl-5-(4-fluorophenyl)-1H-benzo[d]imidazol-2-yl) methanamine.

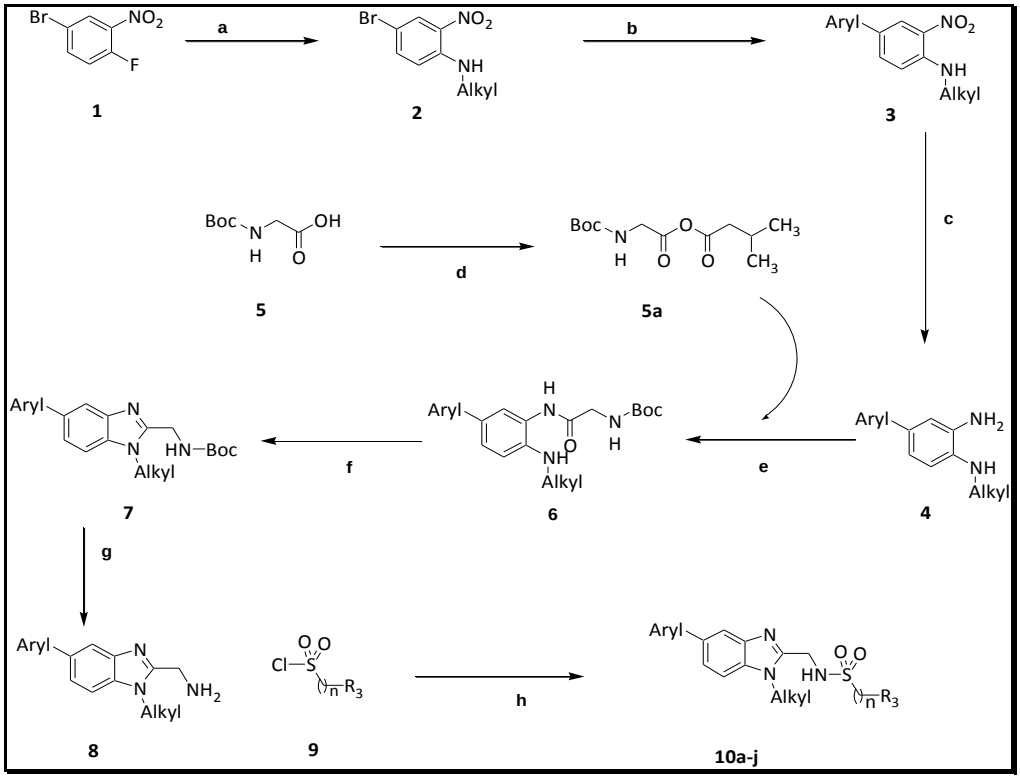
INTRODUCTION

Benzimidazole is a heterocyclic aromatic organic compound. It is an important pharmacophore and a privileged structure in medicinal chemistry. This compound is bicyclic in nature which consists of the fusion of benzene and imidazole. Nowadays is a moiety of choice which possesses many pharmacological properties. The most prominent benzimidazole compound in nature is N-ribosyl-dimethyl benzimidazole, which serves as an axial ligand for cobalt in vitamin B12[1]. The use of Benzimidazole dates many years back [2]. In 1990 various Benzimidazole derivatives were synthesized with substitution of fluorine, propylene, tetrahydroquinoline and cyclised compound which resulted in compounds with increased stability, bioavailability and significant biological activity [3,4]. In 1991 benzimidazole derivatives were synthesized by derivatization at N-H of benzimidazole by electron donating group and substitution with long chain of propyl, acetamido, thio, thiazole-amino, tetramethylpiperidine on pyridine resulting in good antiulcer activity [5,6]. Nowadays Infectious microbial diseases are causing problems world-wide, because of resistance to number of antimicrobial agents (β-lactam antibiotics, macrolides, quinolones and vancomycin). A variety of clinically significant species of microorganisms has become an important health problem globally [7]. One way to fight with this challenge is the appropriate usage of the available marketed antibiotics the other is the development of novel anti-microbial agents [8] Hence, there will always be a vital need to discover new chemotherapeutic agents to overcome the emergence of resistance and ideally shorten the duration of therapy. Due to the structural similarity to purine, antibacterial ability of Benzimidazoles are explained by their competition with purines resulting in inhibition of the synthesis of

