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Synthesis, Characterization and Antimicrobial Screening of Novel Thieno[2,3-*d*]Pyrimidine Derivatives

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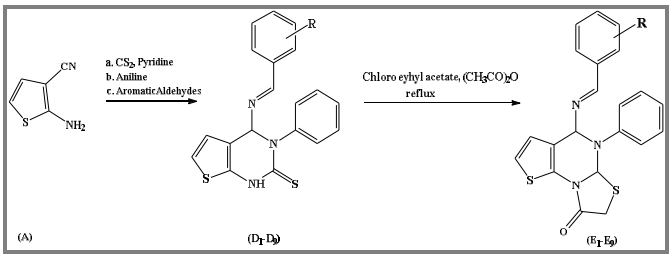
ABSTRACT

A Series of new thieno[2,3-d]pyrimidine derivatives4-{[(E)-(substituted phenyl)methylidene]amino}-5-phenyl-5,5a-dihydro-4H-[1,3]thiazolo [3,2-a]thieno[3,2-e]pyrimidin-8(7H)-one ***(E$_1$-E$_9$)****have been synthesized from 2-aminothiophene-3-carbonitrile. The newly synthesized compounds have been characterized by FT-IR, ^{1}H NMR and elemental analysis. They have also been screened for their antimicrobial activity against two Gram-positive, two Gram-negative and one fungal strain by broth dilution method. Some of the compounds have shown significant activity.*

Graphical Abstract



Synthesis of Thieno[2,3-*d*] Pyrimidine containing Compounds

Keywords: Thieno[2,3-*d*] Pyrimidine, Thiazolidinone, Characterization, Antimicrobial activity.

INTRODUCTION

The formation of novel fused heterocycles is an important task for heterocyclic chemists from various points of view for the development of living things. Many condensed heterocyclic systems, especially when linked to a pyrimidine ring as quinazolines, pyridopyrimidines, triazolopyrimidines, pyrazolopyrimidines, pyrimidoazepines, furo-pyrimidines and pyrrolopyrimidines. Thienopyrimidines occupy a special position among these compounds.As a logical consequence of thiophene-phenyl isosterism, thienopyrimidines can be considered as bioisosteres of quinazolines. The synthesis of thienopyrimidine derivatives as potential surrogates for the quinazoline core structure has therefore

become a routine strategy in modern drug design and development. Thienopyrimidine derivatives have been found to possess wide range of therapeutic activities [1] viz, antitumor [2], antiviral [3], antimalarial [4], analgesic [5], anticancer [6, 7], anti-inflammatory [8, 9], anticonvulsant [10], neurotropic [11, 12], antioxidant [13], antibacterial [14], antifungal [15] and anti-proliferative [16].

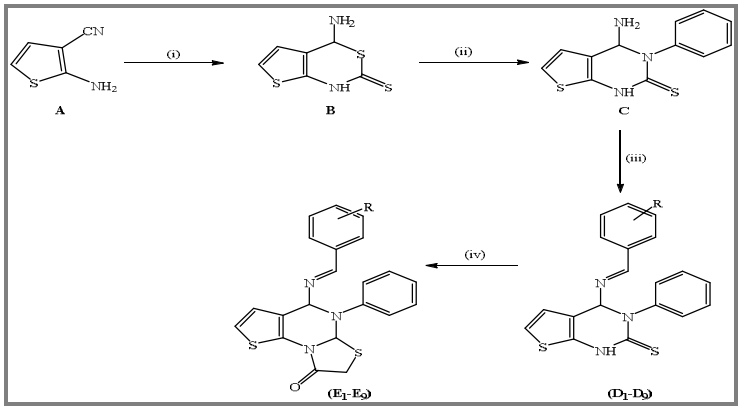
Thiazolidinones are the derivatives of thiazolidine which belong to an important group of heterocyclic compounds containing sulfur and nitrogen in a five member ring. The cyclic structure was assigned after the recognition of mercapto acetic acid as the primary product of hydrolysis of 3-phenyl-2-phenylamino-4-thiazolidinone. 4-thiazolidinone is an important scaffold known to be associated with several biological activities such as anti-inflammatory [17], antiviral [18], antidiabetic [19], antitubercular [20], anticonvulsant [21], anti-HIV [22], analgesic [23], anticancer [23], antifungal [24], antibacterial [25] and antimicrobial [26-28]. Therefore, we focused our attention on the synthesis of some novel thieno[2,3-*d*] pyrimidine derivatives starting with 2-aminothiophene-3-carbonitrile with a view to evaluate their antimicrobial activity.

