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SYNTHESIS AND STUDY OF SOME NOVEL BENZOTHIAZOLE DERIVATIVES AS ANTIMICROBIAL AGENTS

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ABSTRACT

We have synthesized some novel benzothiazole derivatives as antimicrobial agents by condensation of N-(4-Acetyl-phenyl)-2-(benzothiazole-2-ylsulfanyl)-acetamide with different substituted of aniline in the presence of catalytic amount of acetic acid. The intermediate was prepared by reaction of N-(4-acetylphenyl)-2-chloroacetamide with benzthiazol in the presence of K_2CO_3. A new series of benzothiazole having azomethine group were confirmed by IR, ^{1}H NMR, ^{13}C NMR, mass spectroscopy and elemental analysis. The new compounds examined for antibacterial effects again different strain of bacteria and antifungal were high to lowest minimum inhibition concentration (MIC) values.

Key words: Benzothiazole derivatives, Antimicrobial agents.

INTRODUCTION

Increasing of population with new disease required new bioactive molecules into form of drugs. Generally, the prevention and to inhibit the pathogenic action of the drug is depends on some specific linkage, moiety and/or group, which are present in the drug. Benzimidazole, benzoxazole, benzothiazole etc. moiety exhibited a very good biological activity as well as chalcones, Schiff base etc. also.

Generally, azomethines are known as Schiff bases, which are contained characteristic -C=N- group. Several methods have been reported for the synthesis of azomethines. Selvam et al.[1] have prepared sulfonamide and its derivatives as anti-HIV agents. Schiff bases can be synthesized from an aromatic amine and a carbonyl compound by nucleophilic addition forming a hemiaminal. Furthermore, this hemiaminal followed by a dehydration to generate an imine[2]. They are well known intermediates for the preparation of azetidinones, thiazolidinones, oxadiazolines and many other derivatives shown by literature survey. Azomethines exhibit a wide range of pharmacological activities like antiparasitic[3], antimicrobial[4], anticancer[5] and anti-inflammatory[6], antioxidant[7] etc.

Benzothiazole scaffold is a useful structural motif for displaying chemical functionality in biologically active molecules. There are many drugs, which are useful in different diseases containing benzoxazole nucleus. The main reason of that benzothiazole and its derivatives exhibited a wide variety of interesting biological activities such as anti-microbial[8,9], anticancer[10], antidiabetic[11], antitumor[12], anti-inflammatroy[13], anticonvulsant[14], analgesic[15] etc.

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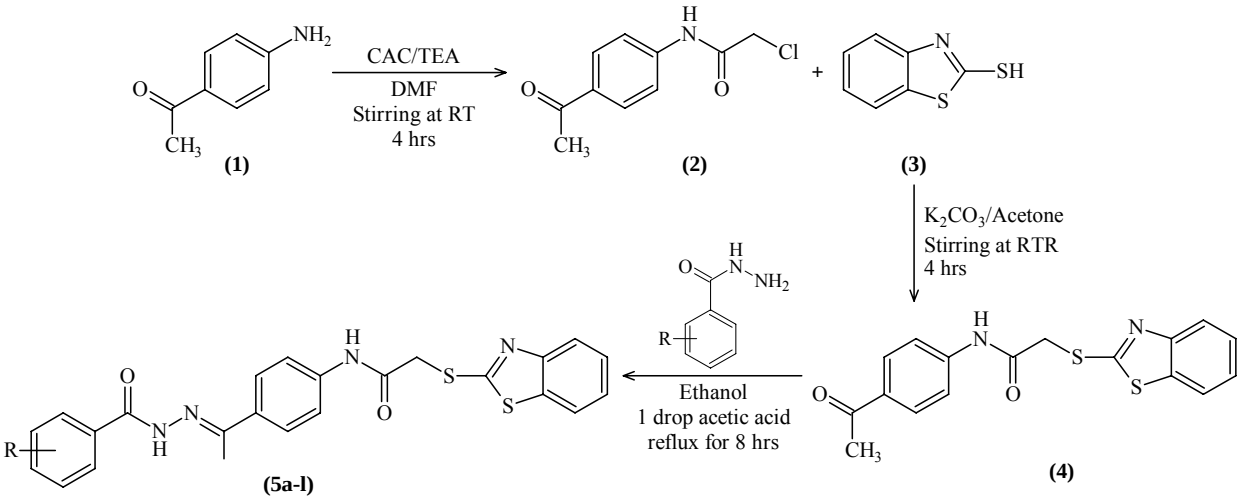
EXPERIMENTAL

