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# Synthesis and *In vitro* antimicrobial evaluation of some novel bioactive heterocyclic compounds

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**ABSTRACT**

*4-(2,5-Dichloro-3-Thienyl)-6-Aryl Pyrimidine -2-Amine* $\mathbf{2}_{a\text{-}m}$ *, 7-Chloro-N-[4-(2,5-dichloro-3-thienyl)-6-Aryl pyrimidine-2-yl] quinoline -4-amine* $\mathbf{3}_{a\text{-}m}$ *and 4-(2,5-dichloro thiophen-3-yl)-2-aryl benzo[1,4]thiazepine* $\mathbf{4}_{a\text{-}m}$ *have been synthesized from (2E)-3-aryl-1-(2,5-dichloro-3-thienyl)prop-2-en-1-one* $\mathbf{1}_{a\text{-}m}$ *by the cyclization with guanidine nitrate and then condensation with 4,7-dichloroquinoline(*$\mathbf{2}_{a\text{-}m}$ *,* $\mathbf{3}_{a\text{-}m}$*) and cyclization with o-amino thiophenol respectively (*$\mathbf{4}_{a\text{-}m}$*). Compounds (2E)-3-aryl-1-(2,5-dichloro-3-thienyl)prop-2-en-1-one* $\mathbf{1}_{a\text{-}m}$ *was synthesized from 1-(2,5-dichloro thiophen-3-yl)-ethanone and various aromatic aldehyde. The structures of novel synthesized compounds have been established on the basis of IR ,* $^{1}$*H NMR,* $^{13}$*C NMR and Mass spectral data and screened for their antimicrobial activities against different microorganisms by micro dilution method. Isoniazid, Rifampicin, chloroquine, quinine, Gentamycin, Ampicilin, Chloramphenicol, Ciprofloxacin, Norfloxacin, Nystatin and Greseofulvin were used as standard drugs for mycobacteria* $H_{37}$*Rv, malarial parasite P.falciparum , bacteria E.coli, P.aeruginosa, S.aureus, S.pyogenus and fungus C.albicans, A.niger, A.clavatus.*

**Keywords**: Chalcone, Pyrimidine, Quinoline, Benzo thiazepine, Antimicrobial activities.

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## INTRODUCTION

Chalcones are natural substances found in a number of plants or synthetically prepared. These compounds are of a high interest due to their use as starting material in the synthesis of a series of heterocyclic compounds [1-2]. Chalcone and pyrimidine are potential bioactive agents due to their wide spectrum of pharmacological activities like antitumor [3], anticancer [4], antibacterial [5-6], anticonvulsant [7], antitubercular [8-9], antiHIV [10] and antiviral [11]. Quinoline and their derivatives have been extensively explored for their biological [12], antifilarial [13], antibacterial [14-15], and antimalarial [16-17]activities. Quinoline containing drugs, particularly 4-amino quinoline such as chloroquine have proven to be the most successful class of the compounds for the treatment and prophylaxis of malaria. Pharmacological studies reported for benzothiazepines class of compounds reveals that these compounds have immense chemotherapeutic importance of antihypertensive, cardiovascular , anticancer [18] , antiherpes [19] and antimicrobial [20] activity.

Tuberculosis (TB) is a worldwide pandemic caused by different species of *mycobacteria* [21]. The latest static reveals that around two million people throughout the world die annually from tuberculosis and there are around eight million new cases each year, in which the developing countries contribute to a greater share [21]. Along with HIV-positive people with a weaken immune system, TB is a leading killer epidemic [22]. It is found that every year

about two million people living with HIV/AIDS die from TB [23]. Additionally, in the current times the form of multidrug resistant TB(MDR-TB), a form of TB that does not respond to the standard therapy is more familiar. Therefore, the need for newer, more effective drugs that can achieve multiple goals in improving TB control is pressing. As part of an ongoing multifaceted program aimed towards the development of new molecules as therapeutic agents, herein we report the synthesis and antimicrobial activities of pyrimidines, quinolines and benzothiazepines.

## MATERIALS AND METHODS

Melting points were determined in open glass capillaries and are uncorrected. The homogeneicity of the compounds was checked by TLC (silica gel G, Merck , Ethyl Acetate : n-Hexane 2:8), IR spectrum ($cm^{-1}$) were recorded by Fourier Transform IR Spectrometer(Shimadzu 8700) using KBr pellet method. $^{1}H$ & $^{13}C$ NMR spectra were recorded on a Bruker DRX-300 instrument, using $CDCl_3$ as solvent & TMS as internal reference (chemical shifts in δ values ). Mass spectra were recorded by using water UPLC-TQD mass spectrometer.