bacterial nucleic acids and proteins [9,10]. Though many synthetic strategies have been reported for the preparation of benzimidazole derivatives. In the view of biological importance of benzimidazole derivatives we aimed the synthesis of a series of novelN-((1-alkyl-5-(substituted phenyl)-1H-benzo[d]imidazol-2-yl) methyl) substituted aryl/alkyl sulfonamide.

MATERIALS AND METHODS

All chemicals were LR grade and used without further purification. The progress of reaction was monitored by Analytical TLC in EtOAc-Hexane/DCM-MeOH solvent systems on precoated plates (silica gel 60, F254) and visualized with UV light. Flash chromatography was performed with silica gel 60(60-120 mesh). NMR spectra (1H at 400 MHz) were recorded using $CDCl_3$ OR DMSO-d6 as a solvent. The specifications of the LC/MS are as follows: electrospray (+) ionization, mass range 100-1500 Da, 20-V cone voltage, and Xterra MS C18 column (2.1 mm x 50 mm x 3.5 µm). Melting points were determined using Lab india V10 Thermovar apparatus and were uncorrected.



Scheme-1

Reagents: **a)**Alkyl amine, K_2CO_3, Acetone, RT; **b)** Aryl boronic acid, $Pd(PPh_3)_4$, Na_2CO_3,Toluene, Ethanol, Water, 80ºC; **c)** Zn Powder, Con. HCl, Methanol, THF, 0°C – RT; **d)** N-Methylmorpholine, Isobutyl chloroformate, THF, 0-5°C; **e)** 5a, THF, 0°C – RT; **f)** Glacial Acetic acid, 50°C; **g)** Trifluoroacetic acid, DCM, RT; **h)** TEA, DCM, RT.

Preparation of 4-bromo-N-ethyl-2-nitroaniline (2): 4-bromo-1-fluoro-2-nitrobenzene 1 (10 g, 45.46 mmol) and potassium carbonate (12.6 g, 90.92 mmol) were taken into acetone (100 mL). Ethyl amine (181.84 mmol, 2.0 meq) was then added to above solution and stirred overnight at room temperature. The mixture was then concentrated and water (100 mL) and EtOAc (100 mL) were added. The layers were separated and the aqueous layer was extracted with EtOAc (2 x 100 mL). The combined organic layers

were dried over anhydrous sodium sulfate, filtered, and concentrated by rotary evaporation to afford the 4-bromo-N-ethyl-2-nitroaniline brown solid (9.2 g, 82.57%).

Preparation of N-ethyl-4'-fluoro-3-nitro-[1,1'-biphenyl]-4-amine (3): To a stirred solution of 4-bromo-N-alkyl-2-nitroaniline 2 (8 g, 32.64 mmol) in Toluene (100 mL), 4-fluorophenylboronic acid (39.17 mmol, 1.2 eq) in ethanol (60 mL) and potassium carbonate (11.25 g, 81.6 mmol) in water (40 mL) were added. Degassed the reaction mixture by N2 for 10 min followed by the addition of tetrakis triphenylphosphinopalladium (0) (1.88 g, 1.63 mmol). The reaction mixture was heated to reflux for 4h. Water (250 mL) and EtOAc (250 mL) was added into the reaction mixture. The layers were separated and the aqueous layer was extracted with EtOAc (2 x 100 mL). The combined organic layers were washed with brine, dried over anhydrous sodium sulfate, filtered, and concentrated by rotary evaporation. The crude material was purified by column chromatography (EtOAc/Hexane, 3:7) to yield the title compound N-ethyl-4'-fluoro-3-nitro-[1,1'-biphenyl]-4-amine 3 (6.5 g, 76.51%).

