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Antimicrobial Activity Evalution of Newly Synthesized *N,N*-Disubstituted Taurinamidobenzenesulfonamide Derivatives

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Abstract: Herein we synthesized 6 new *N,N*-disubstituted taurinamidobenzenesulfonamide derivatives and characterized their structures by means of ^{1}H and ^{13}C NMR, HR-MS analysis. In addition, their *in vitro* antibacterial and antifungal activities were tested against two gram-positive, two gram-negative bacteria, and two fungal strains by using broth microdilution method. Compounds **1** (methoxy substitution) and **2** (methyl substitution) displayed the best antibacterial activity against *Escherichia coli* and *Staphylococcus aureus*, respectively. *E. faecalis* was affected by compounds **1**, **2**, **4**, and **6**, becoming the most susceptible pathogen compared to other tested bacterial and fungal strains. Interestingly, changing fluoro atom in compound **6** with the chloro atom, as in compound **5**, deteriorated the antibacterial activity against all bacterial strains. As a result, these results provide us to investigate the relationship between structural changes and antibacterial/antifungal activity, which can be further used to develop more effective taurine derivatives.

Keywords: Taurine, taurinamidobenzenesulfonamide, antibacterial, antifungal, microdilution.

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INTRODUCTION

Sulfanylamide was first established as a selective toxic agent against bacteria in the 1930s, which ushered in a new era in antibacterial drug development studies. As the sulfonamide and amine parts of the molecule can be functionalized by different groups, a wide range of sulfanylamide derivatives with diverse pharmacokinetic and pharmacodynamic properties have been synthesized (Figure 1). In addition, the clinically useful sulfa drug class of antibacterials was discovered. However, the emerging bacterial resistance against these drugs limits their usage in treatment (1).

Sulfanylamide is a competitive inhibitor of *p*-aminobenzoic acid and exerts its bacteriostatic action via binding to dihydropteroate synthase (DHPS). Although the structure–activity relationship of sulfa drugs indicates that the amino part should be free of substitution in order to show an antimicrobial effect, modification of the amine part might also result in active molecules. A study replacing the amino group in sulfanylamide with the methyl, nitro, or chloro group and substituting the sulfonamide moiety with various heterocycles resulted in compounds with promising *in vitro* antibacterial activity against various bacterial strains (Figure 1) (2).

Recently, it was reported that bacteria encode genetically different carbonic anhydrases (CAs) which are involved in their virulence and growth abilities. In addition, various *N*-substituted sulfanylamide derivatives were found to be potential inhibitors of bacterial CAs. Therefore, CAs considered as druggable targets that serve a new mechanism of action devoid of resistance mechanism (3–5). All these findings support the idea that sulfanylamide derivatives will protect their place in drug development studies in the future, too.

Amino acids with their nontoxic profile and biocompatibility properties represent an interesting tool for constructing new, biologically active molecules (6, 7). Taurine, 2-aminoethanesulfonic acid, is the only free and nonproteogenic amino acid in mammals (8–11). Despite its negatively charged sulfonic acid, it can be transported inside cells with TauT transporters in humans and contributes to various important physiological events. Also, it passes through bacterial membranes with the help of TauABC transporters to be used as a sulfur, carbon, and nitrogen source (12). There is also evidence that bacteria use taurine to biosynthesize natural products. For example, a newly investigated antibiotic bulgacin-A with taurine in its structure was isolated from a gram-negative bacterium *Paraburkholderia acidophila*, which inhibits lytic transglycosylases of bacterial cell wall biosynthesis (13). In contrast to its role in bacteria, taurine shows antibacterial, antifungal, and antiviral activity in humans (14, 15). The mechanism underlying the antibacterial activity of taurine depends on the formation of taurinechloramine from the attack of toxic HOCl on the amine group of taurine during inflammation (Figure 2) (16–18).