MATERIALS AND METHODS

All the chemicals for the synthesis of targeted derivatives were used as of analytical grade. The progress of reactions and the purity of synthesized compounds were checked by TLC on EMerck precoated 60 F_{254} plates and the spots were examined under short-wave UV light and iodine chamber. Melting points of final compounds were determined with Digital Melting Point Apparatus EQ 730 (Equiptronics) using an open capillary tube with the heating rate of 10°C min^{-1}. The IR spectra were recorded with a Thermo Scientific Nicolet iS10 FTIR spectrophotometer at the Department of Chemistry, Veer Narmad South Gujarat University. ^{1}H-NMR spectra of the compounds were recorded with Avance II 400 MHz spectrometer at SAIF, Chandigarh, in DMSO-d6 using TMS as internal standard and chemical shifts are expressed in δ ppm. Elemental analyses were performed on Thermo Scientific FLASH 2000 at G.N.F.C.(Gujarat Narmada Valley Fertilizer Company Ltd., Bharuch).

General synthesis of Intermediates and Products:

Synthesis of 4-amino-1,4-dihydro-2*H*-thieno[2,3-*d*][1,3]thiazine-2-thione, B: To a solution/ suspension of 2-aminothiophene-3-carbonitrile **A** (0.01 mol) in ethanol (50 mL), carbon disulphide (0.01 mol) was added slowly at temperature 5-15°C. Pyridine in catalytic amount was also added. The reaction mixture was stirred for 6h at room temperature. Then it was cooled to 20°C to give precipitates. The resulting precipitated material was filtered off, washed with little amount of chilled methanol, dried and recrystallized from acetic acid Yield: 79% (M.P. 167°C).



Where, R=-2,4-$(Cl)_2$, 3,4-$(OH)_2$, 3-OCH_3, 4-Cl, 4-F, 4-OH, 4-OCH_3, 4-CH_3, 4-NO_2
(i) CS_2, Pyridine (ii) Aniline, Dimethyl Acetamide (iii) Aromatic aldehydes
(iv) Chloro ethyl acetate, acetic anhydride

Scheme 1: 4-{[(*E*)-(substituted phenyl)methylidene]amino}-5-phenyl-5,5*a*-dihydro-4*H*-[1,3]thiazolo[3,2-*a*]thieno [3,2 *e*]pyrimidin-8(7*H*)-one **(E_1-E_9)**

Synthesis of 4-amino-3-phenyl-3,4-dihydrothieno[2,3-*d*]pyrimidine-2(1*H*)-thione, C: To a solution/suspension of 4-amino-1,4-dihydro-2*H*-thieno[2,3-*d*][1,3]thiazine-2-thione **B** (0.01 mol) in dimethyl acetamide (50 mL), aniline (0.01 mol) was added. The mixture was heated and stirred under reflux for 10 h at 160-165°C. Then it Then it was cooled to give precipitates which was filtered off, washed with water, dried and recrystallized from acetic acid. Yield: 70% (M.P. 189°C).

Synthesis of 4-{[(*E*)-(substitutedphenyl)methylidene]amino}-3-phenyl-3,4-dihydrothieno[2,3-*d*] pyrimidine-2(1*H*)-thione, (D_1-D_9): To a solution/suspension of 4-amino-3-phenyl-3,4-dihydro-thienob [2,3-*d*] pyrimidine-2(1*H*)-thione **C** (0.01 mol) in slightly acidic ethanol (50 mL), aromatic aldehyde (0.01 mol) dissolved in ethanol (20 mL) was added and then stirred at reflux temperature for 8-10 h. On cooling, the reaction mixture was dumped into ice-water and the precipitated product was filtered off, washed with chilled water, dried and recrystallized from ethanol. Yield: 68% (M.P. 202°C).

