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Synthesis, Characterization and Antimicrobial Activity of 5,6-Dimethyl thieno[2,3-*d*]Pyrimidine Derivatives

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ABSTRACT

Some N-(substituted)-5,6-dimethylthieno[2,3-d]pyrimidin-4-amine derivatives 3(a-e) and3-(substitutedphenyl)-1-(4-(5,6dimethylthieno[2,3d]pyrimidin4ylamino)phenyl)prop-2-en-1-one derivatives 5(a-e) were synthesized starting from 2-amino thiophene-3-carboxylic acid ester analogue. The structures of all synthesized compounds have been evaluated by physical methods (melting point as well as elemental analyses) and also were confirmed by IR, ^{1}H and ^{13}C NMR spectroscopies. All the newly synthesized compounds were tested for their *in vitro* antimicrobial activity against gram (+)ve and gram (-)ve bacteria and also on different strains of fungi. Some of the compounds showed better antibacterial as well as antifungal activities in comparison with the standard drugs.

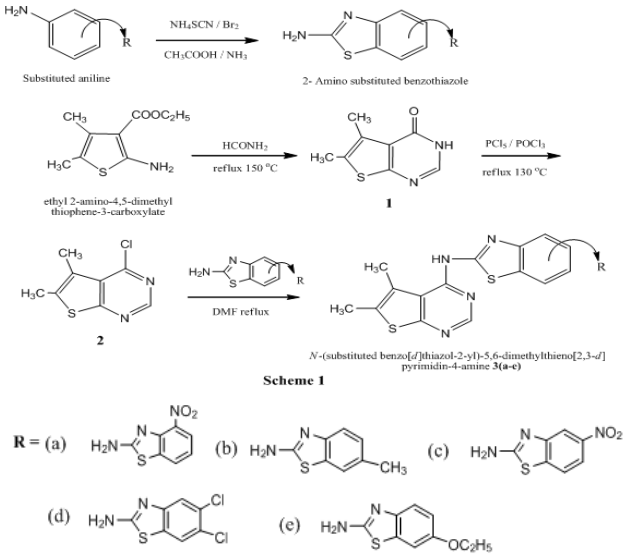
Introduction

Medicinal Chemistry essentially it concerns with the understanding of mechanisms of action of drugs mechanism. It attempts to establish relationship between structure and function (activity) and to link biodynamic behavior with chemical reactivity and physical properties. Chemists have a chance to participate in the fundamentals of prevention, therapy and understanding of diseases and thereby to contribute to a healthier and happier life"[1]. Thienopyrimidines are important class of fused heterocycles that are of considerable interest on account of diverse range of their biological activities[2] such as; antibiotic, radioprotective, anticancer, antimicrobial[3], antiviral, antiproliferative, antifolate, antiamnesic, anaphylactic, antihistaminic, antiglaucoma, antioxidant, anticoccidial, thrombolytic, antifungal, neurotropic, molluscicidal and larvicidal, antipyretic, analgesic, antipsychotic, anticonvulsant, anti-inflammatory, ulcerogenic index, antihypertensive, antibacterial, antiallergic, antiarrhythmic, antidepressant[4-8]. Many thieno[2,3-*d*]pyrimidine derivatives were reported as phosphodiesterase inhibitors, also exhibit good H_1 receptor antagonistic activities and 4-amino thienopyrimidine derivatives show insecticidal, pesticidal and acaricidal activities. Numerous thieno[2,3-*d*]pyrimidines have been proved useful for cerebral ischemia, malaria, tuberculosis, Alzheimer's and Parkinson's diseases[9]. Some thienopyrimidine derivatives have also found as fluorescent dyes for biomolecule detection and as novel ionophores in plasticized poly(vinyl chloride) matrix membrane sensors for uranyl ions[10]. Benzothiazole derivatives exhibit a wide range of biological activities[11-12], Benzothiazole moiety exhibits activity such as antiallagesic, antiparastic, antitumour, anti-glutamate, antifungal, vasdilator, anticancer, brest cancer, antitubercular, CNS, photosynthesis inhibiting activity, anti-inflammatory, antibacterial[13-14] etc. Chalcones are natural compounds that are largely distributed in plants, fruits, and vegetables.