All the required chemicals and solvents used for the synthesis were purchased from HIMEDIA, LOBA chemie, SD fine chemicals and/or Merck Ltd. Melting point was determined by the open end capillary method and are reported uncorrected at the primary stage. Completion of reaction was monitored by aluminum coated TLC plates (TLC silica gel 60 F_{245}, E. Merck) using the different solvent ratio for different steps as mobile phase and spot checked under ultraviolet (UV) light. Bruker Spectrophotometer-400 MHz where Trimethyl silane (TMS) and dimethyl sulfoxide (DMSO)-d6 was used as solvent for the ^1H NMR. Shimadzu mass spectrophotometer was used for the mass spectral analysis. Bruker FT-IR alpha-t (ATR) used for the IR spectral data. Perkin-Elmer 2400 CHN analyzer used for the elemental analysis (% C, H, N).



where R = Different substituents

Scheme 1: Synthetic route for the preparation of title compounds (5a-l).

Synthesis of N-(4-acetylphenyl)-2-chloroacetamide (Comp. 2)

The synthesis of N-(4-acetylphenyl)-2-chloroacetamide (**Compound 2)** was carried out by reacting 4-amino acetophenone (0.01 mol, 135 g/mol, 1.35 g) with chloroacetylchloride (0.015 mol, 113 g/mol, 1.19 mL) and triethylamine (4-5 drops) using DMF (30 mL) as solvent. The reaction mixture was stirred for 4 hrs at room temperature. The completion of reaction was monitored by TLC with mobile phase Toluene : Acetone (7:3). The solution was poured into ice water (50 mL). The product obtained was filter and crystalline in ethanol.

Compound 2: Solide brown crystals; Yield 85%; M.P. 154°C; IR (ν_{max}, cm^{-1}, ATR): 740 (C-Cl str.), 1413 (C=C str. Aromatic ring), 1640 (C=O str.), 2750 (CH_2 str. methylene), 3049 (CH str. aromatic ring), 3232 (NH str.); ^1H NMR (400 MHz, DMSO-d6, δ, ppm): 2.56 (3H, s, -CH_3), 4.89 (2H, s, -CH_2), 7.70-8.10 (4H, d, Ar–H), 9.97 (1H, s, -NH); ^{13}C NMR (400 MHz, DMSO-d6, δ, ppm): 27.2 (C17), 43.2 (C8), 121.0 (C11), 121.0 (C15), 129.2 (C12), 129.2 (C14), 137.2 (C13), 166.0 (C9), 198.2 (C16); (MS (m/z): 212 (M^+).

Synthesis of N-(4-acetylphenyl)-2-(benzo[d]thiazole-2-ylthio)acetamide (Comp. 4)

N-(4-acetylphenyl)-2-chlroacetamide **(2)** (0.01 mol, 211.5 g/mol, 2.11 g) was further reacted with 2-mercatobenzothiazole **(3)** (0.01 mol, 167.25 g/mol, 1.67 g). The reaction mixture was stirred at room

temperature for 4 hrs in presence of K_2CO_3 (0.02 mol, 138 g/mol, 2.76 g) and acetone (25 mL) as a reaction medium. The completion of reaction was monitored by TLC using Toluene: Acetone (8:2) as a mobile phase, product was poured into water and stirred for 1 hr. The obtained precipitate were collected and dried. The product was crystallized into methanol.