Preparation of N-4-ethyl-4'-fluoro-[1,1'-biphenyl]-3,4-diamine (4): N-ethyl-4'-fluoro-3-nitro-[1,1'-biphenyl]-4-amine 3 (6 gm, 23 mmol) was taken in the mixture of THF and MeOH (60 mL, 2:1). Zn powder (3 g, 46.11 mmol) was added to it at room temperature. Conc. Hydrochloric acid (2.5 mL, 23 mmol) was added drop wise to the reaction mass. (Caution: exotherm).The reaction mass was stirred at room temperature for 15 min. After the completion of reaction, solvent was concentrated under reduced pressure and aqueous ammonia solution and EtOAc (100 mL) were added to the residue. The mixture was then stirred for 10 – 15 min and filtered through celite bed and washed it with EtOAc (50 mL). Filtrate was layer separated. Organic layer was then washed with water (150 mL) and brine (150 mL). The organic layers were dried over anhydrous sodium sulphate, filtered, and concentrated by rotary evaporator. The crude material was purified by column chromatography (EtOAc/Hexane, 5:5) to yield N-4-ethyl-4'-fluoro-[1,1'-biphenyl]-3,4-diamine 4 (4.5 g, 84.76 %) as brown solid.

Preparation of compound tert-butyl(2-((4-ethylamino)-4'-fluoro-[1,1'-biphenyl]-3-yl)amino)-2-oxo ethyl)carbamate (6): N-boc glycine 5 (3.3 g, 18.84 mmol) and N-Methylmorpholine (4.2 g, 41.45 mmol) were taken in dry THF (50 mL).Cooled it to 0-5 °C. Isobutyl chloroformate (2.57 g, 18.84 mmol) was added drop wise to above reaction mass. Reaction mass was stirred further for 30 min at 0-5 °C. The reaction mass was filtered through celite bed. Filtrate (5a) was then added drop wise to the solution of N-4-ethyl-4'-fluoro-[1,1'-biphenyl]-3,4-diamine 4 (4.3 g, 18.67 mmol) in dry THF (50 mL) at 0 °C. Reaction mass was slowly allowed to attain room temperature and then stirred at room temperature for 30 min. Reaction progress was monitored with TLC. After the completion of reaction, solvent was concentrated under reduced pressure, Water (50 mL) and EtOAc (100 mL) were added to the residue. The mixture was then stirred for 5-10 min and layers were separated. Organic layer was then washed with water (50 mL) and brine (50 mL).Distilled it under reduced pressure to afford the tert-butyl(2-((4-ethylamino)-4'-fluoro-[1,1'-biphenyl]-3-yl)amino)-2-oxoethyl)carbamate 6 (5 gm, 68.45%) as dark brown solid. Crude material forwarded as such in next step.

Preparation of tert-butyl ((1-ethyl-5-(4-fluorophenyl)-1H-benzo[d] imidazol-2-yl) methyl) carbamate (7): tert-butyl(2-((4-ethylamino)-4'-fluoro-[1,1'-biphenyl]-3-yl)amino)-2-oxoethyl) carba mate 6 (5 g,12.90 mmol) was taken in glacial acetic acid (50 mL). Reaction mass was heated at 50-60 °C for 1.5 h. After the completion of reaction, solvent was concentrated under reduced pressure and aqueous ammonia solution and EtOAc (100 mL) were added to the residue. The mixture was then stirred for 10 – 15 min and filtered through celite bed and washed it with EtOAc (50 mL). Filtrate was layer separated. Organic layer was then washed with water (50 mL) and brine (50 mL). The organic layers were dried over anhydrous sodium sulphate, filtered, and concentrated by rotary evaporator. The crude material was purified by column chromatography (EtOAc/Hexane, 5:5) to yield tert-butyl((1-ethyl-5-(4-fluorophenyl)-1H-benzo[d]imidazol-2-yl)methyl)carbamate 7 (4 g, 57.97 %) as cream solid.