In our previous study, we designed a group of taurine derivative by using molecular hybridization method and tested for their antimicrobial and antifungal properties. Among the final compounds, the derivative comprising a sulfanylamide group showed moderate antibacterial activity only against the gram-positive *Enterococcus faecalis* with a minimum inhibitory concentration (MIC) of 128 µg/mL (Figure 2) (19). In order to find more effective sulfanylamide derivatives and extend our knowledge of antimicrobial taurine derivatives, in this study, we decided to keep the taurinamidobenzenesulfonamide part of the previously investigated molecule unchanged and replace the phthalimide part with a hydrophobic benzyl group in order to obtain *N,N*-disubstituted derivatives with benzyl groups decorated with different electron-withdrawing and electron-donating groups (Figure 3). This modification strategy will give us an opportunity to investigate the contribution of disubstitution to antimicrobial activity.

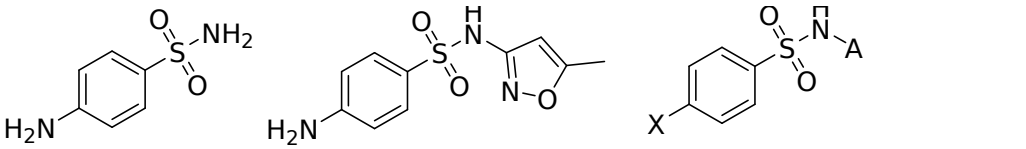

Figure 1. Structures of sulfanylamide, sulfamethoxazole, and previously investigated sulfamethoxazole derivatives

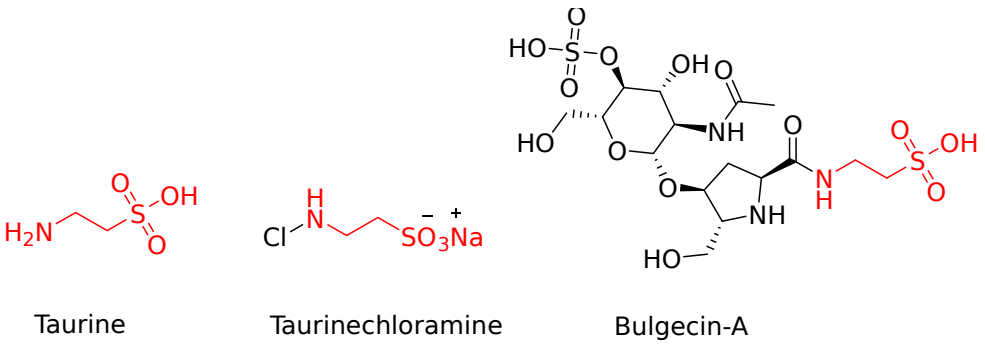

Figure 2. Structures of taurine and its biologically active derivative, and the antibiotic bulgecin-A with taurine in its structure.

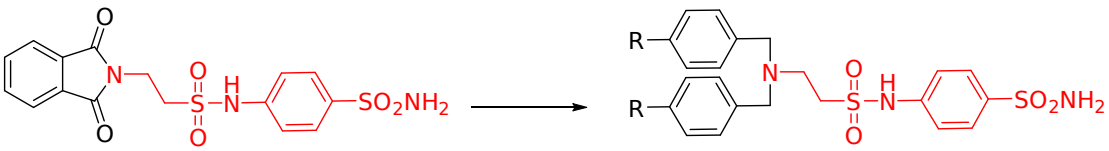

Figure 3. Drug design strategy.