Compound 4: Solid cream yellow; Yield: 80%; M.P.: 168-170^oC; IR (ν_{max}, cm^{-1}, ATR): 1419 (C=C str. aromatic ring), 1644 (C=O str.), 2755 (CH_2 str. methylene), 3054 (CH str. Aromatic ring), 3240 (NH str.); ^1H NMR (400 MHz, DMSO-d6, δ, ppm): 2.52 (3H, s, -CH_3), 4.46 (2H, s, -CH_2), 7.44-8.19 (8H, d, Ar–H), 7.25 (1H, s, -NH); ^{13}C NMR (400 MHz, DMSO-d6, d, ppm): 26.4, 38.7, 121.4, 121.4, 121.6, 121.9, 124.5, 125.5, 129.0, 129.4, 135.4, 136.8, 142.8, 153.8, 166.6, 168.4, 197.5; MS (m/z): 342 (M^+); Elemental Analysis: C, 59.50; H, 4.20; N, 08.22%.

General procedure for the synthesis of the title compounds (5a–l)

N-(4-Acetylphenyl)-2-(benzo[d]thia-2-ylthio)acetamide **(Comp. 4)** (0.01 mol, 326 g/mol, 3.26 g) was further treated with different substituted acid hydrazide (0.01 mol) in ethanol (20 mL) in the presence of catalytic amount of acetic acid and 4-5 drops of fused sodium acetate and refluxed for 8 hrs. The completion of the reaction was monitored by the TLC using Toluene : Acetone (8:2) as mobile phase. Resulting solid was separated out, filtered, and washed with water, dried and crystallized by alcohol (99.9%)[16]. Melting points of each synthesized compound were measured by electrical melting point apparatus. The products were designated as **(5a–l)** and characterized by elemental, IR, NMR, CMR and MS analyses.

Physical constant and characterization of 2-(benzo[d]thiazol-2-ylthio)-N-(4-(1-(2-benzoylhydrazono) ethyl)phenyl) acetamide (5a)

Yield: 74%; M.P.: 190-192°C; ^1H NMR (400 MHz, DMSO- δ6, δ, ppm): 2.32 (3H, s, -CH_3), 4.10 (2H, s, -CH_2), 7.60-8.09 (13H, d, Ar–H), 7.16 (1H, s, -NH); ^{13}C NMR (400 MHz, DMSO- δ6, δ, ppm): 16.6, 38.0, 110.5, 119.5, 121.6, 121.6, 123.7, 124.8, 127.9, 127.9, 128.6, 128.6, 129.8, 129.8, 132.3, 132.9, 133.6, 140.7, 141.8, 147.9, 151.6, 163.0, 165.4, 168.0; MS (m/z): 460 (M^+); Elemental analysis: C, 63.53; H, 4.37; N, 12.18%.

Physical constant and characterization of 2-(benzo[d]thiazol-2-ylthio)-N-(4-(1-(2-(3-nitrobenzoyl) hydrazono)ethyl)phenyl)acetamide (5b)

Yield: 72%; M.P.: 210-212°C; ^1H NMR (400 MHz, DMSO- δ6, δ, ppm): 2.30 (3H, s, -CH_3), 4.42 (2H, s, -CH_2), 7.52-8.70 (12 H, d, Ar–H), 7.00-7.26 (2 H, s, -NH); ^{13}C NMR (400 MHz, DMSO-δ 6, δ, ppm): 16.3, 38.8, 110.6, 119.4, 121.6, 121.6. 123.1, 123.8, 124.8, 127.6, 129.4, 129.4, 129.8, 132.5, 133.0, 133.6, 135.4, 140.8, 141.6, 148.0, 151.6, 163.4, 165.4, 168.5; MS (m/z): 505 (M^+); Elemental analysis : C, 57.03; H, 3.78; N, 13.84%.

Physical constant and characterization of 2-(benzo[d]thiazol-2-ylthio)-N-(4-(1-(2-(4-nitrobenzoyl) hydrazono)ethyl)phenyl) acetamide (5c)

Yield: 75%; M.P.: 214-216°C; ^1H NMR (400 MHz, DMSO-δ 6, δ, ppm): 2.36 (3H, s, -CH_3), 4.37 (2H, s, -CH_2), 7.50-8.45 (12H, d, Ar–H), 6.95-7.24 (2H, s, -NH); ^{13}C NMR (400 MHz, DMSO- δ6, δ, ppm): 16.4, 39.5, 110.3, 119.8, 121.8, 121.8, 123.5, 124.3, 124.3, 125.0, 128.8, 128.8, 129.2, 129.2, 133.4, 137.6, 138.6, 141.5, 147.8, 151.4, 151.9, 163.9, 165.0, 168.2; MS (m/z): 506 (M^+); Elemental analysis: C, 57.06; H, 3.77; N, 13.88%.