Synthesis of 4-{[(*E*)-(substituted phenyl)methylidene]amino}-5-phenyl-5,5*a*-dihydro-4*H*-[1,3] thiazolo[3,2-*a*]thieno[3,2-*e*]pyrimidin-8(7*H*)-one(E_1-E_9): Chloro ethyl acetate (0.01 mol) was added to solution/suspension of 4-{[(*E*)-(substituted phenyl)methylidene]amino}-3-phenyl-3,4-dihydro-thieno [2,3-*d*] pyrimidine-2(1*H*)-thione(**D_1-D_9**)(0.01 mol) in acetic anhydride (50 mL) and heated and stirred under reflux for 12 h. The reaction mass was cooled to 20°C. The precipitated product was filtered off, washed with little amount of chilled water, dried and recrystallized from ethanol to get title compounds (Table 1).

Table 1. Physical data of Compounds (E_1-E_9)

Compound No.	R	Molecular Formula	Molecular Weight (g mol^{-1})	Yield (%)	M.P. (°C)
E_1	2,4-$(Cl)_2$	$C_{21}H_{15}Cl_2N_3OS_2$	460.39	62	275
E_2	3,4-$(OH)_2$	$C_{21}H_{17}N_3O_3S_2$	423.51	47	272
E_3	3-OCH_3	$C_{22}H_{19}N_3O_2S_2$	421.53	63	281
E_4	4-Cl	$C_{21}H_{16}ClN_3OS_2$	425.95	65	254
E_5	4-F	$C_{21}H_{16}FN_3OS_2$	409.50	66	241
E_6	4-OH	$C_{21}H_{17}N_3O_2S_2$	407.51	57	226
E_7	4-OCH_3	$C_{22}H_{19}N_3O_2S_2$	421.53	71	283
E_8	4-CH_3	$C_{22}H_{19}N_3OS_2$	405.53	73	261
E_9	4-NO_2	$C_{21}H_{16}N_4O_3S_2$	436.50	75	>300

RESULTS AND DISCUSSION

The structures of newly synthesized compounds were established on the basis of elemental analyses, IR and ^{1}H NMR Spectroscopy. All the synthesized compounds were screened for antimicrobial activity.

Characterization of Synthesized Compounds:

4-amino-1,4-dihydro-2*H*-thieno[2,3-*d*][1,3]thiazine-2-thione(B): IR (KBr, ν, cm^{-1}): 3450-3340 (NH-NH_2), 1180 (C=S); ^{1}H NMR (DMSO-d6, δ ppm): 2.01 (s, 2H, NH_2), 2.21 (s, 1H, NH), 6.42 (d, 1H, CH), 7.15 (d, 1H, CH), 5.85 (s, 1H, CH).

4-amino-3-phenyl-3,4-dihydrothieno[2,3-*d*]pyrimidine-2(1*H*)-thione (C): IR (KBr, ν, cm^{-1}): 3420-3260 (NH-NH_2), 1220 (C=S; ^{1}H NMR (DMSO-d6, δ ppm): 2.03 (s, 2H, NH_2), 2.25 (s, 1H, NH), 6.40 (d, 1H, CH), 7.12 (d, 1H, CH), 7.17-7.28 (m, 5H, Ar-H).

4-{[(*E*)-(2,4-dichlorophenyl)methylidene]amino}-3-phenyl-3,4-dihydrothieno[2,3-*d*]pyrimidine-2 (1*H*)-thione (D_1): ^{1}H NMR (DMSO-d6, δ ppm): 5.47 (s, 1H, CH),6.81 (d, 1H, CH), 7.09 (d, 1H, CH), 7.16-7.40 (m, 8H, Ar-H), 8.52 (s, 1H, N=CH).