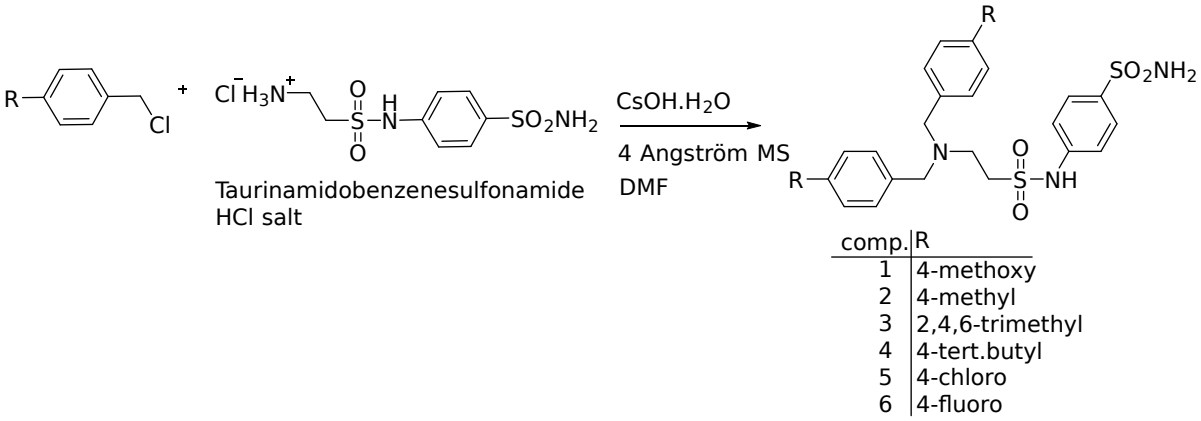

Figure 4. General synthesis of the final compounds **1-6**.

MATERIAL AND METHODS

Chemistry

Anhydrous solvents and all reagents were purchased from Sigma-Aldrich and Interlab (Germany). All reactions were performed under an argon atmosphere. ^{1}H and ^{13}C NMR spectra were performed in DMSO-d_6 on an Agilent 600 MHz PremiumCOMPACT NMR spectrometer. Chemical shifts and coupling constants (J) were reported in parts per million (ppm) and in Hertz (Hz) respectively. Merck silica gel F-254 plates were used for TLC analyses and the products were visualized by UV detection. The products were purified by flash chromatography employing Merck silica gel 60 (230–400 mesh ASTM) as stationary phase. Stuart® (SMP30) melting point apparatus was used to measure melting points in open capillary tubes and the results were uncorrected. High-resolution mass spectrometry (HR-MS) analyses were recorded on Agilent Technologies 6530 Accurate-Mass Q-TOF LC/MS.

General Procedure for the Synthesis of the Final Compounds

Taurinamidobenzenesulfonamide hydrochloride salt was prepared by following the reaction conditions previously described by us (19, 20). For obtaining final compounds; various benzyl chloride (2 mmol) and taurinamidobenzenesulfonamide.HCl (1.7 mmol) was added to a mixture of cesium hydroxide monohydrate ($CsOH.H_2O$, 1.7 mmol), activated powdered 4 Angström molecular sieves (500 mg) in anhydrous *N,N*-dimethyl formamide (DMF, 8.3 mL) and stirred at room temperature for 18 hr (21, 22). After the completion of the reaction the mixture was filtered, and the solvent was evaporated under reduced pressure. The residue was subjected to flash chromatography eluting with ethyl acetate: n-hexane (EtOAc: Hxn) and the obtained residue was crystallized with ethanol: water to afford the desired compounds **1-6** as white powders.

*4-((2-(Bis(4-methoxybenzyl)amino)ethyl)sulfonamido) benzenesulfonamide **1***

Elution with EtOAc: Hxn (25%) and crystallized with ethanol: water afforded **1** as a white solid (yield 3%); Mp: 120.2°C; ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 2.76-2.78 (m, 2H, CH_2), 3.41-3.43 (m, 2H, CH_2), 3.48 (m, 4H, benzylic-CH_2), 3.75 (s, 6H, OCH_3), 6.85 (d, J = 8.2 Hz, 4H, Ar-H), 7.16 (d, J = 8.2 Hz, 4H, Ar-H), 7.23 (d, J = 8.8 Hz, 2H, Ar-H), 7.35 (s, 2H, SO_2NH_2), 7.79 (d, J = 8.1 Hz, 2H, Ar-H), 10.28 (brs, 1H, SO_2NH-); ^{13}C NMR (100 MHz, DMSO-d_6, δ, ppm): 159.1 (2 × Ar-C), 142.2, 139.4, 131.2 (2 × Ar-C), 130.6 (4 × Ar-C), 128.1 (2 × Ar-C), 118.8 (2 × Ar-C), 114.5 (4 × Ar-C), 57.0 (2 × benzylic-C), 55.9 (2 × OCH_3), 48.5, 46.5; ESI-HRMS (*m/z*) $[M+H]^+$, calculated for $C_{24}H_{30}N_3O_6S_2$ 520.1571; found 520.15743.