**Step 1 : Synthesis of (2*E*)-3-Aryl-1-(2,5-dichloro-3-thienyl)prop-2-en-1-one $1_{a-m}$**
A mixture of 1-(2,5-dichloro -3-thienyl)ethanone (1.0mol), various aromatic aldehyde (1.2 mol) and 5% sodium methoxide solution in methanol (30ml) was taken in a R.B.F. The reaction mixture was stirred overnight at room temperature. The progress of reaction was monitored by TLC (Mobile Phase Ethyl Acetate : n-Hexane 2:8). The solid thus obtained was filtered, washed with chilled methanol and purified by recrystallization from methanol.

**Step 2 : Synthesis of 4-(2,5-Dichloro-3-Thienyl)-6-aryl pyrimidine -2-amine $2_{a-m}$**
A mixture of (2*E*)-3-Aryl-1-(2,5-dichloro-3-thienyl)prop-2-en-1-one(0.01 mol), guanidine nitrate (0.01 mol) and NaOH in DMF was heated at reflux temperature for 5-6 hrs. The reaction mixture was then cooled, poured into crushed ice. The product obtained was filtered, washed with water and recrystallized from acetone.

**Step 3 : Synthesis of 7-Chloro-N-[4-(2,5-dichloro-3-thienyl)-6-aryl pyrimidine-2-yl] quinoline -4-amine $3_{a-m}$**
4-(2,5-Dichloro-3-Thienyl)-6-aryl Pyrimidine -2-Amine in hydrochloric acid was taken in R.B.F and heated at 70-80 $^{0}C$ . Then 4,7-dichloro quinoline in toluene was added in portion to it. The temperature was maintain at 70-80 $^{0}C$ for 7-8 hrs .The mixture was then pourd into crushed ice . From the separated organic and aqueous layers ; aquous layer on neutralization with NaOH give product which was filtered , washed and recrystallized from acetone.

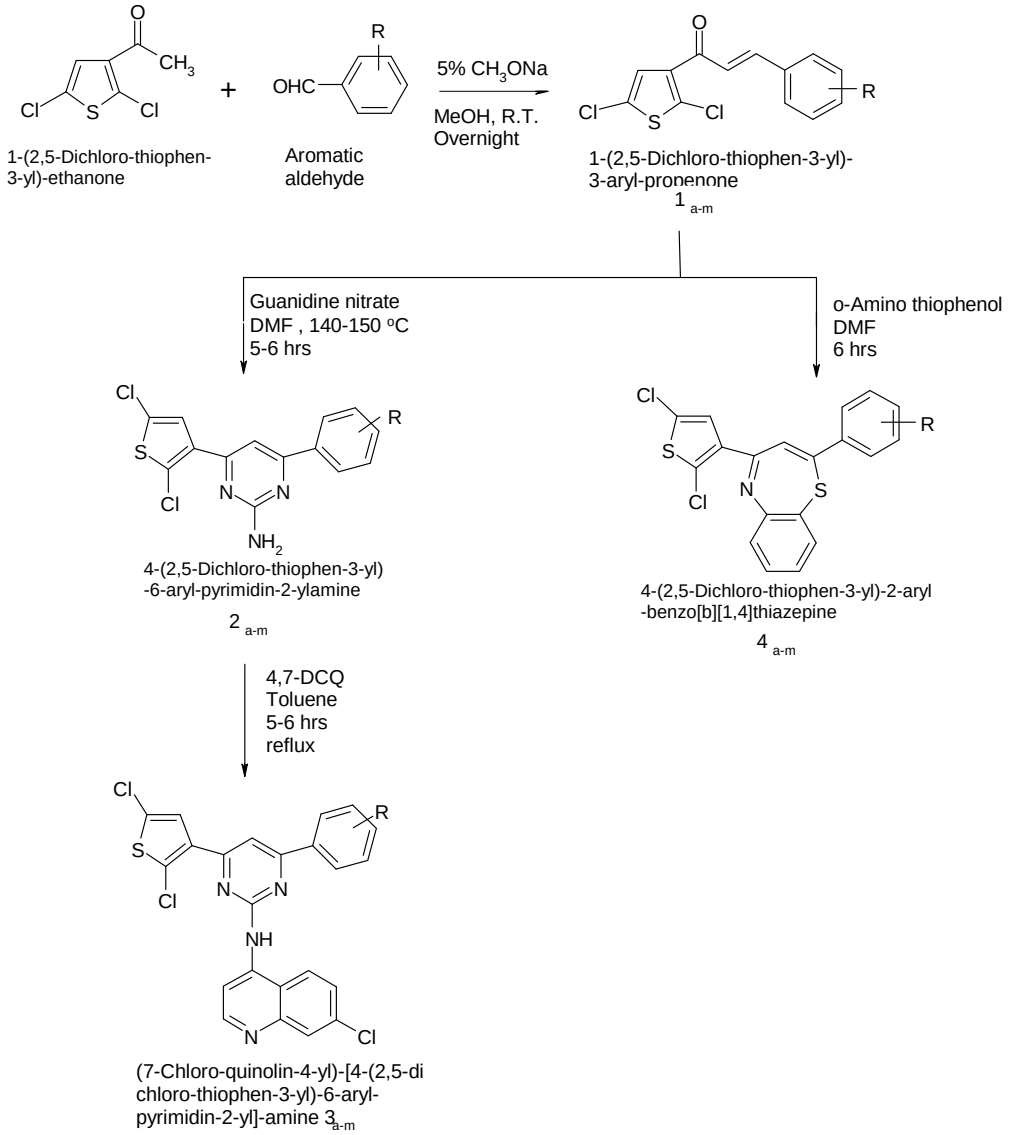
**Step 4 : Synthesis of 4-(2,5-Dichloro thiophen-3-yl)-2-aryl benzo [1,4]thiazepine $4_{a-m}$**
A mixture of 2E-3-aryl-1-(2,5-dichloro-3-thienyl)-prop-2-en-1-one , o-amino thiophenol and few drops of glacial acetic acid in DMF was refluxed for 8-9 hrs. The reaction mixture was then cooled and left overnight. The solid thus obtained was filtered, washed and recrystallized from acetone.