Physical constant and characterization of 2-(benzo[d]thiazol-2-ylthio)-N-(4-(1-(2-(3-methylbenzoyl) hydrazono)ethyl)phenyl) acetamide (5d)

Yield: 68%; M.P.: 208-210°C; ^{1}H NMR (400 MHz, DMSO-δ6, δ, ppm): 2.30-2.36 (6H, s, -CH_3), 4.38 (2H, s, -CH_2), 7.32-8.22 (12H, d, Ar–H), 6.90-7.22 (2H, s, -NH); ^{13}C NMR (400 MHz, DMSO-δ 6, δ, ppm): 16.5, 21.6, 38.6, 114.8, 116.2, 121.4, 121.4, 123.0, 123.8, 124.5, 128.2, 128.4, 129.7, 129.7, 131.7, 134.6 136.7,137.9, 138.4, 139.3, 140.2, 145.8, 147.6, 163.6, 167.4; MS (m/z): 474 (M^+); Elemental analysis: C, 63.26; H, 4.64; N, 11.80%.

Physical constant and characterization of 2-(benzo[d]thiazol-2-ylthio)-N-(4-(1-(2-(4-methylbenzoyl) hydrazono)ethyl)phenyl) acetamide (5e)

Yield: 66%; M.P.: 202-204°C; ^{1}H NMR (400 MHz, DMSO-δ 6, δ, ppm): 2.30-2.36 (6H, s, -CH_3), 4.44 (2H, s, -CH_2), 7.38-8.18 (12H, d, Ar–H), 7.05-7.25 (2H, s, -NH); ^{13}C NMR (400 MHz, DMSO- δ6, δ, ppm): 16.6, 21.4, 38.6, 110.6, 119.4, 121.3, 121.3, 123.6, 124.6, 127.3, 127.3, 129.1, 129.1, 129.5, 129.5, 129.9, 133.6, 140.8, 141.6, 141.9, 147.8, 151.9, 163.3, 165.2, 168.2; MS (m/z): 475 (M^+); Elemental analysis: C, 63.35; H, 4.62; N, 11.85%.

Physical constant and characterization of 2-(benzo[d]thiazol-2-ylthio)-N-(4-(1-(2-(4-methoxy-benzoyl) hydrazono)ethyl)phenyl) acetamide (5f)

Yield: 64 %; M.P.: 214-216°C; ^{1}H NMR (400 MHz, DMSO- δ6, δ, ppm): 2.32-3.85 (6H, s, -CH_3), 4.40 (2H, s, -CH_2), 7.15–8.20 (12H, d, Ar–H), 6.90-7.20 (2H, s, -NH); ^{13}C NMR (400 MHz, DMSO- δ6, δ, ppm): 16.6, 38.5, 55.6, 110.6, 114.8, 114.8, 119.2, 121.4, 121.4, 123.7, 124.7, 128.3, 128.3, 129.6, 129.6, 129.9, 133.4, 140.7, 141.6, 147.6, 151.9, 163.3, 164.3, 165.2, 168.6; MS (m/z): 490 (M^+); Elemental analysis: C, 61.17; H, 4.52; N, 11.45%.

Physical constant and characterization of 2-(benzo[d]thiazol-2-ylthio)-N-(4-(1-(2-(2-chlorobenzoyl) hydrazono)ethyl)phenyl) acetamide (5g)

Yield: 71 %; M.P.: 212-214°C; ^{1}H NMR (400 MHz, DMSO-δ 6, δ, ppm): 2.34 (3H, s, -CH_3), 4.42 (2H, s, -CH_2), 7.41–8.14 (12H, d, Ar–H), 6.96-7.25 (2H, s, -NH); ^{13}C NMR (400 MHz, DMSO- δ 6, δ, ppm): 16.5, 38.2, 110.6, 119.2, 121.6, 121.6, 124.6, 126.6, 128.9, 129.5, 129.5, 129.9, 130.2, 132.5, 133.5, 133.6, 134.8, 140.7, 147.6, 151.9, 163.3, 164.1, 165.2, 168.4 ; MS (m/z): 494 (M^+); Elemental analysis: C, 58.02; H, 3.84; N, 11.34%.