Preparation of 1-ethyl-5-(4-fluorophenyl)-1*H*-benzo[d]imidazol-2-yl)methanamine (8): To a stirred solution of tert-butyl((1-ethyl-5-(4-fluorophenyl)-1H-benzo[d] imidazol-2-yl)methyl)carbamate 7 (4 g, 10.32 mmol) in dichloromethane (60 mL) was added trifluoroacetic acid (60 mL). The reaction mixture was stirred at room temperature for 2 h. The reaction mixture was concentrated by rotary evaporation. The residue was dissolved in DCM (100 mL) and aqueous solution of NaOH (2 M) was added until the solution reached to pH of 8, washed the organic layer by water (3 x 50 mL). The combined organic layers were dried over anhydrous sodium sulphate, filtered, and concentrated by rotary evaporation. The crude material was purified by column chromatography (EtOAc/Hexane, 7:3) to yield 1-ethyl-5-(4-fluorophenyl)-1H-benzo[d]imidazol-2-yl)methanamine 8 (3 g,78.68%) as a brown solid.

General Procedure for the Preparation of N-((1-ethyl-5-(4-fluorophenyl)-1H-benzo[d]imidazol-2-yl)methyl)substitutedbenzene sulfonamide (10a-j): To a stirred solution of 1-ethyl-5-(4-fluorophenyl)-1H-benzo[d]imidazol-2-yl) methanamine 8 (0.2 g, 0.74mmol) in dry DCM (15 mL), triethylamine (0.2 mL, 1.49mmol) was added to the reaction mixture followed by the addition of substituted phenylsulfonyl chloride 9 (0.147 g, 0.76mmol) at room temperature under N_2. The reaction mixture was stirred at room temperature for 2 h. The mixture was then concentrated and water (15 mL) and EtOAc (30 mL) was added. The layers were separated and the aqueous layer was extracted with EtOAc (3 x 15 mL). The combined organic layers were washed with 1N HCl, followed by saturated aqueous $NaHCO_3$ and brine. The combined organic layers were dried over anhydrous sodium sulphate, filtered, and concentrated by rotary evaporation. The crude material was purified by column chromatography (MeOH/DCM, 1:9) to yield the N-((1-ethyl-5-(4-fluorophenyl)-1H-benzo[d]imidazol-2-yl)methyl)4-methoxybenzenesulfonamide (0.2 g, 63.21 %) as a brown solid.

All the compounds were found to be off white to brown solid.10 new compounds (10a-j) were synthesized in similar manner and characteristic physical data are shown in table 1.

N-((1-cyclopropyl-5-(4-fluorophenyl)-1H-benzo[d]imidazol-2-yl) methyl) cyclopropane sulfonamide (10a): Yield: 86 %. 1H NMR (400 MHz, CDCl3):δ =8.299-8.271(t,1H), 7.568-7.540(m,3H), 7.476-7.451(m,1H),7.148-7.104(m,2H),4.332-4.268(m,2H),1.415-1.370(m,1H),1.351-1.268(m,2H), 1.148-1.121 (m,2H), 1.054-0.884(m,3H), 0.790-0.750(m,2H). MS: m/z 386 (M+H)+.

N-((1-ethyl-5-(4-fluorophenyl)-1*H*-benzo[d]imidazol-2-yl) methyl)-4-methoxybenzene sulfonamide (10b): Yield: 63 %. 1H NMR (400 MHz, DMSO-d6):δ =8.298-8.270(t,1H), 7.910-7.711(m,5H), 7.662-7.641(m,1H), 7.570-7.550(m,1H), 7.314-7.269(m,2H), 7.093-7.071(m,2H), 4.332-4.268(m,4H), 3.796(s,3H), 1.368-1.332(t,3H)ppm. MS: m/z 440 (M+H)+.

N-((1-ethyl-5-(4-fluorophenyl)-1*H*-benzo[d] imidazol-2-yl) methyl)-4-fluoro-2-methylbenzene sulfonamide (10c): Yield: 62 %. 1H NMR (400 MHz, DMSO-d6):δ =8.582(t,1H), 7.884-7.847(m,1H), 7.800-7.749(m,1H), 7.738-7.714(m,2H), 7.670-7.649(m,1H), 7.578-7.558(m,1H), 7.32-7.239 (m,3H), 7.155-7.105(m,1H), 4.379-4.272(m,4H), 2.609(s,3H), 1.351-1.315(t,3H) ppm. MS: m/z 442 (M+H)+.