4-{[(*E*)-(3,4-dihydrophenyl)methylidene]amino}-3-phenyl-3,4-dihydrothieno[2,3-*d*]pyrimidine-2 (1*H*)-thione (D_2): ^{1}H NMR (DMSO-d6, δ ppm): 4.39 (s, 1H, OH), 4.50 (s, 1H, OH), 5.46 (s, 1H, CH), 6.73 (d, 1H, CH), 7.10 (d, 1H, CH), 7.12-7.37 (m, 8H, Ar-H), 8.53 (s, 1H, N=CH).

4-{[(*E*)-(3-methoxyphenyl)methylidene]amino}-3-phenyl-3,4-dihydrothieno[2,3-*d*]pyrimidine-2(1*H*)-thione (D_3): ^{1}H NMR (DMSO-d6, δ ppm): 3.79 (s, 3H, CH_3), 5.49 (s, 1H, CH), 6.78 (d, 1H, CH), 7.12 (d, 1H, CH), 7.14-7.51 (m, 9H, Ar-H), 8.52 (s, 1H, N=CH).

4-{[(*E*)-(4-chlorophenyl)methylidene]amino}-3-phenyl-3,4-dihydrothieno[2,3-*d*]pyrimidine-2(1*H*)-thione (D_4): ^{1}H NMR (DMSO-d6, δ ppm): 5.47 (s, 1H, CH), 6.80 (d, 1H, CH), 7.10 (d, 1H, CH), 7.16-7.50 (m, 9H, Ar-H), 8.50 (s, 1H, N=CH).

4-{[(*E*)-(4-fluorophenyl)methylidene]amino}-3-phenyl-3,4-dihydrothieno[2,3-*d*]pyrimidine-2(1*H*)-thione (D_5): ^{1}H NMR (DMSO-d6, δ ppm): 5.48 (s, 1H, CH), 6.78 (d, 1H, CH), 7.11 (d, 1H, CH), 7.16-7.52 (m, 9H, Ar-H), 8.51 (s, 1H, N=CH).

4-{[(*E*)-(4-hydroxyphenyl)methylidene]amino}-3-phenyl-3,4-dihydrothieno[2,3-*d*]pyrimidine-2(1*H*)-thione (D_6): ^{1}H NMR (DMSO-d6, δ ppm): 4.00 (s, 1H, OH), 5.46 (s, 1H, CH), 6.70 (d, 1H, CH), 7.11 (d, 1H, CH), 7.17-7.42 (m, 9H, Ar-H), 8.50 (s, 1H, N=CH).

4-{[(*E*)-(4-methoxyphenyl)methylidene]amino}-3-phenyl-3,4-dihydrothieno[2,3-*d*]pyrimidine-2(1*H*)-thione (D_7): ^{1}H NMR (DMSO-d6, δ ppm): 3.78 (s, 3H, CH_3), 5.47 (s, 1H, CH), 6.72 (d, 1H, CH), 7.10 (d, 1H, CH), 7.16-7.46 (m, 9H, Ar-H), 8.47 (s, 1H, N=CH).

4-{[(*E*)-(4-methylphenyl)methylidene]amino}-3-phenyl-3,4-dihydrothieno[2,3-*d*]pyrimidine-2(1*H*)-thione (D_8): ^{1}H NMR (DMSO-d6, δ ppm): 2.35 (s, 3H, CH_3), 5.48 (s, 1H, CH), 6.78 (d, 1H, CH), 7.13 (d, 1H, CH), 7.18-7.53 (m, 9H, Ar-H), 8.45 (s, 1H, N=CH).

4-{[(*E*)-(4-nitrophenyl)methylidene]amino}-3-phenyl-3,4-dihydrothieno[2,3-*d*]pyrimidine-2(1*H*)-thione (D_9): ^{1}H NMR (DMSO-d6, δ ppm): 5.46 (s, 1H, CH), 6.74 (d, 1H, CH), 7.10 (d, 1H, CH), 7.17-7.57 (m, 9H, Ar-H), 8.45 (s, 1H, N=CH).