**[1d]** $^{1}H$ NMR [300 MHz δ] 7.105 (1H, Thiophene ring) , 7.546-7.311 (4H, Ar-H) , 7.708-7.656 (2H,-CH=CH) $^{13}C$ NMR [75MHz δ] 137.05($C_1$), 129.91($C_2$), 129.09($C_3$), 137.87 ($C_4$), 129.09($C_5$), 129.91($C_6$), 133.18($C_7$), 124.19($C_8$), 183.68($C_9$), 144.01($C_{10}$), 131.51($C_{11}$), 127.32($C_{12}$), 129.50($C_{13}$) M/S(m/z relative intensity) 318.5(M), 320.5(M+2), 322.5(M+6), 324.6(M+6), 239, 199, 122.

**[1f]** $^{1}H$ NMR [300MHz δ] 7.146 (1H, Thiophene ring), 7.650-7.477 (4H, Ar-H), 7.920-7.894 (2H,-CH=CH). $^{13}C$ NMR [75MHz δ] 148.99($C_1$), 122.20($C_2$), 137.53($C_3$), 132.23($C_4$), 127.25($C_5$), 122.87($C_6$), 134.38($C_7$), 125.16($C_8$), 183.23($C_9$), 142.30($C_{10}$), 130.31($C_{11}$), 127.02($C_{12}$), 129.77($C_{13}$) M/S(m/z relative intensity) 327.5(M), 329.5(M+2), 331.5(M+4), 300.6, 259.6, 244.7, 200, 183.1,122.1 .

**[2f]** $^{1}H$ NMR [300 MHz δ] 7.877 (1H,pyrimidine ring), 7.682-7.583(4H, Ar-H), 7.107 (1H,thiophenering), 5.287 (2H,-$NH_2$) $^{13}C$ NMR [75MHz δ] 148.90($C_1$), 121.55($C_2$), 139.25($C_3$), 132.98($C_4$), 127.50($C_5$), 122.37($C_6$), 163.72($C_7$), 160.65($C_8$), 106.03($C_9$), 162.88($C_{10}$), 139.41($C_{11}$), 130.12($C_{12}$), 127.29($C_{13}$), 129.99($C_{14}$) M/S(m/z relative intensity) 375.2(M), 377.1(M+2), 379.1(M+4),239.5,203.5,205.6,180.4 .

**[2i]** $^{1}H$ NMR [300 MHz δ] 7.955 (1H,pyrimidine ring), 7.545-7.262(4H, Ar-H), 7.085 (1H,thiophenering), 5.232 (2H,-$NH_2$), 3.853(3H,-$OCH_3$) $^{13}C$ NMR [75MHz δ] 161.52($C_1$), 114.54($C_2$), 127.60($C_3$), 136.26($C_4$), 127.28($C_5$), 114.32($C_6$), 165.92($C_7$), 159.54($C_8$), 105.62($C_9$), 164.72($C_{10}$), 142.52($C_{11}$), 130.08($C_{12}$), 127.05($C_{13}$), 129.81($C_{14}$), 55.55($C_{15}$). M/S(m/z relative intensity) 355.2(M), 357.8(M+2), 359.1(M+4),237.4, 239.5, 241.5, 120.3 .




**SCHEME I**

**[3d]** $^{1}$H NMR [300 MHz δ] 8.134 (1H,pyrimidine ring), 7.262 (1H,thiophene ring), 4.200 (1H,-NH-), 8.801-6.911(9H,Ar-H) M/S(m/z relative intensity) 365.1(M), 367.1(M+2), 369.1 (M+4), 198.3, 200.4 240.6,242.6 IR (cm$^{-1}$) -Cl(767.67), -NH(3283.63), quinoline & pyrimidine ring (1571.99).