Physical constant and characterization of 2-(benzo[d]thiazol-2-ylthio)-N-(4-(1-(2-(3-chlorobenzoyl) hydrazono)ethyl)phenyl) acetamide (5h)

Yield: 70 %; M.P.: 214-216°C; ^{1}H NMR (400 MHz, DMSO-δ 6, δ, ppm): 2.32 (3H, s, -CH_3), 4.36 (2H, s, -CH_2), 7.50–8.10 (12H, d, Ar–H), 7.14-7.28 (2H, s, -NH); ^{13}C NMR (400 MHz, DMSO- δ6, δ, ppm): 16.4, 39.6, 110.8, 119.4, 121.6, 121.6, 124.3, 126.3, 128.9, 129.8, 129.8, 130.4, 130.6, 132.7, 133.7, 133.7, 134.5, 140.4, 147.6, 151.6, 163.9, 164.4, 165.6, 168.2; MS (m/z): 496 (M^+); Elemental analysis: C, 58.21; H, 3.84; N, 11.33%.

Physical constant and characterization of 2-(benzo[d]thiazol-2-ylthio)-N-(4-(1-(2-(4-chlorobenzoyl) hydrazono)ethyl)phenyl) acetamide (5i)

Yield: 72 %; M.P.: 206-208°C; ^{1}H NMR (400 MHz, DMSO- δ6, δ, ppm): 2.32 (3H, s, -CH_3), 4.43 (2H, s, -CH_2), 7.46–8.14 (12H, d, Ar–H), 6.93-7.23 (2H, s, -NH); ^{13}C NMR (400 MHz, DMSO- δ 6, δ, ppm): 16.6, 39.8, 110.8, 119.4, 121.3, 121.3, 124.4, 128.9, 128.9, 129.9, 129.9, 130.3, 130.3, 132.7, 133.4,

133.4, 134.9, 140.4, 147.4, 151.9, 163.4, 164.2, 165.4, 168.2; MS (m/z): 496 (M^+); Elemental analysis: C, 58.23; H, 3.83; N, 11.35%.

Physical constant and characterization of 2-(benzo[d]thiazol-2-ylthio)-N-(4-(1-(2-(2-hydroxy-benzoyl)hydrazono)ethyl)phenyl) acetamide (5j)

Yield: 66%; M.P.: 212-214°C; ^{1}H NMR (400 MHz, DMSO- δ6, δ, ppm): 2.30 (3H, s, -CH_3), 5.37 (1H, s, -OH), 4.41 (2H, s, -CH_2), 6.98–8.12 (12H, d, Ar–H), 6.96-7.23 (2H, s, -NH); ^{13}C NMR (400 MHz, DMSO-δ 6, δ, ppm): 16.6, 38.6, 110.7, 117.4, 117.8, 119.4, 121.4, 121.7, 121.7, 123.6, 124.6, 128.9, 129.2, 133.1, 133.9, 140.9, 141.7, 147.8, 151.6, 153.4, 159.8, 163.5, 165.2, 165.6; MS (m/z): 476 (M^+); Elemental analysis: C, 60.45; H, 4.26; N, 11.79%.

Physical constant and characterization of 2-(benzo[d]thiazol-2-ylthio)-N-(4-(1-(2-(3-hydroxy-benzoyl)hydrazono)ethyl)phenyl) acetamide (5k)

Yield: 66%; M.P.: 220-222°C; ^{1}H NMR (400 MHz, DMSO-δ 6, δ, ppm): 2.32 (3H, s, -CH_3), 5.32 (1H, s, -OH), 4.35 (2H, s, -CH_2), 7.13–8.22 (12H, d, Ar–H), 6.84-7.28 (2H, s, -NH); ^{13}C NMR (400 MHz, DMSO- δ6, δ, ppm): 16.6, 38.7, 110.3, 117.6, 117.6, 119.4, 121.1, 121.8, 121.8, 123.3, 124.4, 128.7, 129.3, 133.0, 133.7, 140.8, 141.7, 147.9, 151.5, 153.4, 159.6, 163.8, 165.0, 165.5; MS (m/z): 474 (M^+); Elemental Analysis: C, 60.66; H, 4.26; N, 11.82%.