4-{[(*E*)-(2,4-dichlorophenyl)methylidene]amino}-5-phenyl-5,5*a*-dihydro-4*H*-[1,3]thiazolo[3,2-*a*] thieno[3,2-*e*]pyrimidin-8(7*H*)-one (E_1): IR (KBr, ν, cm^{-1}): 2981, 2870 (CH), 1680 (C=O), 1548 (C=N), 1153 (-SCH_2-), 732 (Ar-Cl); ^{1}H NMR (DMSO-d6, δ ppm): 3.50 (s, 2H, CH_2), 5.48 (s, 1H, CH), 6.01 (s, 1H, CH), 6.95 (d, 1H, CH), 7.12 (d, 1H, CH), 7.18-7.50 (m, 8H, Ar-H), 8.46 (s, 1H, N=CH); Anal. Calcd. for $C_{21}H_{15}Cl_2N_3OS_2$: C, 54.79; H, 3.28; N, 9.13; S, 13.93; Found: C, 54.68; H, 3.35; N, 9.06; S, 13.85.

4-{[(*E*)-(3,4-dihydroxyphenyl)methylidene]amino}-5-phenyl-5,5*a*-dihydro-4*H*-[1,3]thiazolo[3,2-*a*] thieno[3,2-*e*]pyrimidin-8(7*H*)-one (E_2): IR (KBr, ν, cm^{-1}): 2982, 2875 (CH), 1688 (C=O), 1552 (C=N), 1152 (-SCH_2-), 3420 (Ar-OH); ^{1}H NMR (DMSO-d6, δ ppm): 3.48 (s, 2H, CH_2), 4.34 (s, 1H, OH), 4.68 (s, 1H, OH), 5.43 (s, 1H, CH), 6.00 (s, 1H, CH), 6.94 (d, 1H, CH), 7.10 (d, 1H, CH), 7.16-7.32 (m, 8H, Ar-H), 8.45 (s, 1H, N=CH); Anal. Calcd. for $C_{21}H_{17}N_3O_3S_2$: C, 59.56; H, 4.05; N, 9.92; S, 15.14; Found: C, 59.62; H, 4.10; N, 9.97; S, 15.21.

4-{[(*E*)-(3-methoxyphenyl)methylidene]amino}-5-phenyl-5,5*a*-dihydro-4*H*-[1,3]thiazolo[3,2-*a*] thieno[3,2-*e*]pyrimidin-8(7*H*)-one (E_3): IR (KBr, ν, cm^{-1}): 2981, 2869 (CH), 1686 (C=O), 1553 (C=N), 1152 (-SCH_2-); ^{1}H NMR (DMSO-d6, δ ppm): 3.49 (s, 2H, CH_2), 3.80 (s, 3H, CH_3), 5.46 (s, 1H, CH), 6.03 (s, 1H, CH), 6.97 (d, 1H, CH), 7.14 (d, 1H, CH), 7.19-7.48 (m, 9H, Ar-H), 8.40 (s, 1H, N=CH); Anal. Calcd. for $C_{22}H_{19}N_3O_2S_2$: C, 62.69; H, 4.54; N, 9.97; S, 15.21; Found: C, 62.61; H, 4.49; N, 9.90; S, 15.13.

4-{[(*E*)-(4-chlorophenyl)methylidene]amino}-5-phenyl-5,5*a*-dihydro-4*H*-[1,3]thiazolo[3,2-*a*] thieno[3,2-*e*]pyrimidin-8(7*H*)-one (E_4): IR (KBr, ν, cm^{-1}): 2982, 2869 (CH), 1685 (C=O), 1554 (C=N), 1158 (-SCH_2-), 730 (Ar-Cl); ^{1}H NMR (DMSO-d6, δ ppm): 3.48 (s, 2H, CH_2), 5.47 (s, 1H, CH), 6.01 (s, 1H, CH), 6.95 (d, 1H, CH), 7.10 (d, 1H, CH), 7.16-7.49 (m, 9H, Ar-H), 8.49 (s, 1H, N=CH); Anal. Calcd. for $C_{21}H_{16}ClN_3OS_2$: C, 59.22; H, 3.79; N, 9.87; S, 15.05; Found: C, 59.17; H, 3.73; N, 9.92; S, 15.11.