**[3f]** $^{1}$H NMR [300 MHz δ] 8.134 (1H,pyrimidine ring), 7.265 (1H,thiophene ring), 4.200 (1H,-NH-), 8.199-6.911(9H,Ar-H) M/S(m/z relative intensity) 498.3(M), 376.5, 378.5, 198.3, 200.4, 207.3, 209.3, 211.3 . IR (cm$^{-1}$) -Cl(767.67), -NH(3283.63), quinoline & pyrimidine ring (1571.99).

**[3i]** $^{1}$H NMR [300 MHz δ] 8.130 (1H,pyrimidine ring), 7.265 (1H,thiophene ring), 4.200 (1H,-NH-), 8.799-6.911(9H,Ar-H), 3.900(3H,-$OCH_3$ ) M/S(m/z relative intensity) 505.1(M), 461.2, 361.2, 198.4, 200.4, 207.3, 353.2, 355.2, 357.2 IR (cm$^{-1}$) -Cl(765.74), -NH(3481.0), quinoline & pyrimidine ring (1579.7), -$OCH_3$(1249.87).

**[4d]** $^{1}$H NMR [300 MHz δ] 8.946 (1H,thiophene ring), 7.537-7.280(8H,Ar-H), 3.105(1H,-CH=C) $^{13}$C NMR [75MHz δ] 124.39($C_1$), 125.56($C_2$), 129.84($C_3$), 129.49($C_4$), 130.86($C_5$), 123.07($C_6$), 126.43($C_7$), 129.83($C_8$), 133.3($C_9$), 128.93($C_{10}$), 126.43($C_{11}$), 123.07($C_{12}$), 122.03 . M/S(m/z relative intensity) 419.1(M), 157.5 , 113.5 .

**[4k]** $^{1}$H NMR [300 MHz δ] 9.003 (1H,thiophene ring), 7.532-7.260(6H,Ar-H), 2.952(1H,-CH=C), 3.988 (9H,-$OCH_3$) $^{13}$C NMR [75MHz δ] 127.59($C_1$), 154.14($C_2$), 126.40($C_3$), 144.01($C_4$), 123.83($C_5$), 129.5($C_6$), 61.04($C_7$), 56.40($C_8$), 61.04($C_9$), 125.77($C_{10}$), 123.83($C_{11}$), 122.07($C_{12}$), 122.03 . M/S(m/z relative intensity) 484(M), 334, 254.5.

## RESULTS AND DISCUSSION

The compounds were synthesized as per **scheme I**
Compounds (2*E*)-3-aryl-1-(2,5-dichloro-3-thienyl)prop-2-en-1-one $\mathbf{1_{a\text{-}m}}$ were synthesized from 1-(2,5-dichloro thiophen-3-yl)-ethanone and various aromatic aldehyde, which upon cyclization with guanidine nitrate yields 4-(2,5-Dichloro-3-Thienyl)-6-Aryl Pyrimidine -2-Amine $\mathbf{2_{a\text{-}m}}$ and then condensation of $\mathbf{2_{a\text{-}m}}$ with 4,7-dichloroquinoline resulted in the synthesis of 7-Chloro-N-[4-(2,5-dichloro-3-thienyl)-6-Aryl pyrimidine-2-yl] quinoline -4-amine $\mathbf{3_{a\text{-}m}}$ . Similarly compounds 4-(2,5-dichloro thiophen-3-yl)-2-aryl benzo[1,4]thiazepine $\mathbf{4_{a\text{-}m}}$ were synthesized from compounds (2*E*)-3-aryl-1-(2,5-dichloro-3-thienyl)prop-2-en-1-one $\mathbf{1_{a\text{-}m}}$ by the cyclization with o-amino thiophenol. We have described the synthesis and biological activities of a new chalcones, pyrimidines, quinolines and benzothiazepine derivatives. The proposed structures of all the synthesized compounds were well supported by IR, $^{1}$H NMR, $^{13}$C NMR and Mass spectral data. The formation of compounds $\mathbf{1_{a\text{-}m}}$ were confirmed by disappearance of signals for the aldehydic proton in δ 9-10 and appearance of ethylinic proton in the range of δ 7.708-7.656 . The $^{1}$H NMR spectrum also displayed signals for the presence of amino proton at δ 5.287 for $–NH_2$ and at δ 4.200 for –NH . Aromatic protons were observed in the usual region as multiplet between δ 7.650-7.311 , δ 7.682-7.262 , δ 8.799-6.911 and δ 7.537-7.260 .