They belong to the flavonoid group of molecules and some of them exhibit numerous biological activities. They are precursors in flavonoid biosynthesis. The enzymatic cyclization of the 6'-hydroxychalcones leads to the formation of flavanones and subsequently to a large number of flavonoid groups including flavones, flavonols, dihydroflavonols, aurones and isoflavones[15]. Chalcone moiety exhibits activity such as antiallagesic, antiparastic, antihypertensive, anti-inflammatory, antibacterial etc[16-18].

Experimental

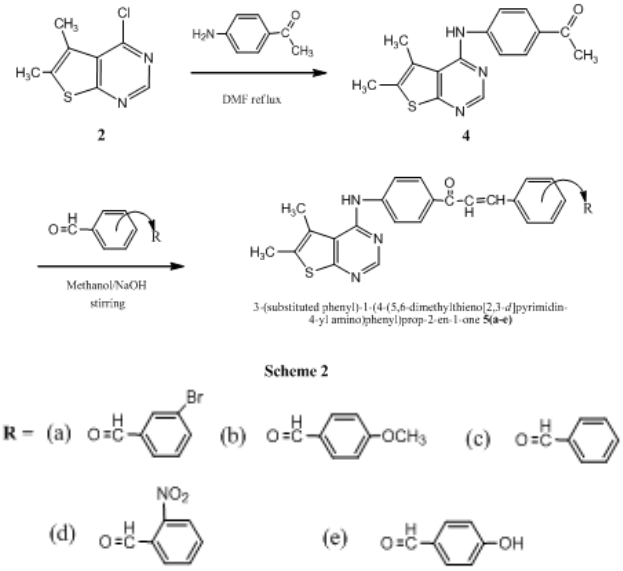
Chemical and instrumentation: This present work deals with the synthesis and studies of some thieno[2,3-*d*] pyrimidine derivatives 3(a-e) *N*-(substitutedbenzo[*d*]thiazol-2-yl)-5,6-di methylthieno[2,3-*d*]pyrimidin-4-amine and 5(a-e) 3-(substituted phenyl)-1-(4-(5,6-dimethylthieno [2,3-*d*]pyrimidin-4-ylamino)phenyl)prop-2-en-1-one have been synthesized from the key compound ethyl-2-amino-4,5-dimethyl thiophene-3-carboxylate.



Scheme 1

Tele:

E-mail address: himanshu4p_2765@yahoo.com



Scheme 2

The final compounds The progress of the reaction and purity of the compounds were checked on TLC [Aluminium sheet silica gel 60 F_{245} (E.Merck)] plates using ethyl acetate:*n*-hexane (2:8) as an irrigator and the plates were developed in an iodine chamber. Infrared spectra (ν_{max} in cm^{-1}) of synthesized derivatives have been scanned in KBr pellets by using Nicolet is10 FTIR spectrophotometer instrument at Dept. of Chemistry, VNSG University, Surat. NMR spectra were recorded on BRUKER AVANCE II 400 MHz NMR spectrometer using DMSO-d_6 as solvent and TMS as internal reference (chemical shifts in δ, ppm) at SAIF, Department of Chemistry, Punjab University, Chandigarh. Synthetic pathways are depicted in the below Scheme 1 & 2.

Synthesis of 2-amino substituted benzothiazole intermediates:

To the glacial acetic acid (20 mL) cooled to 5˚C were added 8 g (0.08 mol) of ammonium thiocyanate and (0.01 mol) of substituted aniline. The mixture was placed in freezing mixture of ice and salt and mechanically stirred while 1.6 mL of bromine in 6 mL of glacial acetic acid was added from a dropping funnel at such a rate that the temp does not rise beyond 0˚C. After all the bromine has been added (15 min), the solution was stirred for an additional 2 hour at 0˚C and at room temperature for 10 hrs. It was then allowed to stand overnight during which period coloured precipitate settled at the bottom, water (6 mL) was added quickly and slurry was heated at 85˚C on a steam bath and filtered hot. The residue was placed in a reaction flask and treated with 10 mL of glacial acetic acid heated again to 85˚C and filtered hot. The combined filtrate was cooled and neutralized with conc. ammonia solution to pH~6 when the coloured precipitate was collected. Recrystallisation from benzene [twice] after treatment with charcoal gave colour plates of 2-aminobenzothiazole. Yield 74 %.