4-{[(*E*)-(4-fluorophenyl)methylidene]amino}-5-phenyl-5,5*a*-dihydro-4*H*-[1,3]thiazolo[3,2-*a*] thieno[3,2-*e*]pyrimidin-8(7*H*)-one (E_5): IR (KBr, ν, cm^{-1}): 2990, 2878 (CH), 1680 (C=O), 1550 (C=N), 1270 (Ar-F), 1157 (-SCH_2-); ^{1}H NMR (DMSO-d6, δ ppm): 3.47 (s, 2H, CH_2), 5.49 (s, 1H, CH), 6.05 (s, 1H, CH), 6.97 (d, 1H, CH), 7.11 (d, 1H, CH), 7.18-7.54 (m, 9H, Ar-H), 8.44 (s, 1H, N=CH); Anal. Calcd. for $C_{21}H_{16}FN_3OS_2$: C, 61.60; H, 3.94; N, 10.26; S, 15.66; Found: C, 61.65; H, 3.99; N, 10.31; S, 15.59.

4-{[(*E*)-(4-hydroxyphenyl)methylidene]amino}-5-phenyl-5,5*a*-dihydro-4*H*-[1,3]thiazolo[3,2-*a*] thieno[3,2-*e*]pyrimidin-8(7*H*)-one (E_6): IR (KBr, ν, cm^{-1}): 2982, 2871 (CH), 1681 (C=O), 1552 (C=N), 3431 (Ar-OH), 1155 (-SCH_2-); ^{1}H NMR (DMSO-d6, δ ppm): 3.50 (s, 2H, CH_2), 4.16 (s, 1H, OH), 5.45 (s, 1H, CH), 5.99 (s, 1H, CH), 6.94 (d, 1H, CH), 7.11 (d, 1H, CH), 7.15-7.40 (m, 9H, Ar-H), 8.39(s, 1H, N=CH); Anal. Calcd. for $C_{21}H_{17}N_3O_2S_2$: C, 61.90; H, 4.21; N, 10.31; S, 15.73; Found: C, 61.86; H, 4.17; N, 10.29; S, 15.80.

4-{[(*E*)-(4-methoxyphenyl)methylidene]amino}-5-phenyl-5,5*a*-dihydro-4*H*-[1,3]thiazolo[3,2-*a*] thieno[3,2-*e*]pyrimidin-8(7*H*)-one (E_7): IR (KBr, ν, cm^{-1}): 2979, 2879 (CH), 1681 (C=O), 1551 (C=N), 1152 (-SCH_2-); ^{1}H NMR (DMSO-d6, δ ppm): 3.48 (s, 2H, CH_2), 3.82 (s, 3H, CH_3), 5.45 (s, 1H, CH), 6.00 (s, 1H, CH), 6.96 (d, 1H, CH), 7.11 (d, 1H, CH), 7.18-7.53 (m, 9H, Ar-H), 8.46 (s, 1H, N=CH); Anal. Calcd. for C22H19N3O2S2: C, 62.69; H, 4.54; N, 9.97; S, 15.21; Found: C, 62.72; H, 4.47; N, 9.91; S, 15.14.

4-{[(*E*)-(4-methylphenyl)methylidene]amino}-5-phenyl-5,5*a*-dihydro-4*H*-[1,3]thiazolo[3,2-*a*] thieno[3,2-*e*]pyrimidin-8(7*H*)-one (E_8): IR (KBr, ν, cm^{-1}): 2982, 2870 (CH), 1680 (C=O), 1551 (C=N), 1154 (-SCH_2-); ^{1}H NMR (DMSO-d6, δ ppm): 3.48 (s, 2H, CH_2), 2.37 (s, 3H, CH_3), 5.46 (s, 1H, CH), 6.00 (s, 1H, CH), 6.94 (d, 1H, CH), 7.10 (d, 1H, CH), 7.17-7.50 (m, 9H, Ar-H), 8.43 (s, 1H, N=CH); Anal. Calcd. for C22H19N3OS2: C, 65.16; H, 4.72; N, 10.36; S, 15.81; Found: C, 65.22; H, 4.78; N, 10.41; S, 15.86.