*4-((2-(Bis(4-methylbenzyl)amino)ethyl)sulfonamido) benzenesulfonamide **2***

Elution with EtOAc: Hxn (25%) and crystallized from ethanol: water afforded **2** as a white solid (yield 20%); Mp: 177.8°C; ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 2.30 (s, 6H, CH_3), 2.79-2.77 (m, 2H, CH_2), 3.43-3.41 (m, 2H, CH_2), 3.51 (s, 4H, benzylic-CH_2), 7.10 (d, J = 7.7 Hz, 4H, Ar-H), 7.15 (d, J = 7.9 Hz, 4H, Ar-H), 7.21 (d, J = 8.6 Hz, 2H, Ar-H), 7.36 (s, 2H, SO_2NH_2), 7.77 (d, J = 8.6 Hz, 2H, Ar-H), 10.27 (1H, brs, SO_2NH-); ^{13}C NMR (100 MHz, DMSO-d_6, δ, ppm): 142.2, 139.4, 136.9 (2 × Ar-C), 136.3 (2 × Ar-C), 129.7 (4 × Ar-C), 129.4 (4 × Ar-C), 128.1 (2 × Ar-C), 118.8 (2 × Ar-C), 57.6 (2 × benzylic-C), 48.6, 46.8, 21.6 (2 × alip-C); ESI-HRMS (*m/z*) $[M+H]^+$, calculated for $C_{24}H_{30}N_3O_4S_2$ 488.1672; found 488.16769.

*4-((2-(Bis(2,4,6-trimethylbenzyl)amino)ethyl)sulfonamido) benzenesulfonamide **3***

Elution with EtOAc: Hxn (25%) and crystallized from ethanol: water afforded **3** as a white powder (yield 24%). Mp: 229.0°C; ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 2.15 (m, 12H, CH_2), 2.21 (m, 6H, CH_2), 2.76-

2.73 (m, 2H, CH_2), 3.25-3.22 (m, 2H, CH_2), 3.47 (s, 4H, benzylic-CH_2), 6.77 (s, 4H, Ar-H), 7.13 (d, J = 8.2 Hz, 2H, Ar-H), 7.35 (m, 2H, SO_2NH_2), 7.74 (d, J = 9.0 Hz, 2H, Ar-H), 10.28 (1H, brs, SO_2NH-); ^{13}C NMR (100 MHz, DMSO-d_6, δ, ppm): 142.0, 139.5, 138.4 (4 × Ar-C), 136.6 (2 × Ar-C), 132.1 (2 × Ar-C), 129.6 (4 × Ar-C), 128.0 (2 × Ar-C), 118.9 (2 × Ar-C), 52.4 (2 × benzylic-C), 50.3, 47.8, 21.4 (2 × aliph-C), 20.5 (4 × aliph-C); ESI-HRMS (*m/z*) $[M+H]^+$, calculated for $C_{28}H_{38}N_3O_4S_2$ 544.2298; found 544.23027.

4-((2-(Bis(4-(tert-butyl)benzyl)amino)ethyl)sulfonamido) benzenesulfonamide ***4***

Elution with EtOAc: Hxn (25%) and crystallized from ethanol: water afforded **4** as a white powder (yield 2%). Mp:172.2°C; ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 1.31 (m, 18H, CH_2), 2.84-2.81 (m, 2H, CH_2), 3.59-3.57 (m, 4H, CH_2), 4.79 (s, 2H, benzylic-CH_2), 7.14 (d, J = 8.4 Hz, 2H, Ar-H), 7.22 (d, J = 8.0 Hz, 2H, Ar-H), 7.33-7.31 (m, 4H, Ar-H), 7.35 (m, 2H, SO_2NH_2), 7.42 (d, J = 8.0 Hz, 3H, Ar-H), 7.69 (d, J = 8.3 Hz, 1H, Ar-H); ^{13}C NMR (100 MHz, DMSO-d_6, δ, ppm): 150.8, 150.3 (2 × Ar-C), 136.7 (2 × Ar-C), 134.1, 129.2 (2 × Ar-C), 128.8, 128.7, 128.3 (2 × Ar-C), 127.2, 126.1 (2 × Ar-C), 126.0 (2 × Ar-C), 125.9, 57.4 (benzylic-C), 53.6 (benzylic-C), 40.9, 35.1, 32.1 (6 × aliph-C), 32.0 (2 × aliph-C); ESI-HRMS (*m/z*) $[M+H]^+$, calculated for $C_{30}H_{42}N_3O_4S_2$ 572.2611; found 572.26138.