**Antimicrobial activities**
The antitubercular screening was carried out by Lowenstain-Jensen egg medium (L J Medium) as described by watt against $H_{37}$Rv strain. L J Medium containing standard drug as well as control L J Medium was also inoculated with mycobacterium tuberculosis of $H_{37}$Rv strain. The medium inoculated was incubated for $37^0$C for 6 weeks. At the end of 6 weeks readings were taken. Isoniazid and Rifampicin was taken as standard drugs. **( Table – II )**

The antimalarial activity of the compounds $\mathbf{3_{a\text{-}m}}$ were determined by their inhibiton of parasite growth using the Chloroquine resistant strain Plasmodium falciparum (IC50 =0.020 µg/ml). **( Table –III )**

Good activity was observed in compound **3a, 3h, 3i** compare to standard drug quinine and chloroquine drugs.

Following common standard strains were used for screening of antibacterial and antifungal activities: *E.Coli*, *P.Aeruginosa*, *S.Aureus*, *S.Pyogenus*, *C.Albicans*, *A.Niger*, *A.Clavatus*. The strains were procured from Institute of Microbial Technology, Chandigarh. DMSO was used as diluents / vehicle to get desired concentration of drugs to test upon standard bacterial strains. Each synthesized drug was diluted for obtaining 2000 microgram /ml concentration, as a stock solution. In primary screening 1000 microgram/ml, 500 microgram /ml, and 250 microgram /ml concentrations of the synthesized drugs were taken. The active synthesized drugs found in this primary screening were further tested in a second set of dilution against all microorganisms. The drugs found active in primary screening were similarly diluted to obtain 200 microgram/ml, 100 microgram/ml, 50 microgram/ml, 25 microgram/ml, 12.5 microgram/ml and 6.250 microgram/ml concentrations. The highest dilution showing at least 99 % inhibition zone is taken as MIC. The result of this is much affected by the size of the inoculums. Synthesized comopounds were evaluated for antimicrobial activity by micro dilution method against MTCC 443 (*E.coli*), MTCC 441 (*P. aeruginosa*), MTCC 96 (*S. aureus*), MTCC 442 (*S. pyogenus*), MTCC 227 (*C.albicans*), MTCC 282 (*A. niger*) and MTCC 1323 (*A. clavatus*) respectively using the standard drugs Gentamycin, Ampicillin, Chloramphenicol, Ciprofloxacin, Norfloxacin, Nystatin and Greseofulvin.The Comparative activities of the newly synthesized compound ($\mathbf{4_{a\text{-}m}}$) & the control antibiotics on bacterial & fungal strains respectively were summarized in **Table IV**.

Excellent to good activity was observed in compounds **4d , 4e , 4f & 4j** (against *E.coli*), compounds **4j** (against *P.aeruginosa*), compounds **4a, 4b, 4c, 4f, 4g, 4h, 4i, 4j, 4l & 4m** (against *S.aureus*), compounds **4a, 4c, 4h, 4f & 4l** (against *S.pyogenus*), compound **4i** (against C.albicans,A. *niger & A. clavatus*) and compound **4b, 4c, 4d, 4g, 4h, 4i, 4k & 4m** (against *C.albicans* ) . The remaining compounds were found effective at a much higher concentration as compared to the standard drugs.