Synthesis of 5,6-dimethylthieno[2,3-d]pyrimidin-4(3H)-one (1): A mixture of ethyl 2-amino-4,5-dimethylthiophene-3-carboxylate (0.01 mol) and formamide (20 mL) were heated for 8-10 hrs at 150-160˚C under stirring with a magnetic stirrer. Then the mixture was poured onto ice-water and stirred for another 30 minutes. The precipitate was collected by filtration and recrystallized from ethanol to give compound (1). Yield 69 % (m.p. 136-138˚C).

Synthesis of 4-chloro-5,6-dimethylthieno[2,3-d]pyrimidine (2): A mixture of compound (1) (0.01 mol), phosphorus pentachloride (0.015 mol) and phosphorus oxychloride (16 mL) were heated and stirred under reflux for 8 hrs at 115-118˚C. Excess of phosphorus oxychloride was then removed by distillation. The residue obtained was acidified with sodium bicarbonate solution (5%w/v). The resulting precipitate was collected by filtration, washed with water and dried to give compound (2). Yield 62%. (m.p. 150-152˚C).

General procedure for N-(substitutedbenzo[d]thiazol-2-yl)-5,6-dimethylthieno[2,3-d] pyrimidin-4-amine (3(a-e)): A stirred mixture of compound (2) (0.04 mol), 2-amino substituted benzothiazole (0.05 mol) and potassium carbonate (0.02 mol) in DMF (20 mL) was heated at 130˚C for 4-5 hrs. After the completion of reaction, it cooled to room temperature then add 1 N HCl till pH~4. The precipitated solid, crude product was collected by filtration and recrystallized from ethanol to give title compounds (3(a-e)) are summarized in Table 1.

Synthesis of 5,6-dimethyl-N-(4-nitrobenzo[d]thiazol-2-yl)thieno[2,3-d]pyrimidin-4-amine (3a): Yield 68%; m.p. 180 °C; Anal. Calcd. For $C_{15}H_{11}N_5O_2S_2$ (357.41 gm/mole): C, 50.41; H, 3.10; N, 19.59. Found: C, 50.33; H, 3.02; N, 19.66. IR (KBr, cm-1): 3430 (-NH-), 2910, 2830, 1550, 1350, 1450, 1375, 1260, 675. ^{1}H NMR (400 MHz, DMSO-d_6, δ ppm): 2.14 (s, 3H, -CH_3), 2.37 (s, 3H, -CH_3), 4.2 (s, 1H, -NH-), 7.4-8.45 (m, 4H, Ar-H). ^{13}C NMR (100 MHz, DMSO-d_6, δ ppm): 174.0, 145.1, 125.1, 132.0, 144.0, 113.7, 134.9, 154.5, 152.1, 141.6, 128.0, 121.8, 125.6, 10.0, 12.0.

Synthesis of 5,6-dimethyl-N-(6-methylbenzo[d]thiazol-2-yl)thieno[2,3-d]pyrimidin-4-amine (3b): Yield 70%; m.p. 178 °C; Anal. Calcd. For $C_{16}H_{14}N_4S_2$ (326.44 gm/mole): C, 58.87; H, 4.32; N, 17.16. Found: C, 58.98; H, 4.37; N, 17.10. IR (KBr, cm-1): 3425 (-NH-), 2940, 2860, 1450, 1380, 1260, 680. ^{1}H NMR (400 MHz, DMSO-d_6, δ ppm): 2.11 (s, 3H, -CH_3), 2.20 (s, 3H, -CH_3), 2.34 (s, 3H, -CH_3), 4.4 (s, 1H, -NH-), 7.34-8.59 (m, 4H, Ar-H). ^{13}C NMR (100 MHz, DMSO-d_6, δ ppm): 173.8, 147.0, 131.0, 131.1, 151.3, 114.0, 134.4, 157.0, 154.1, 120.7, 117.0, 134.3, 133.4, 127.6, 10.0, 12.0, 21.1.