4-{[(*E*)-(4-nitrophenyl)methylidene]amino}-5-phenyl-5,5*a*-dihydro-4*H*-[1,3]thiazolo[3,2-*a*] thieno[3,2-*e*]pyrimidin-8(7*H*)-one (E_9): IR (KBr, ν, cm^{-1}): 2983, 2873 (CH), 1681 (C=O), 1551 (C=N), 1153 (-SCH_2-), 1340 (Ar-NO_2); ^{1}H NMR (DMSO-d6, δ ppm): 3.52 (s, 2H, CH_2), 5.47 (s, 1H, CH), 6.04 (s, 1H, CH), 6.96 (d, 1H, CH), 7.11 (d, 1H, CH), 7.16-7.52 (m, 9H, Ar-H), 8.43 (s, 1H, N=CH); Anal. Calcd. for $C_{21}H_{16}N_4O_3S_2$: C, 57.78; H, 3.69; N, 12.84; S, 14.69; Found: C, 57.84; H, 3.74; N, 12.79; S, 14.76.

APPLICATION

One of the purposes of the present work is to synthesize new heterocyclic compounds that might be of certain biological interest. All the newly synthesized compounds were tested against *S.aureus* (ATCC-96) and *S.pyogenes* (ATCC-443) as Gram positive and *E.coli* (ATCC- 442) and *P.aeruginosa* (ATCC-441) as Gram negative bacterial strains. Antifungal activities of the compounds were tested against *A.niger* (ATCC-282) as fungal strain. The prepared compounds were screened *in vitro* for their antibacterial and antifungal activities by broth dilution method (Table 2). The lowest concentration inhibiting growth of the organism is recorded as the MIC. DMSO was used as diluent. Ampicillin and Chloramphenicol were used as standard antibacterial and Nystatin and Gresefulvin were used as standard antifungal drugs. From the screening results, it can be seen that compound E_2

showed excellent activity and compound E_6 showed good activity against Gram positive bacteria *S.aureus*. Compound E_6 and E_7 exhibited considerable activity against Gram positive bacteria *S.pyogenes.* Compound E_2 and E_3 showed good activity against Gram negative bacteria *E.coli*. Rest of the compounds showed good to moderate activity against other bacteria compared with the standard drugs. Antifungal screening data showed that the compounds were poor to moderate active against *A.niger* compared to the standard drugs.

Table 2. Antimicrobial activity of synthesized compounds

Compound No.	Minimum Inhibitory Concentration (µg mL^{-1})				
	Antibacterial				Antifungal
	Gram-positive		Gram-negative		
	S.aureus ATCC-96	*S.pyogenes* ATCC-443	*E.coli* ATCC-442	*P.aeruginosa* ATCC-441	*A.niger* ATCC-282
E_1	500	500	200	250	1000
E_2	25	200	62.5	250	250
E_3	250	500	100	500	1000
E_4	250	200	250	200	1000
E_5	200	500	250	200	250
E_6	62.5	125	200	500	250
E_7	200	100	250	250	500
E_8	250	500	500	500	1000
E_9	250	200	250	200	>1000
Ampicillin	250	100	100	100	-
Chloramphenicol	50	50	50	50	-
Gresefulvin	-	-	-	-	100
Nystatin	-	-	-	-	100

CONCLUSION

In this present work, we have synthesized some novel thieno[2,3-*d*]pyrimidine derivatives (E_1-E_9) and screened for their antibacterial and antifungal activities. The structures of all the prepared compounds were confirmed successfully by IR and ^{1}H NMR spectra and elemental analysis. Antibacterial activity of title compounds showed that hydroxyl group present at 3rd and 4th position of phenyl ring in compound E_2 could be responsible for increased activity against *S.aureus* as Gram-positive bacteria and *E.coli* as Gram-negative bacteria. All synthesized compounds showed poor to moderate antifungal activity.

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