**Table -I Physical, characterization of Compounds $1_{a-m}$ ,$2_{a-m}$ ,$3_{a-m}$ & $4_{a-m}$**

| Sr.No. | R | Mol.Formula | Mol.Wt. | M.P. $^0$C | Yield % |
|---|---|---|---|---|---|
| 1a | H | $C_{13}H_8OSCl_2$ | 283 | 78 | 90 |
| 1b | 2-Cl | $C_{13}H_7OSCl_3$ | 317.5 | 100 | 85 |
| 1c | 3-Cl | $C_{13}H_7OSCl_3$ | 317.5 | 92 | 85 |
| 1d | 4-Cl | $C_{13}H_7OSCl_3$ | 317.5 | 102 | 88 |
| 1e | 2-$NO_2$ | $C_{13}H_7NO_3SCl_2$ | 328 | 142 | 80 |
| 1f | 3- $NO_2$ | $C_{13}H_7NO_3SCl_2$ | 328 | 158 | 86 |
| 1g | 4- $NO_2$ | $C_{13}H_7NO_3SCl_2$ | 328 | 140 | 80 |
| 1h | 4-OH | $C_{13}H_8O_2SCl_2$ | 299 | 84 | 81 |
| 1i | 4- $OCH_3$ | $C_{14}H_{10}O_2SCl_2$ | 313 | 80 | 87 |
| 1j | 3,4-di $OCH_3$ | $C_{15}H_{12}O_3SCl_2$ | 343 | 136 | 83 |
| 1k | 3,4,5-tri $OCH_3$ | $C_{16}H_{14}O_4SCl_2$ | 373 | 78 | 79 |
| 1l | 4- N-$(CH_3)_2$ | $C_{15}H_{13}NOSCl_2$ | 326 | 74 | 80 |
| 1m | 4- OH-3- $OCH_3$ | $C_{14}H_{10}O_3SCl_2$ | 329 | 69 | 75 |
| 2a | H | $C_{14}H_9N_3SCl_2$ | 322 | 90 | 72 |
| 2b | 2-Cl | $C_{14}H_8N_3SCl_3$ | 356.5 | 130 | 66 |
| 2c | 3-Cl | $C_{14}H_8N_3SCl_3$ | 356.5 | 118 | 64 |
| 2d | 4-Cl | $C_{14}H_8N_3SCl_3$ | 356.5 | 132 | 70 |
| 2e | 2-$NO_2$ | $C_{14}H_8N_4O_2SCl_2$ | 367 | 86 | 64 |
| 2f | 3- $NO_2$ | $C_{14}H_8N_4O_2SCl_2$ | 367 | 96 | 70 |
| 2g | 4- $NO_2$ | $C_{14}H_8N_4O_2SCl_2$ | 367 | 78 | 62 |
| 2h | 4-OH | $C_{14}H_9N_3OSCl_2$ | 338 | 98 | 73 |
| 2i | 4- $OCH_3$ | $C_{15}H_{11}N_3OSCl_2$ | 352 | 78 | 71 |
| 2j | 3,4-di $OCH_3$ | $C_{16}H_{13}N_3O_2SCl_2$ | 382 | 100 | 70 |
| 2k | 3,4,5-tri $OCH_3$ | $C_{17}H_{15}N_3O_3SCl_2$ | 412 | 80 | 72 |
| 2l | 4- N-$(CH_3)_2$ | $C_{16}H_{14}N_4SCl_2$ | 365 | 92 | 67 |
| 2m | 4- OH-3- $OCH_3$ | $C_{15}H_{11}N_3O_2SCl_2$ | 368 | 78 | 65 |
| 3a | H | $C_{23}H_{13}N_4SCl_3$ | 483.5 | 102 | 60 |
| 3b | 2-Cl | $C_{23}H_{12}N_4SCl_4$ | 518 | 150 | 58 |
| 3c | 3-Cl | $C_{23}H_{12}N_4SCl_4$ | 518 | 128 | 60 |
| 3d | 4-Cl | $C_{23}H_{12}N_4SCl_4$ | 518 | 144 | 70 |
| 3e | 2-$NO_2$ | $C_{23}H_{12}N_5O_2SCl_3$ | 528.5 | 98 | 60 |
| 3f | 3- $NO_2$ | $C_{23}H_{12}N_5O_2SCl_3$ | 528.5 | 118 | 66 |
| 3g | 4- $NO_2$ | $C_{23}H_{12}N_5O_2SCl_3$ | 528.5 | 96 | 62 |
| 3h | 4-OH | $C_{23}H_{13}N_4OSCl_3$ | 499.5 | 88 | 70 |
| 3i | 4- $OCH_3$ | $C_{24}H_{15}N_4OSCl_3$ | 513.5 | 110 | 70 |
| 3j | 3,4-di $OCH_3$ | $C_{25}H_{17}N_4O_2SCl_3$ | 543.5 | 124 | 68 |
| 3k | 3,4,5-tri $OCH_3$ | $C_{26}H_{19}N_4O_3SCl_3$ | 573.5 | 106 | 76 |
| 3l | 4- N-$(CH_3)_2$ | $C_{25}H_{18}N_5SCl_3$ | 526.5 | 112 | 70 |
| 3m | 4- OH-3- $OCH_3$ | $C_{24}H_{16}N_4O_2SCl_3$ | 530.5 | 98 | 68 |
| 4a | H | $C_{19}H_{11}NS_2Cl_2$ | 388 | 110 | 76 |
| 4b | 2-Cl | $C_{19}H_{10}NS_2Cl_3$ | 422.5 | 120 | 70 |
| 4c | 3-Cl | $C_{19}H_{10}NS_2Cl_3$ | 422.5 | 110 | 64 |
| 4d | 4-Cl | $C_{19}H_{10}NS_2Cl_3$ | 422.5 | 128 | 68 |
| 4e | 2-$NO_2$ | $C_{19}H_{10}N_2O_2S_2Cl_2$ | 433 | 176 | 66 |
| 4f | 3- $NO_2$ | $C_{19}H_{10}N_2O_2S_2Cl_2$ | 433 | 162 | 76 |
| 4g | 4- $NO_2$ | $C_{19}H_{10}N_2O_2S_2Cl_2$ | 433 | 172 | 65 |
| 4h | 4-OH | $C_{19}H_{11}NOS_2Cl_2$ | 404 | 114 | 60 |
| 4i | 4- $OCH_3$ | $C_{20}H_{13}NOS_2Cl_2$ | 418 | 96 | 67 |
| 4j | 3,4-di $OCH_3$ | $C_{21}H_{15}NO_2S_2Cl_2$ | 448 | 182 | 71 |
| 4k | 3,4,5-tri $OCH_3$ | $C_{22}H_{17}NO_3S_2Cl_2$ | 478 | 124 | 70 |
| 4l | 4- N-$(CH_3)_2$ | $C_{21}H_{16}N_2S_2Cl_2$ | 431 | 118 | 70 |
| 4m | 4- OH-3- $OCH_3$ | $C_{20}H_{13}NO_2S_2Cl_2$ | 434 | 130 | 69 |