Physical constant and characterization of 2-(benzo[d]thiazol-2-ylthio)-N-(4-(1-(2-(4-hydroxy-benzoyl)hydrazono)ethyl)phenyl) acetamide (5l)

Yield: 62%; M.P.: 220-222°C; ^{1}H NMR (400 MHz, DMSO-δ 6, δ, ppm): 2.29 (3H, s, -CH_3), 5.31 (1H, s, -OH), 4.32 (2H, s, -CH_2), 7.08–7.99 (12H, d, Ar–H), 6.88-7.24 (2H, s, -NH); ^{13}C NMR (400 MHz, DMSO- δ 6, δ, ppm): 16.6, 38.6, 110.4, 116.2, 119.1, 119.4, 120.2, 121.8, 121.8, 123.9, 124.6, 128.9, 128.9, 129.5, 133.2, 135.8, 140.9, 141.4, 147.8, 151.9, 158.8, 163.5, 165.2, 168.3; MS (m/z): 476 (M^+); Elemental analysis: C, 60.62; H, 4.28; N, 11.76%.

RESULTS AND DISCUSSION

Scheme 1 was completed by three various steps and final compounds were designated at **(5a-l)**. Compounds **(5a-l)** have not been reported previously confirmed by using the Scifinder search into the CSMCRI, Bhavnagar. The newly synthesized compounds were confirmed by various spectrograph using spectroscopic instruments like FT–IR, ^{1}H NMR, ^{13}C NMR, MS and CHN analyzer. The data of FT-IR spectroscopy provides valuable information regarding the nature of functional group in present structure. In order to study the bonding mode of compound **(4)** to the compound **(5a-l)**, the IR spectrum of compound **(4)** was compared with the spectra of compound **(5a–l)**. Considerable differences to be expected were observed and it's a significant that the reaction was proceed out. The general structure of compounds **(5a-l)** designated as below, where R is different substitute group or atom.

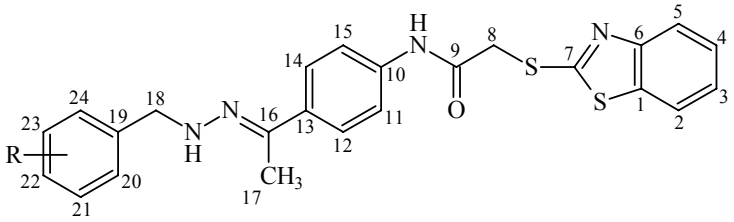


Fig. 1: Compound (5a-l)

The structures of the final compounds **(5a-l)** were established by their spectral analysis. Using compound **(5a)** as a representative example, its FTIR spectrum of **(5a)** showed the most relevant peaks of benzothiazole-acetylphenyl ring. Stretching vibration at 3228 cm^{-1} indicates that compound containing a secondary amine. The vibration at 1588 cm^{-1} and 3048 cm^{-1} over the range showed intensity absorption peaks corresponding to aromatic C-H stretching vibrations. The absorption peaks at 1660 cm^{-1} is due to the carbonyl groups present structure as amide group.

^{1}H NMR: It has been observed from the chemical structure of compound that C-11,C-12, C-14 and C-15 are pairs of chemically equivalent protons which appear at δ = 7.66 ppm and δ = 7.83 ppm indicates that this all four carbon are presence in same aromatic ring. As well as C-2, C-3, C-4 and C-5 are pairs of chemically equivalent protons which appeared at δ = 7.56, δ = 8.02 ppm and δ = 8.16 ppm value indicates that benzothiazole ring. C-20, C-21, C-22, C-23 and C-24 are also pairs of chemically equivalent protons, which indicates that this all carbon presence of same aromatic ring. The protons attached at C-8 appeared as a singlet at δ = 4.10 ppm due to sulfur and C-9 carbonyl group atmosphere. Carbon C-17 contains a proton gives singlet at δ = 2.32 ppm indicates that azomethine group present in the structure. The mass spectrum of **(5a)** showed a molecular ion peak at m/z 460 (M + 1), which is in agreement with its proposed structure.