4-((2-(Bis(4-chlorobenzyl)amino)ethyl)sulfonamido) benzenesulfonamide ***5***

Elution with EtOAc: Hxn (25%) and crystallized from ethanol: water afforded **5** as a white powder (yield 23%). Mp:119.4°C; ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 2.78-2.80 (m, 2H, CH_2), 3.47-3.49 (m, 2H, CH_2), 3.55 (s, 4H, benzylic-CH_2), 7.22 (d, J = 8.7 Hz, 2H, Ar-H), 7.30 (d, J = 8.7 Hz, 4H, Ar-H), 7.36-7.37 (m, 6H, Ar-H, SO_2NH_2), 7.79 (d, J = 8.7 Hz, 2H, Ar-H), 10.30 (brs, 1H, SO_2NH-); ^{13}C NMR (100 MHz, DMSO-d_6, δ, ppm): 142.1, 139.5, 138.5 (2 × Ar-C), 132.5 (2 × Ar-C), 131.2 (4 × Ar-C), 129.1 (4 × Ar-C), 128.1 (2 × Ar-C), 118.8 (2 × Ar-C), 56.9 (2 × benzylic-C), 48.4, 46.9; ESI-HRMS (*m/z*) $[M+H]^+$, calculated for $C_{22}H_{24}Cl_2N_3O_4S_2$ 528.0580; found 528.05806.

4-((2-(Bis(4-fluorobenzyl)amino)ethyl)sulfonamido) benzenesulfonamide ***6***

Elution with EtOAc: Hxn (25%) and crystallized from ethanol: water afforded **6** as a white powder (yield 7%). Mp:110.1°C; ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 2.77-2.79 (m, 2H, CH_2), 3.46-3.49 (m, 2H, CH_2), 3.55 (s, 4H, benzylic-CH_2), 7.13 (t, J = 8.7 Hz, 4H, Ar-H), 7.22 (d, J = 8.7 Hz, 2H, Ar-H), 7.29-7.31 (m, 4H, Ar-H), 7.36 (m, 2H, SO_2NH_2), 7.78 (d, J = 8.7 Hz, 2H, Ar-H), 10.28 (1H, brs, SO_2NH-); ^{13}C NMR (100 MHz, DMSO-d_6, δ, ppm): 162.2 (d, J = 237.6 Hz, 2 × Ar-C), 142.1, 139.4, 135.6 (d, J = 2.9 Hz, 2 × Ar-C), 131.3 (d, J = 8.2 Hz, 3 × Ar-C), 128.1 (3 × Ar-C), 118.7 (3 × Ar-C), 115.9 (d, J = 21.2 Hz, 3 × Ar-C), 56.8 (2 × benzylic-C), 48.4, 46.7; ESI-HRMS (*m/z*) $[M+H]^+$, calculated for $C_{22}H_{24}F_2N_3O_4S_2$ 496.1171; found 496.11818.

Antimicrobial Activity

Establishment of minimum inhibitory concentration (MIC)

The microorganisms that were used in study (*Staphylococcus aureus* (ATCC 29213), *Enterococcus faecalis* (ATCC 29212), *Escherichia coli* (ATCC 25922), *Pseudomonas aeruginosa* (ATCC 27853), *Candida albicans* (ATCC 90028) and *Candida parapsilosis* (ATCC 22019) were stored in Brain-Heart Infusion Broth (Merck, Germany) with 10% glycerol at -80 °C. Titled compounds were screened for their antimicrobial activity against each strain employing broth microdilution method and MICs of synthesized compounds were determined according to the European Committee on Antimicrobial Susceptibility Testing (EUCAST) document (23). The solid growth medium Mueller-Hinton Agar (Merck, Germany) and Sabouraud Dextrose Agar (Oxoid, UK) were exploited for the bacteria and yeasts grown at 37 °C for 24 h, respectively. Then, bacteria and yeasts were suspended in saline. The turbidity of bacterial and fungal inocula was fixed to 0.5 McFarland by densitometer (Biosan, DEN-1), and the suspensions were diluted 100-fold and 10-fold for bacteria and yeasts, respectively. Mueller-Hinton broth (Merck, Germany) (50 µl) and RPMI (Sigma, UK) with 2% of glucose (RPMI 2% G) were added into the each well of sterile 96-well microdilution plates for bacteria and yeasts, respectively. 50 µL from each of the tubes containing the corresponding concentration of 6 new compounds were included into first wells each column of the microdilution plate and serial dilutions were accomplished. Bacterial and yeast inoculum suspensions were inoculated each well of plate with 50 µL, and the plates were incubated for 24 h at 37 °C. Growth control for each organisms and sterility control for medium were also tested. The final concentrations of the compounds were ranged from 2048 to 512 µg/ml. The MIC value was defined as the lowest concentration of the compound that entirely inhibited the microbial growth. The well-known antibiotic ciprofloxacin (Santa Cruz, US) and antifungal drug fluconazole (Sigma, UK) were used as reference drugs. Also, the study was performed by using the quality control ranges that were recommended by EUCAST. All test conditions were carried out at least in triplicate and DMSO was also tested independently for its antimicrobial activity.