Synthesis of 5,6-dimethyl-N-(5-nitrobenzo[d]thiazol-2-yl)thieno[2,3-d]pyrimidin-4-amine (3c): Yield 72%; m.p. 184 °C; Anal. Calcd. For $C_{15}H_{11}N_5OS_2$ (357.41 gm/mole): C, 50.41; H, 3.10; N, 19.59. Found: C, 50.35; H, 3.13; N, 19.52. IR (KBr, cm-1): 3433 (-NH-), 2911, 2829, 1554, 1351, 1455, 1370, 1265, 674. ^{1}H NMR (400 MHz, DMSO-d_6, δ ppm): 2.01 (s, 3H, -CH_3), 2.30 (s, 3H, -CH_3), 4.1 (s, 1H, -NH-), 8.20-9.20 (m, 4H, Ar-H). ^{13}C NMR (100 MHz, DMSO-d_6, δ ppm): 175.0, 147.1, 135.8, 131.7, 150.3, 113.9, 135.3, 156.6, 152.7, 121.4, 117.1, 120.1, 10.7, 12.1.

Synthesis of N-(5,6-dichlorobenzo[d]thiazol-2-yl)-5,6-dimethylthieno[2,3-d]pyrimidin-4-amine (3d): Yield 65%; m.p. 181 °C; Anal. Calcd. For $C_{15}H_{11}FN_4S_2$ (381.30 gm/mole): C, 47.25; H, 2.64; N, 14.69. Found: C, 47.17; H, 2.57; N, 14.72. IR (KBr, cm-1): 3435 (-NH-), 2920, 2855, 1440, 1370, 1251, 675. ^{1}H NMR (400 MHz, DMSO-d_6, δ ppm): 2.05 (s, 3H, -CH_3), 2.40 (s, 3H, -CH_3), 4.05 (s, 1H, -NH-), 8.00-8.70 (m, 3H, Ar-H). ^{13}C NMR (100 MHz, DMSO-d_6, δ ppm): 173.4, 146.0, 129.8, 131.0, 150.0, 115.1, 135.2, 131.3, 129.7, 156.8, 154.1, 121.4, 123.3, 9.7, 13.0.

Synthesis of N-(6-ethoxybenzo[d]thiazol-2-yl)-5,6-dimethylthieno[2,3-d]pyrimidin-4-amine (3e): Yield 63%; m.p. 178 °C; Anal. Calcd. For $C_{17}H_{16}N_4OS_2$ (356.47 gm/mole): C, 57.28; H, 4.52; N, 15.72. Found: C, 57.26; H, 4.55; N, 15.67. IR (KBr, cm-1): 3432 (-NH-), 2930, 2850, 1445, 1330, 1270, 665. ^{1}H NMR (400 MHz, DMSO-d_6, δ

ppm): 2.10 (s, 3H, -CH_3), 2.50 (s, 3H, -CH_3), 1.50 (t, 3H, -CH_3), 4.00 (q, 2H, -CH_2-), 4.15 (s, 1H, -NH-), 6.95-8.70 (m, 4H, Ar-H). ^{13}C NMR (100 MHz, DMSO-d_6, δ ppm): 173.7, 146.1, 131.2, 130.8, 144.9, 114.4, 134.6, 152.7, 155.7, 151.4, 104.8, 115.9, 115.2, 65.2, 10.6, 12.0, 14.1.

Synthesis of 1-(4-(5,6-dimethylthieno[2,3-d]pyrimidin-4-ylamino) phenyl)ethanone (4): A stirred mixture of compound (2) (0.01 mol), *p*-aminoacetophenone 2.7g (0.02 mol) and potassium carbonate (0.02 mol) in DMF (30 mL) was heated at 130˚C for 4-5 hrs. After the completion of reaction, it cooled to room temperature then add 1 N HCl till pH~4. The precipitated solid, crude product was collected by filtration and recrystallized from ethanol to give compound (4). Yield 71%. (M.P. 127-129˚C).

General procedure for 3-(substituted phenyl)-1-(4-(5,6-dimethylthieno[2,3-d] pyrimidin-4-ylamino) phenyl)prop-2-en-1-one (5(a-e)): A mixture of the appropriate aromatic aldehyde (0.01 mol) and a solution of compound (4) 3.5g (0.01 mol) in DMF (20 mL) containing potassium hydroxide (10%, 2 mL) heated under reflux for 5 hrs. The reaction mixture was then cooled, poured into ice-cold water, filtered, and the crude was recrystallized from the absolute ethanol to give title compounds (5(a-e)) are summarized in Table 1.