**Table-II**

| ANTI TUBERCULOSIS ACTIVITY TABLE | | | |
|---|---|---|---|
| | | | |
| METHOD | | L.J.MEDIUM [CONVENTIONAL METHOD] | |
| BACTERIA | | H37RV | |
| STANDARD DRUG | | ISONIAZID, RIFAMPICIN | |
| | | | |
| SR.NO | CODE NO | MIC µg/ml | REMARKS |
| 1 | 1a | 500 | ISONIAZID = 0.20 µg/ml |
| 2 | 1b | 250 | RIFAMPICIN = 0.25 µg/ml |
| 3 | 1c | 500 | |
| 4 | 1d | 62.5 | |
| 5 | 1e | 50 | |
| 6 | 1f | 100 | |
| 7 | 1g | 62.5 | |
| 8 | 1h | 100 | |
| 9 | 1i | 250 | |
| 10 | 1j | 50 | |
| 11 | 1k | 100 | |
| 12 | 1l | 100 | |
| 13 | 1m | 50 | |
| 14 | 2a | 1000 | |
| 15 | 2b | 100 | |
| 16 | 2c | 1000 | |
| 17 | 2d | 1000 | |
| 18 | 2e | >1000 | |
| 19 | 2f | >1000 | |
| 20 | 2g | >1000 | |
| 21 | 2h | 500 | |
| 22 | 2i | 250 | |
| 23 | 2j | 62.5 | |
| 24 | 2k | 250 | |
| 25 | 2l | 500 | |
| 26 | 2m | 1000 | |

**Table-III ANTI MALARIAL ACTIVITY**

*Plasmodium falciparum*

**MINIMAL INHIBITION CONCENTRATION**

| SR.NO | COMPOUND ID | MEAN IC50 VALUESa |
|---|---|---|
| 1 | **3a** | **0.42 µg/ml** |
| 2 | 3b | 0.92 µg/ml |
| 3 | 3c | 0.75 µg/ml |
| 4 | 3d | 0.58 µg/ml |
| 5 | 3e | 1.11 µg/ml |
| 6 | 3f | 0.96 µg/ml |
| 7 | 3g | 0.76 µg/ml |
| 8 | **3h** | **0.073 µg/ml** |
| 9 | **3i** | **0.48 µg/ml** |
| 10 | 3j | 1.45 µg/ml |
| 11 | 3k | 1.35 µg/ml |
| 12 | 3l | 1.27 µg/ml |
| 13 | 3m | 0.67 µg/ml |

*chloroquine : IC50 0.020 micrograme/ml quinine : IC 50 0.268 microgramme / ml*

**Table-IV Antimicrobial activity of compound 4a-m**

| Minimum Inhibition Concentration | | | | | | | |
|---|---|---|---|---|---|---|---|
| **comp.** | **Antibacterial** | | | | **Antifungal** | | |
| | ***E.coli*** **MTCC443** | ***P.aeruginosa*** **MTCC441** | ***S.aureus*** **MTCC96** | ***S.pyogenus*** **MTCC442** | ***C.albicans*** **MTCC227** | ***A.niger*** **MTCC282** | ***A.clavatus*** **MTCC1323** |
| 4a | 250 | 250 | **200** | **100** | 1000 | 500 | 500 |
| 4b | 62.5 | 100 | **250** | 200 | **100** | 1000 | 1000 |
| 4c | 125 | 200 | **200** | **100** | **500** | >1000 | >1000 |
| 4d | **100** | 125 | 500 | 200 | **500** | >1000 | >1000 |
| 4e | **100** | 250 | 500 | 250 | 1000 | >1000 | >1000 |
| 4f | **62.5** | 200 | **100** | **100** | >1000 | 250 | 500 |
| 4g | 500 | 250 | **200** | 200 | **500** | 1000 | 1000 |
| 4h | 250 | 200 | **125** | **100** | **250** | 1000 | 1000 |
| 4i | 125 | 200 | **250** | 250 | **500** | **200** | **200** |
| 4j | **100** | **62.5** | **250** | 250 | 1000 | 500 | 500 |
| 4k | 125 | 250 | 500 | 500 | **500** | 500 | 1000 |
| 4l | 250 | 250 | **125** | **125** | 1000 | 250 | 250 |
| 4m | 125 | 250 | **200** | 200 | **500** | 1000 | 1000 |
| Gentamycin | 0.05 | 1 | 0.25 | 0.5 | | | |
| Ampicilin | 100 | - | 250 | 100 | | | |
| Chloramphenicol | 50 | 50 | 50 | 50 | | | |
| Ciprofloxacin | 25 | 25 | 50 | 50 | | | |
| Norfloxacin | 10 | 10 | 10 | 10 | | | |
| Nystatin | | | | | 100 | 100 | 100 |
| Greseofulvin | | | | | 500 | 100 | 100 |