RESULTS AND DISCUSSION

Synthesis and Characterization of the Final Compounds

Herein, 6 new 4-((2-(bis(4-substituted benzyl)amino)ethyl)sulfonamido)benzenesulfonamide derivatives have been prepared. The starting compound taurinamidobenzenesulfonamide hydrochloride salt was established by a 4 step reaction, as previously described (19,20). To obtain the final compounds, taurinamidobenzenesulfonamide hydrochloride salt was reacted with

various benzyl chlorides in the presence of a 4 Å molecular sieve and cesium hydroxide monohydrate in *N,N*-dimethylformamide solution at room temperature for 18 h (Figure 4). Final compounds **1-6** were achieved in yields of 2%-24%, as described in the Experimental Section. All six compounds were characterized by ^{1}H and ^{13}C NMR and high-resolution mass spectrometric (HR-MS) analysis, and all spectral data obtained were consistent with the proposed structures (see the Experimental section for details).

In the ^{1}H NMR spectra, the aromatic protons located at the amine part of compound **4** were observed as a singlet signal having four proton integration while the other compounds displayed the same protons as two signals with four-proton integration. Together with these protons, the signals of the benzylic protons (3.47-4.79 ppm) were indicative for the formation of disubstitution. On the other hand, the hydrogens of sulfanylamide displayed two separate signals, indicating the AA'BB' aromatic system. All aromatic proton signals were detected at 6.77-7.79 ppm region. The protons of the taurine scaffold exhibited two separate signals in aliphatic field at 2.76-3.59 ppm. The primary and secondary sulfonamide peaks were assigned as singlet at 7.22-7.31 ppm and 10.38-10.42 ppm respectively, though secondary sulfonamide hydrogen of compound **4** did not have any signal. The signals corresponding to methoxy, methyl, trimethyl and *tert*-butyl groups were located in the expected regions which also verified the disubstitution, since these substitutions were doubled. In ^{13}C NMR spectra, aromatic carbon signals were detected in the range of 115.88-162.2 ppm. Benzylic carbon signals were detected at 52.4-57.6 ppm region. In addition, the alkyl substitutions and taurine carbon atoms were observed in the expected regions. The splitting of carbon-fluoro atoms were also detected in ^{13}C NMR. On the other hand, HR-MS data were consistent with the proposed molecular weights.

Biological Activity

Antimicrobial activity

Final compounds were tested for their *in vitro* antibacterial and antifungal activities against two gram-positive bacteria*;* two gram-negative bacteria and two fungal strains using broth microdilution method with ciprofloxacin and fluconazole as reference drugs. Table 1 summarizes the structure–activity relationship from biological activity results.

Table 1. *In vitro* antibacterial and antifungal activity (MIC, µg/mL) of compounds **1–6** compared to ciprofloxazin and fluconazole.