4-(difluoromethoxy)-N-((1-ethyl-5-(4-fluorophenyl)-1*H*-benzo[d] imidazol-2-yl) methyl) benzene sulfonamide (10d): Yield: 45 %. 1H NMR (400 MHz, DMSO-d6):δ =8.452(t,1H), 7.900-7.878(m,2H), 7.790-7.786(m,1H), 7.734-7.699(m,1H), 7.622-7.601(d,1H), 7.535-7.350(m,2H), 7.331-7.328 (m,2H), 7.313-7.259(m,2H), 4.314-4.261(m,4H), 1.359-1.323(t,3H)ppm. MS: m/z 476 (M+H)+.

N-((1-ethyl-5-(4-methoxyphenyl)-1*H*-benzo[d]imidazol-2-yl) methyl)-4-fluorobenzene sulfonamide (10e): Yield: 79 %. 1H NMR (400 MHz, DMSO-d6):δ =8.301-8.270(t,1H), 7.911-7.713(m,5H),7.662-7.644(m,1H),7.568-7.549(m,1H),7.317-7.271(m,2H),7.093-7.073(m,2H),4.327-4.262(m,4H), 3.803(s,3H), 1.370-1.334(t,3H)ppm. MS: m/z 440 (M+H)+.

N-((1-ethyl-5-phenyl-1*H*-benzo[d]imidazol-2-yl) methyl)-2-fluoro-4-methoxybenzene sulfonamide (10f): Yield: 48 %. 1H NMR (400 MHz, DMSO-d6):δ =8.295-8.273(t,1H), 7.907-7.715(m,5H), 7.666-7.641(m,1H), 7.570-7.567(m,1H), 7.314-7.274(m,2H), 7.101-7.080(m,2H), 4.334-4.270(m,4H), 3.798(s,3H), 1.372-1.332(t,3H)ppm. MS: m/z 440 (M+H)+.

N-((1-ethyl-5-(4-fluorophenyl) -1*H*-benzo[d] imidazol-2-yl) methyl)-2-fluoro-4-methylbenzene sulfonamide (10g): Yield: 72 %. 1H NMR (400 MHz, DMSO-d6):δ =8.579(t,1H), 7.891-7.855(m,1H), 7.798-7.751(m,1H), 7.733-7.710(m,2H), 7.664-7.655(m,1H), 7.571-7.551(m,1H), 7.320-7.237(m,3H), 7.150-7.100(m,1H), 4.374-4.267(m,4H),2.600(s,3H), 1.347-1.311(t,3H) ppm. MS: m/z 442 (M+H)+.

N-((5-(4-(difluoromethoxy) phenyl)-1-ethyl-1*H*-benzo[d] imidazol-2-yl) methyl)-4-flurobenzene sulfonamide (10h): Yield: 51 %. 1H NMR (400 MHz, DMSO-d6):δ =8.455(t,1H), 7.905-7.882(m,2H), 7.797-7.792(m,1H), 7.736-7.701(m,1H), 7.628-7.607(d,1H), 7.539-7.354(m,2H), 7.338-7.335 (m,2H), 7.317-7.263(m,2H), 4.319-4.266(m,4H), 1.356-1.330(t,3H)ppm. MS: m/z 476 (M+H)+.

N-((5-(2,4-difluorophenyl) -1-ethyl-1*H*-benzo[d]imidazol-2-yl) methyl)-4-methylbenzene sulfonamide (10i): Yield: 85 %. 1H NMR (400 MHz, DMSO-d6):δ =8.586(t,1H), 7.888-7.851 (m,1H), 7.805-7.754(m,1H), 7.743-7.719(m,2H), 7.677-7.656(m,1H), 7.585-7.565(m,1H), 7.327-7.244(m,3H), 7.159-7.109(m,1H), 4.385-4.277(m,4H),2.614(s,3H), 1.357-1.321(t,3H) ppm. MS: m/z 442 (M+H)+.