## CONCLUSION

In conclusion, we have described the synthesis and biological activities of a new chalcones , pyrimidines, quinolines and benzothiazepine derivatives. These chalcones and pyrimidine derivatives showed poor antitubercular activity than parent isoniazid, rifampicin; while compounds **3a,3h,3i** exhibited good growth inhibition to the standard drug chloroquine and quinine. Compounds **4j,4i** exhibited the growth inhibition almost qual to the standard drug against all bacterial and fungal strains respectively.

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## REFERENCES

[1] Bhat B A , Dhar K L , Puri S C , Saxena A K , Shanmugavel M & Qazi G N , *Bio Org Med Chem Lett*, **2005**,15,3177.
[2] Ansari F L , Vmbreen S , Hussain L , Makhmoor T , Nawaz S A , Lodhi M A , Khan S N , Shaheen F , Choudhary M I & Rahman A , *Chem Biodiversity*,**2005**,2,487.
[3] Cocco M T , Congiu C , Lilliu V & Onnis V, *Bio Org Med Chem Lett*,**2006**,14,366.
[4] Pattan S , Hole M , Pattan J , Dengale S , Shinde H , Muluk R , Nirmal S & Jadhav R , *Indian J Chem*, **2012**,51B,774.
[5] Singh G , Singh G , Yadav A K & Mishra A K , *Indian J Chem*,**2002**,41B,430.
[6] Kanth S R , Reddy G V , Rao P S , Narsalah B & Murthy V S N , *Eur J Chem*, **2006**,41,1011.
[7] Clausen R P , Moltzen E K , Perregaard J , Lenz S M , Sanchez C , Falch E , Frolund B , Bolvig T , Sarup A , Larsson O M , Schousboe A & Krogsgaard-Larsen P , *Bio Org Med Chem Lett*,**2005**,3,895.
[8] Faldu V J , Gothalia V K & Shah V H , *Indian J Chem*,**2015**,54B,391.
[9] Alam S , Panda R & Kachroo M , *Indian J Chem*,**2014**,53B,440.
[10] Gadhachanda V R , Wu B , Wang Z , Kuhen K L , Caldwell J , Zondler H , Zondler H , Walter H , Havenhand M & He Y , *Bio Org Med Chem Lett*,**2007**,17,260.
[11] Nasr M N & Gineinah M M , *Arch Pharm*,**2002**,335(6),289.
[12] Gupta R , Gupta A K & Paul S , *Indian J Chem*,**2002**,39B,847.
[13] Tiwari S , Chauhan P M S & Bhaduri D P , *Bio Org Med Chem Lett*,**2000**,10,1409.
[14] Kidwai M , Bhushan K R , Sapra P , Gupta R & Saxena R K , *Bio Org Med Chem*,**2000**,8,69.
[15] Modh R P , Shah D & Chikhalia K H , *Indian J Chem*,**2013**,52B,1318.

[16] Ziegler J , Linck R & Wright D W , *Curr Med Chem*,**2001**,8,171.
[17] Chauhan P M S & Srivastava S K , *Curr Med Chem*,**2001**,8,1535.
[18] Mulvihill M J and Miller M J , *Tetrahedron*,**1998**,54,6605.
[19] Verhegger I , Aerschot A V , Meervelt, Rozenski J , Wiebe L , Clereq E-De and Herdewjin *P J.Med Chem*.,**1995**,38,826.
[20] Pant U C , Pant S , Chandra H and Sharma P , *Indian J Chem*,**2006**,45B,1525.
[21] Eswaran S , Adhikari A V , Pal N K & Chowdhary I H , *Bio Org Med Chem Lett*,**2010**,20,1040.
[22] Zulma A , Malon P , Henderson J & Grange J M , *Postgrad Med J*,**2000**,76,259.
[23] Corbett E L , Watt C J , Walker N , Maher D , Williams B G , Raviglione M C & Dye C , *Arch Of Inter Med*,**2003**,163,1009.