3-(3-bromophenyl)-1-(4-(5,6-dimethylthieno[2,3-d]pyrimidin-4-ylamino) phenyl)prop-2-en-1-one (5a): Yield 63%; m.p. 178 °C; Anal. Calcd. For $C_{23}H_{18}BrN_3OS$ (464.38 gm/mole): C, 59.49; H, 3.91; N, 9.05. Found: C, 59.43; H, 3.94; N, 9.01. IR (KBr, cm-1): 3415(-NH-), 2905, 2850, 1660, 1550, 1440, 1380, 1260, 680, 610. ^{1}H NMR (400 MHz, DMSO-d_6, δ ppm): 2.17 (s, 3H, -CH_3), 2.41 (s, 3H, -CH_3), 4.53 (s, 1H, -NH-), 6.32 (d, 1H, =CH-CO-), 6.65 (d, 1H, =CH-), 6.62-7.27 (m, 9H, Ar-H). ^{13}C NMR (100 MHz, DMSO-d_6, δ ppm): 145.3, 130.5, 115.5, 136.3, 122.7, 154.2, 152.0, 147.2, 128.3, 136.2, 132.6, 110.4, 131.0, 126.8, 131.2, 110.6, 131.2, 130.1, 188.9, 11.2, 12.1, 145.8, 120.7.

Synthesis of 1-(4-(5,6-dimethylthieno[2,3-d]pyrimidin-4-ylamino)phenyl)-3-(4-methoxy phenyl)prop-2-en-1-one (5b): Yield 70%; m.p. 152 °C; Anal. Calcd. For $C_{24}H_{21}N_3O_2S$ (415.51 gm/mole): C, 69.37; H, 5.09; N, 10.11. Found: C, 69.34; H, 5.17; N, 10.01. IR (KBr, cm-1): 3431 (-NH-), 2922, 2854, 1630, 1545, 1260, 1430, 1380, 640. ^{1}H NMR (400 MHz, DMSO-d_6, δ ppm): 2.20 (s, 3H, -CH_3), 2.51 (s, 3H, -CH_3), 3.82 (s, 3H, -OCH_3), 4.54 (s, 1H, -NH-), 6.95 (d, 1H, =CH-CO-), 7.05 (d, 1H, =CH-), 6.60-8.59 (m, 9H, Ar-H). ^{13}C NMR (100 MHz, DMSO-d_6, δ ppm): 144.0, 130.6, 115.7, 136.2, 160.0, 155.1, 148.1, 127.3, 127.0, 114.8, 112.0, 131.2, 130.2, 113.1, 110.0, 130.1, 131.5, 188.2, 55.1, 11.2, 12.4, 144.2, 120.9.

Synthesis of 1-(4-(5,6-dimethylthieno[2,3-d]pyrimidin-4-ylamino)phenyl)-3-phenylprop-2-en-1-one (5c): Yield 68%; m.p. 124 °C; Anal. Calcd. For $C_{23}H_{19}N_3OS$ (385.48 gm/mole): C, 71.66; H, 4.97; N, 10.90. Found: C, 71.58; H, 5.02; N, 10.81. IR (KBr, cm-1): 3420(-NH-), 2915, 2855, 1650, 1535, 1442, 1370, 1255, 685, 615. ^{1}H NMR (400 MHz, DMSO-d_6, δ ppm): 2.10 (s, 3H, -CH_3), 2.28 (s, 3H, -CH_3), 4.40 (s, 1H, -NH-), 7.65 (d, 1H, =CH-CO-), 8.12 (d, 1H, =CH-), 7.30-8.30 (m, 10H, Ar-H). ^{13}C NMR (100 MHz, DMSO-d_6, δ ppm): 146.8, 130.7, 115.1, 135.7, 156.0, 154.2, 147.0, 127.0, 134.8, 110.8, 131.0, 129.0, 110.5, 131.4, 128.1, 128. 7, 128.5, 126.7, 190.2, 10.0, 12.1, 146.2, 121.6.