N-((1-ethyl-5-(4-fluoro-2-methylphenyl) -1*H*-benzo[d] imidazol-2-yl) methyl)-2-fluoro-4-fluorobenzene sulfonamide (10j): Yield: 71 %. 1H NMR (400 MHz, DMSO-d6):δ =8.580(t,1H), 7.882-7.847(m,1H), 7.799-7.749(m,1H), 7.735-7.710(m,2H), 7.666-7.645(m,1H), 7.577-7.558(m,1H), 7.316-7.235(m,3H), 7.151-7.100(m,1H), 4.374-4.267(m,4H),2.611(s,3H), 1.346-1.310 (t,3H) ppm. MS: m/z 442 (M+H)+.

RESULTS AND DISCUSSION

Chemistry: Synthesis of novel N-((1-alkyl-5-substituted aryl/hetroaryl)-1 H-benzo[d] imidazol-2-yl) methyl) substituted aryl/alkyl sulfonamide is outlined in Scheme 1. 5-bromo-2-fluoro nitrobenzene 1 was reacted with alkyl amine to produce 5-bromo-2(N-alkyl amino) nitro benzene 2 which was then reacted with various aryl or hetroaryl boronic acids by means of Suzuki coupling using sodium carbonate and $Pd(PPh_3)_4$ led to the formation of the compound 3. Compound 3 was then converted in to 5-bromo-2(N-alkylamino) aniline 4 by nitro reduction using zinc powder and hydrochloric acid in methanol, THF mixture at room temperature. Parallely N-Boc glycine 5 was converted to anhydride 5a using isobutyl chloro formate in the presence of N-methylmorpholine. The product 5a was then reacted with 5-bromo-2(N-alkyl amino) aniline 4 at 0-5 °C to furnish the Boc-protected diamino intermediate 6. The product was then cyclized in acetic acid at 50-60 °C furnished the cyclized product 7. BOC deprotection was done with trifluoroacetic acid in dichloromethane at room temperature produced trifluoroacetic acid salt of amine, this was basified using 2N NaOH to obtain the free amine 8. Amine derivative 8 was reacted with various aryl, hetroaryl or sulfonyl chlorides 9 in the presence of triethyl amine to yield corresponding sulfonamide derivatives (10a-j). These new compounds were purified by column chromatography using 2-3 % methanol in DCM as the eluent. All the reactions were smooth, and provided the products in the range of 55-85% yield.

Table 1: Characteristic physical data of sulfonamide derivatives 10a-j.

Sr. No	Comp Code	Aryl	Alkyl	R	M.P(°C)	Yield (%)
1	10a	4-Fluorophenyl	Cyclopropyl	Cyclopropyl	180-182	86
2	10b	4-Fluorophenyl	Ethyl	4-Methoxyphenyl	176-178	63
3	10c	4-Fluorophenyl	Ethyl	4-Fluoro-2-methylphenyl	190-192	62
4	10d	4-Fluorophenyl	Ethyl	4-Difluoromethyl phenyl	172-174	45
5	10e	4-Methoxyphenyl	Ethyl	4-Fluorophenethyl	175-177	79
6	10f	Phenyl	Ethyl	4-Methoxy-2-luorophenyl	188-190	48
7	10g	4-Fluorophenyl	Ethyl	2-Fluoro-4-Methyl phenyl	193-195	72
8	10h	4-Difluoro methylphenyl	Ethyl	4-Fluorophenyl	170-172	51
9	10i	2,4-Difluorophenyl	Ethyl	4-Methylphenyl	160-162	85
10	10j	4-Fluoro-2-ethylphenyl	Ethyl	4-Fluorophenyl	157-159	71

All compounds are either crystalline or amorphous solid.