Table 1: Antimicrobial screening results of compounds (5a–l)

Entry	R	Minimum Inhibitory Concentration (MIC) µg/mL					
		Gram positive bacteria		Gram negative bacteria		Fungi	
		S. aureus	***E. faecalis***	***E. coli***	***P. aeruginosa***	***C. albicans***	***A. niger***
5a	-H	31.25	125	15.62	31.25	62.5	62.5
5b	3-NO_2	250	125	62.5	31.25	62.5	31.25
5c	4-NO_2	125	125	62.5	31.25	31.25	31.25
5d	3-CH_3	250	125	62.5	31.25	31.25	31.25
5e	4-CH_3	15.62	62.5	15.62	15.62	15.62	15.62
5f	4-OCH_3	15.62	62.5	15.62	15.62	15.62	15.62
5g	2-Cl	125	125	62.5	62.5	125	125
5h	3-Cl	500	125	250	62.5	62.5	31.25
5i	4-Cl	125	125	15.62	62.5	125	125
5j	2-OH	125	125	15.62	62.5	125	62.5
5k	3-OH	125	125	62.5	62.5	125	125
5l	4-OH	125	125	125	125	125	125
Chloramphenicol		50	50	50	50	-	-
Ketoconazole		-	-	-	-	50	50

Minimum Inhibitory Concentration for bacteria (MICb) of all the newly synthesized compounds was determined for their *in vitro* antimicrobial activity against different bacterial and fungal strains by the conventional broth-dilution method[17] using standard drugs which aer Chloramphenicol for bacterial strain and Ketoconazole for fungal strain. The results of antimicrobial studies are presented in Table 1. Intermediates 2 and 4 showed poor antimicrobial activity against all tested bacterial and fungal strains as compared to final derivatives **(5a-l)**. Newly synthesized derivatives showed improved antibacterial activity compared to antifungal activity. Compounds **5a**, **5e** and **5f** were found to be highly active against the gram

positive bacterial strains and all the compounds showed except very good activity against gram bacteria strains except **5h** and **5l** shows average activity, showing inhibition in the range of 15.62-125 µg/mL. Among them, compounds **5e** and **5f** emerged as the most effective antibacterial agents with a 2 to 4-fold higher MIC (15.62 mg/mL) than the reference drug Chloramphenicol. Compounds **5e** and **5f** substituted with inductively electron donating methyl and methoxy groups, respectively, at the para position showed the highest antibacterial activity. The presence of electron donating groups on the phenyl ring resulted in a significant increase in antimicrobial activity of compounds **5d**, **5e**, **5f**, **5j**, **5k** and **5l**. From these results, it can be observed that the antibacterial activity was considerably affected by the substitution pattern on the phenyl ring. Further, the results of the antifungal activity indicated that compound **5e** and **5f** endowed with methyl and methoxy emerged as the most effective antifungal agent and showed an MIC in the value of 15.62 mg/mL against two fungal strains using ketoconazole as a positive control.

CONCLUSION

From the study of the above results and from all the spectral and physical data of the synthesized compounds, it can be clearly concluded that designed compounds were synthesized successfully. We have accomplished the synthesis of new derivatives of benzothiazole (**5a-l)** having a schiff base with the hope of generating new bioactive molecules that could be useful as potent antimicrobial agents. A series of compounds when substituted by electron-donating group like -CH_3 and -OCH_3 enhances the antimicrobial activity when present on the aromatic ring. On the other side, the used of electron accepting group didn't enhances the antimicrobial activity when present on aromatic ring as compared to the electron donating group. Among the twelve newer derivatives analogs **5d**, **5e** possessing electron donating group such as methyl and methoxy at the para position were identified as the most potent antibacterial agents and also compound **5e** and **5f** were found to be the most effective antifungal agent. The results lead us to further studies to acquire more information about newer derivatives of benzothiazole.

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