Synthesis of 1-(4-(5,6-dimethylthieno[2,3-d]pyrimidin-4-ylamino)phenyl)-3-(2-nitro phenyl)prop-2-en-1-one (5d) Yield 70%; m.p. 136 °C; Anal. Calcd. For $C_{23}H_{18}N_4O_3S_2$ (430.48 gm/mole): C, 64.17; H, 4.21; N, 13.01. Found: C, 64.14; H, 4.27; N, 12.93. IR (KBr, cm-1): 3415 (-NH-), 2920, 2845, 1620, 1560, 1240, 1415, 1375, 625. ^{1}H NMR (400 MHz, DMSO-d_6, δ ppm): 2.13 (s, 3H, -CH_3), 2.42 (s, 3H, -CH_3), 4.20 (s, 1H, -NH-), 7.59 (d, 1H, =CH-CO-), 8.50 (d, 1H, =CH-), 7.60-8.90 (m, 9H, Ar-H). ^{13}C NMR (100 MHz, DMSO-d_6, δ ppm): 147.0, 130.7, 114.2, 135.5, 155.9, 153.0, 147.2, 146.2, 127.1, 126.8, 123.0, 111.1, 127.0, 132.0, 111.0, 132.7, 128.3, 134.1, 190.0, 10.1, 12.2, 144.8, 120.7.

Synthesis of 1-(4-(5,6-dimethylthieno[2,3-d]pyrimidin-4-ylamino)phenyl)-3-(4-hydroxy phenyl)prop-2-en-1-one (5e): Yield 75%; m.p. 164 °C; Anal. Calcd. For $C_{23}H_{19}N_3O_2S$ (401.48 gm/mole): C, 68.81; H, 4.77; N, 10.47. Found: C, 68.84; H, 4.70; N, 10.43. IR (KBr, cm-1): 3425 (-NH-), 2910, 2840, 1610, 1540, 1262, 1420, 1370, 645. ^{1}H NMR (400 MHz, DMSO-d_6, δ ppm): 2.02 (s, 3H, -CH_3), 2.25 (s, 3H, -CH_3), 4.24 (s, 1H, -NH-), 5.30 (s, 1H, -OH), 7.49 (d, 1H, =CH-CO-), 8.20 (d, 1H, =CH-), 6.55-8.50 (m, 9H, Ar-H). ^{13}C NMR (100 MHz, DMSO-d_6, δ ppm): 146.0, 131.1, 114.5, 135.9, 157.8, 156.4, 153.6, 146.0, 128.0, 127.7, 115.0, 111.0, 132.1, 130.1, 115.0, 111.1, 130.0, 132.7, 188.4, 10.1, 12.1, 144.8, 120.7.

Results and Discussion

Spectral characteristics: The structures of all the synthesized compounds 3(a-e) and 5(a-e) were confirmed by various spectroscopic techniques including IR, ^{1}H and ^{13}C NMR. The IR spectra[19] of the compounds 3(a-e) and 5(a-e) showed a broad band within the range of 3415-3435 cm^{-1} corresponding to the stretching vibration of the amine group which confirmed the presence of a secondary amino group. The methyl group was confirmed by the presence of two stretching bands within the range of 2905-2940 cm^{-1} and bending vibration within the range of 1330-1455 cm^{-1}. The band within the range of 1251-1275 cm^{-1} was due to the stretching vibration of the -CN tertiary amine group, which confirmed the pyrimidine ring. The band within the region of 674-680 cm^{-1} was due to the stretching vibration of the C-S linkage, which confirmed the thiophene ring. The band within the region of 1610-1660 cm^{-1} was due to the stretching vibration of the >C=O of chalcone group. The band within the region of 1535-1550 cm^{-1} was due to the stretching vibration of the -CH=CH- linkage of chalcone group. The ^{1}H NMR spectra[20] of all the compounds 3(a-e) and 5(a-e) showed a singlet signal within the region of 2.01-2.51 δ ppm which can be attributed for -CH_3 protons. Compounds 3(a-e) and 5(a-e) showed a singlet at 4.00-4.54 δ ppm which was due to the -NH- protons. All the compounds 5(a-e) showed doublets at 6.32-7.65 δ ppm and this was due to the =CH-CO- protons. All the compounds 5(a-e) showed doublets at 6.65-8.50 δ ppm and this was due to the =CH- protons. The aromatic protons showed signals at 6.55-9.20 δ ppm. The ^{13}C NMR spectra of all the compounds 3(a-e) and 5(a-e) showed signals within the range of 10.0-13.0 δ ppm due to the presence of -CH_3 carbons. Compounds 3(a-e) and 5(a-e) showed signals within the range of 10.0-188.9 δ ppm due to the presence other carbons. Aromatic carbons showed signals between 117.1-174.5 δ ppm.