Biological activities

Antibacterial and antifungal activities: The newly synthesized derivatives were evaluated for their in vitro antibacterial activity against gram positive Staphylococcus aureus and Bacillus subtilis, gram negative Escherichia coli & Pseudomonas aeruginosa, and antifungal activity against Aspergillus niger & Aspergillus flavus by micro broth dilution method[13-15]. The standard drugs used for antibacterial activity were ampicillin and streptomycin and nystatin for antifungal activity. Mueller Hinton Broth was used as neutriant medium for bacteria and Sabouraud Dextrose Broth for fungal to grow. Inoculums size for test strain was adjusted to 10^5CFU/mL by comparing the turbidity. The serial dilutions were prepared in primary and secondary screening. The target compounds and standard drugs were disolved in DMSO-water at a concentration of 2.0 mg/mL. In primary screening1000µg/ml, 500µg/ml, 250µg/ml, 125µg/ml, 62.5µg/ml concentrations of the synthesized drugs were taken. Data were not taken for the initial solution because of the high DMSO concentration (10%). The actively synthesized drugs found in this primary screening were further tested in a second set of dilution against all microorganisms. In secondary screening, the drugs found active in primary screening were similarly diluted to obtain 100 µg/mL, 50 µg/mL, and 25 µg/mL, 12.5 µg/mL and 6.25 µg/mL concentrations. The inoculated wells were incubated overnight at 37ºC in a humid atmosphere overnight. The highest dilution showing at least 99% inhibition zone is taken as MIC.

The MIC values revealed that some of the newly synthesized compounds showed moderate to good inhibition. Compound 10b shows overall moderate activity against all bacterial and fungal strain, While compound 10a shows moderate activity against bacterial and fungal strain except Pseudomonas aeruginosa and Aspergillus flavus. Compound 10d shows moderate activity against both fungal strains. Compound 10e shows moderate activity against S.aureus, good activity against B.subtilis and E.coli and better activity against Pseudomonas aeruginosa. Compound 10g demonstrate excellent activity against gram positive

bacterial strains and moderate activity against fungal strains. Compound 10i shows overall moderate to excellent activity against all strains except S. aureus. Compound 10j shows inhibition against gram positive and gram negative bacterial strains. All other compounds displayed poor activity against all bacterial strains compared to standard drugs.

Table 2: Antibacterial and antifungal activity of sulfonamidederivatives 10a-j.

	Antibacterial MIC (µg/mL)				*Antifungal MIC (µg/mL)*	
Compounds	***Bacillus subtilis***	***Staphylococcus aureus***	***Escherichia coli***	***Pseudomonas aeruginosa***	***Aspergillus niger***	***Aspergillus flavus***
Streptomycin			50	50		
Ampicillin	100	100				
Nystatin					100	100
10a	500	500	500	1000	500	1000
10b	500	500	500	500	500	500
10c	1000	1000	1000	1000	1000	1000
10d	1000	1000	1000	1000	500	500
10e	250	500	250	125	1000	1000
10f	1000	1000	1000	1000	1000	1000
10g	125	125	1000	1000	500	500
10h	1000	1000	1000	1000	1000	1000
10i	500	1000	500	500	125	250
10j	250	500	500	250	1000	1000

APPLICATIONS

In the present study the derivatives which we have synthesized were screened for their antimicrobial activity, which are promising as active pharmacophore. Further studies are undergoing to explore the scope of the various biological activities.

CONCLUSIONS

An efficient method for preparation of N-((1-ethyl-5-(4-fluorophenyl)-1H-benzo[d]imidazol-2-yl)methyl)substitutedbenzene sulfonamide derivatives was described and the structure of synthesized compounds was determine by ^{1}H NMR, and LC-Mass spectroscopic analysis and evaluated their in vitro antimicrobial activity by broth dilution method.

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REFERENCES

[1] Barker HA, Smyth RD, Weissbach H, Toohey JI, Ladd JN and Volcani BE, Isolation and properties of crystalline cobamide coenzymes containing Benzimidazole or 5,6-Dimethyl benzimidazole, *Journal of Biological Chemistry,* **1960,** 235(2):480-488.

[2] Patil A, Ganguly S and Surana S, A systematic review of benzimidazole derivatives as an antiulcer agent, *Rasayan J Chem,* **2008**, 1(3):447-460.