Compound			**Gram (+) bacterial strains**				**Gram (-) bacterial strains**				**Fungal strains**			
		R		*S. a.*		*E. f.*		*E. c.*		*P. a.*		*C. a.*		*C. p.*
1	**2**	4-OCH_3	3	2048	4	512	5	512	6	1024	7	>2048	8	>2048
9	**10**	4-CH_3	11	512	12	512	13	1024	14	2048	15	1024	16	1024
17	**18**	2,4,6-$(CH_3)_3$	19	1024	20	1024	21	>2048	22	2048	23	>2048	24	>2048
25	**26**	4-$C(CH_3)_3$	27	1024	28	512	29	1024	30	1024	31	>2048	32	>2048
33	34	4-Cl	35	2048	36	2048	37	>2048	38	>2048	39	>2048	40	>2048
41	42	4-Fl	43	1024	44	512	45	1024	46	1024	47	>2048	48	>2048
Ciprofloxacin	0.25		1		0.008		0.5		nt		nt			
Fluconazole	*nt*		*nt*		*nt*		*nt*		*32*		*2*			

S. a., *Staphylococcus aureus*; *E. f.*, *Enterococcus faecalis*; *E. c.*, *Escherichia coli*; *P. a.*, *Pseudomonas aeruginosa; C. a.*, *Candida albicans*; *C. p.*, *Candida parapsilosis*; nt, not tested.

Compound **2** comprising an electron-donating methyl group as a substituent on the phenyl ring showed the highest MIC (512 µg/mL) against the gram-positive *Staphylococcus aureus*. Adding two methyl groups to the ortho position, as in compound **3**, or replacing the methyl group with a bulky *tert*-butyl group, as in compound **4**, yielded a twofold decrease in the MIC (1024 µg/mL). Halogenation of the phenyl ring with a fluoro (compound **6**) or a chloro (compound **5**) atom also resulted in a two- and fourfold decrease in antibacterial activity compared to compound **2**.

The other gram-positive bacterium *E. faecalis* displayed higher susceptibility to all compounds **1–6** compared to other tested bacterial and fungal strains. Substitution with an electron-donating methyl, methoxy, or even bulky *tert*-butyl group (compounds **1**, **2**, and **4**) resulted in the same activity profile with an MIC of 512 µg/mL (Table 1). Interestingly, replacement of the methyl group with a halogen like a fluoro atom, as in compound **6**, restored the activity (MIC = 512 µg/mL), while

chloro substitution, as in compound **5**, deteriorated antibacterial activity (MIC = 2048 µg/mL).

The gram-negative bacterium *Escherichia coli* was inhibited with the methoxy-substituted compound **1** with a MIC of 512 µg/mL, showing the best antibacterial activity profile among the tested compounds. The increased affinity of compound **1** against gram-negative bacteria might be ascribed to the hydrogen-bonding capability of the methoxy substituent. Replacing the methoxy group (compound **1**) with other electron-donating methyl or bulky *tert*-butyl groups or with an electron-withdrawing atom like fluoro decreased the antibacterial activity twofold, resulting in an MIC of 1028 µg/mL, while the other substitutions decreased the antibacterial activity against *E. coli.*

Among the bacterial strains, *Pseudomonas aeruginosa* was the least susceptible pathogen against the tested compounds **1–6**. Compounds **1**, **4**, and **6** showed twofold better antibacterial activities compared to compounds **2**, **3**, and **5** with an MIC of 1024 µg/mL.

Interestingly, only compound **2** showed antifungal activity against *Candida albicans* and *C. parapsilosis*. Introduction of other substitutions rather than a methyl group deteriorated antifungal activity.

CONCLUSION

In this study, we synthesized six new taurinamidobenzenesulfonamide derivatives and evaluated their *in vitro* antibacterial and antifungal activity against two gram-positive bacteria (*S. aureus* and *E. faecalis*), two gram-negative bacteria (*E. coli* and *P. aeruginosa*), and two fungal strains (*C. albicans* and *C. parapsilosis*) using broth microdilution method. All compounds showed significantly poor antibacterial activity (MIC = 512–2048 µg/mL), while only compound **2** showed antifungal activity with an MIC of 1024 µg/mL. The poor inhibition profile of the compounds may be explained by their low water solubility which probably prevent their diffusion from the lipid membrane to the hydrophilic cytoplasmic environment. It can be concluded that changing phthalimido with substituted benzyl groups did not increase the antibacterial/antifungal activity of taurinamidobenzensulfonamide core structure.

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CONFLICT OF INTERESTS

The authors have declared no conflict of interest.

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