Antimicrobial activity: All the synthesized compounds were screened for their antimicrobial activity by broth dilution method[21-22]. DMSO was used as diluents to get desired concentration of drugs to test upon standard bacterial and fungal strains. Serial dilutions were prepared in primary and secondary screening. All the tubes not showing visible growth are subcultured and incubated overnight at 37˚C. The tubes were then incubated overnight.

The MIC and MFC of the control organism were read to check the accuracy of the drug concentrations. Prepared stock solution of antibiotics of concentrations 2000 mg/L, as required. Arrange micro well plate 8×12 well of sterile well in the rack. The lowest concentration inhibiting growth of the organism was recorded as the MIC and MFC. The growth, inhibition is measured and compound is applied in the method to determine the activity in µg/mL concentration. All the compounds were screened against Gram-positive bacteria [*Staphylococcus aureus* (MTCC-96) and *Streptococcus pyogenus* (MTCC-442)] and Gram-negative bacteria [*Escherichia coli* (MTCC-443) and *Pseudomonas aeruginosa* (MTCC-1688)]. The antifungal activity was tested against Gram-positive fungi [*Candida albicans* (MTCC-227)] and Gram-negative fungi [*Aspergillus niger* (MTCC-282) and *Aspergillus clavatus* (MTCC-1323)]. The results were compared with Ampicillin, Chloramphenicol and Ciprofloxacin and Nystatin and Greseofulvin as a reference drugs. The results are shown in Table 1.

All the synthesized compounds containing thieno[2,3-*d*]pyrimidine derivatives 3(a-e) and 5(a-e) were tested for their antimicrobial activity. Antimicrobial activity of title compounds showed that chloro group present at 5^{th} and 6^{th} position of benzothiazole ring in compound 3d could be responsible for increase activity against *S.pyogenes*, *P.aeruginosa* and *E.coli*. Compound 5b, 5c,5d and 5e has bromo group at 3^{rd} position and methoxy group at 4^{th} position of chalcone derivative to show highest activity against *S.aureus S. pyogenes*, *P.aeruginosa* and *E.coli*. The activity varies with the different substituents on benzothiazole and chalcone derivative.

From the antibacterial results of above series, compounds 3d and 3e exhibited highly active against *P.aeruginosa* and *E.coli* respectively. Compounds 5b, 5d and 5e found highly active against *S.aureus*, *S.pyogenes*, *P.aeruginosa* respectively. Rest of compounds showed good to moderate activity.

The antifungal results of this series indicated that compounds 3c and 3d exhibited good active against *A.clavatus* and *A.niger* respectively. Compounds 5a, 5b and 5c found good active against *A.clavatus C.albicans* and *A.clavatus* respectively. Rest of the compounds showed moderate activity.

Conclusion

Some benzothiazole and chalcone containing thieno[2,3-*d*]pyrimidine derivatives were synthesized and confirmed by spectral techniques and evaluated their antimicrobial activity. The activity varies with the different substituent on benzothiazole and chalcone derivatives. It is noted that the minimum inhibitory concentration decreases. Some of the compounds showed better antibacterial as well as antifungal activities in comparison with the standard drugs. In future, thieno[2,3-*d*]pyrimidine derivatives can be used for designing and development of more potent and selective antimicrobial agents.

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Table 1. Antimicrobial activities of synthesized compounds 3(a-e) and 5(a-e).

Compd. No.	Minimal Inhibition Concentration (µg/mL)				Minimal Fungicidal Concentration (µg/mL)		
	Gram +ve		Gram -ve				
	S. aureus	*S. pyogenes*	*E. coli*	*P. aeruginosa*	*C. albicans*	*A. niger*	*A. clavatus*
3a	200	250	250	250	500	1000	500
3b	100	125	250	200	500	500	500
3c	250	125	125	125	500	500	250
3d	200	100	100	62.5	1000	250	500
3e	250	250	62.5	100	500	500	500
5a	100	100	125	200	500	500	250
5b	62.5	125	200	250	250	500	1000
5c	100	100	250	200	500	500	250
5d	125	62.5	100	500	500	500	500
5e	250	200	100	62.5	1000	500	500
Ampicillin	250	100	100	100	-	-	-
Chloramphenicol	50	50	50	50	-	-	-
Ciprofloxacin	50	50	25	25	-	-	-
Nystatin	-	-	-	-	100	100	100
Greseofulvin	-	-	-	-	500	100	100

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