[3] Kubo K, Oda K, Kaneko T, Satoh H and Nohara A, Synthesis of 2-(4-Fluoroalkoxy-2-pyridyl) methyl] sulfinyl]-1H-benzimidazoles as Antiulcer Agents, *Chem Pharm Bull*, **1990**, 38(10):2853-2858.
[4] Uchida M, Chihiro M, Morita S, Yamashita H, Yamasaki K, Kanbe T, Yabuuchi Y and Nakagawz K, Synthesis and Antiulcer Activity of 4-Substituted 8-[(2-Benzimidazolyl) sulfinylmethyl]-1,2,3,4-tetrahydro quinolines and Related Compounds, *Chem Pharm Bull*,**1990,** 38(6):1575-1586.
[5] Grassi A, Ippen J, Bruno M, Thomas G and Bay P, A thiazolylamino benzimidazole derivative with gastroprotective properties in the rat, *Eur J Pharmaco,*. **1991,** 195(2):251-9.
[6] Ozkay Y, Tunali Y, Karaca H. and Isikdag I, Antimicrobial activity and a SAR study of some novel benzimidazole derivatives bearing hydrazones moiety, *Eur. J. Med. Chem*, **2010,** 45(8): 3293-3298.
[7] Yun H, Baogen W, Yang J, Robinson D, Risen L, Ranken R, Blyn L, Eric SS. and Swayze E, 2-Piperidin-4-ylbenzimidazoles with Broad Spectrum antibacterial activities, *Bioorg Med Chem Lett*, **2003**,13:3253-3256.
[8] Metwally KA, Abdel-Aziz LM, Lashine el-SM, Husseiny MI and Badawy RH, Hydrazones of 2-aryl- -4-carboxylic acid hydrazides: synthesis and preliminary evaluation as antimicrobial agents, *Bioorg Med Chem*, **2006,** 14(24): 8675-82.
[9] Spasov A, Yozhitsa L, Bugaeva I and Anisimova VA, Benzimidazole derivatives: Spectrum of pharmacological activity and toxicological properties, *Pharmaceutical Chemistry Journal*, 33, 5:232-243.
[10] Arjmand F, Mohani B and Ahmad S, Synthesis, antibacterial, antifungal activity and interaction of CT-DNA with a new benzimidazole derived Cu (II) complex, *Eur J Med Chem*, **2005**, 40(11), 1103-1110.
[11] a) Dharmesh Pansuriya, Kalpesh Menpara, Naresh Kachhadiya, Jignesh Menpara and Kartik Ladva, Synthesis, Characterization & Biological evaluation of sulfonamide analogue of Tetrazolo[1,5-a]pyrimidines, *J. Applicable. Chem*, **2014**, 3 (6): 2335-2342.; b) Kalpesh Menpara, Dharmesh Pansuriya, Naresh Kachhadiya, Jignesh Menpara and Kartik Ladva, Synthesis, Characterization And Biological Evaluation Of Novel Amides Containing Spiro[Chromeno[4,3-D]Thiazole-4,1'-Cyclohexan]-2-Amine Derivatives, *J. Applicable. Chem*, **2014**, 3 (2): 535-540. c) Naresh Kachhadiya, Kalpesh Menpara, Dharmesh Pansuriya, Jignesh Menpara, Kartik Ladva, Synthesis, Characterization and Biological Evaluation of N-((1-ethyl-5-(substituted phenyl)-1H-indol-3-yl) methyl) Substituted Alkyl/Aryl Carboxamides Derivatives, *J. Applicable. Chem*, **2017**, 6 (5).
[12] National committee for clinical laboratory standards. Methods for dilution, antimicrobial susceptibility tests for bacteria that grow aerobically approved standard, (M7A5), 5th ed.; national committee for clinical laboratory standards: Wayne, PA, **2000**.
[13] shadomy, S. In Manual of Clinical microbiology, albert, B. Ed, ASM press: Washington, DC, **1991,** p. 1173.
[14] Rattan A, antimicrobial in laboratory medicine, BI Churchill Livingstone, India, **2000,** p. 85.

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