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STUDIES OF SOME NEW THIAZOLE CLUBBED SCHIFF BASE AND 4-OXO-THIAZOLIDINE DERIVATIVES AS POTENT ANTIMICROBIAL, ANTITUBERCULAR AND ANTICANCER AGENTS

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Abstract: Thiazole clubbed three new series of Schiff bases **(3a-h)**, 2,3-disubstituted-4-oxo-thiazolidines **(4a-h)** and 2,3-disubstituted-5-methyl-4-oxo-thiazolidines **(5a-h)** were synthesized by using Dean-Stark water separator. The structures of the synthesized compounds were confirmed on the basis of FTIR, ^{1}H-NMR, ^{13}C-NMR, LCMS data as well as elemental analysis. The prepared analogues were screened for their preliminary *in vitro* antimicrobial activity, antitubercular activity and anticancer activity. Majority of the compounds showed excellent antimicrobial activity against the tested strains. A few of them displayed significant antitubercular activity compared with the first line drugs. Some of the compounds exerted significant anticancer activity.

Keywords: 2-Amino-5-methylthiazole, Schiff base, 4-oxothiazolidine, biological activity.

Introduction

Cancer is the uncontrolled growth of cells coupled with malignant behaviour, invasion and metastasis which is the global health problem leading cause of human death in developing as well as advance countries after cardiovascular diseases[1]. Thus inventions of novel structures that can be potentially active and less toxic are become a major challenge for medicinal chemistry researchers worldwide[2].

2-Amino-5- methyl-thiazole moiety was reported to possess various broad spectrum biological activities[3-6]. Therefore in view of these findings, it was thought of interest to undertake the synthesis of Schiff base and 4-thiazolidinones having a 2-amino-5-methylthiazol moiety with hoping that these compounds may possess certain biological activity.

The study of Schiff base has been rapid increasing because they shows excellent characteristics such as structural similarities with natural biological substances, relatively simple preparation procedures and the synthetic flexibility that enables design of suitable structural properties. Schiff bases have been used as synthons in the preparation of a number of industrial and biologically active compounds like formazans[7], 4-thiazolidinines[8], benzoxazines[9], and so forth, via ring closure, cycloaddition, and replacement reactions[10].

Instead of these, Schiff bases are now attracting the attention of biochemists because of their physiological and pharmacological activities such as anti HIV[11], anticancer[12], anti mycobacterial[13], antimicrobial[14] etc.

In present years, a large number of modern drugs containing the thiazolidinone moiety have been developed like Pioglitazone (hypoglycemic), Darbufelon (dual COX-2/5-LOX inhibitors), Etozolin (new generation diuretics)[15] etc. Moreover, thiazolidinone ring has been incorporated into a broad range of known biologically active compounds, either as a substitutuent group or as a replacement of another ring to synthesize several compounds containing this moiety. There are several reports in the literature describing the thiazolidinone derivatives for their various biological activities such as antiarrhythmic[16], anticancer[17], antimicrobial[18], antitubercular[19], anticonvulsant[20] etc. Keeping these observations in view and in continuation of our work on the synthesis of biologically active nitrogen and sulphur containing heterocycles[21-25], we have undertaken the synthesis of *N*-(substituted benzylidene/2'-thienylidene)-5-methylthiazol-2-amine **(3a-h)**, 2-(substitutedphenyl/2'-thienyl)-3-(5'-methylthiazolyl)-thiazolidine-4-ones **(4a-h)** and 2-(substitutedphenyl/2'-thienyl)-3-(5'-methylthiazolyl)-5-methyl-thiazolidine-4-ones **(5a-h)** and carried out their antimicrobial, antitubercular and anticancer screening studies.

Experimental

All the solvents and reagents are analytical reagent grade and used without further purification. All products were traced by thin-layer chromatography (TLC), performed on E-Merck pre-coated 60 F254 Silica Gel Uniplates and visualized under UV light or keeping the plates in iodine chamber. Melting points were determined by using open capillary tubes and are uncorrected. IR spectra were recorded on a Shimadzu FTIR 8401 spectrophotometer using potassium bromide pellets. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker Avance 400 MHz spectrometer using $CDCl_3$ as a solvent and TMS as an internal standard at 400 and 100 MHz respectively. Mass spectra were scanned on a Shimadzu LCMS 2010 spectrometer (Shimadzu, Tokyo, Japan). Elemental analyses were carried out by Perkin-Elmer 2400 series-II elemental analyser.

General procedure for the synthesis of *N*-(substituted benzylidene/2'-thienylidene)-5-methylthiazol-2-amine (3a-h)

A 250 ml round bottom flask equipped with a Dean-Stark water separator was charged with a mixture of 2-amino-5-methylthiazole **(1)** (1.14 g, 0.01 mol) and an appropriate aromatic/heterocyclic aldehyde **(2a-h)** in toluene (50 ml). During the course of the reaction the water was removed continuously. The reaction mixture was heated under reflux for 6-7 hours. The reaction progress was checked by taking TLC using toluene and methanol (10:3 v/v) as mobile phase. After completion of the reaction, the resulting mixture was cooled, the excess solvent was evaporated. Finally the solid product obtained was filtered, washed with water, dried and crystallized from ethanol to get the residue of **(3a-h).**

***N*-(2'-Methoxybenzylidene)-5-methylthiazol-2-amine (3a):** Yield: 83 %, m.p: 118 ^{0}C. Anal. Calcd. for $C_{12}H_{12}N_2OS$: C, 62.04; H, 5.21; N, 12.06. Found: C, 62.10; H, 5.25; N, 12.12. IR (KBr, cm^{-1}): 3073 (C-H aromatic), 1599 (C=C aromatic), 1597 (C=C thiazole) 1583 (CH=N Schiff base), 1523 (C=N thiazole), 1394 (CH_3), 1248 (C-O-C linkage), 839 (C-H thiazole), 680 (C-S-C linkage); ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 2.4 (s, 3H, C<u>H</u>$_3$), 3.4 (s, 3H, OC<u>H</u>$_3$), 7.2-7.9 (m, 5H, Ar <u>H</u> + 1H thiazole), 9.7 (s, 1H, C<u>H</u>=N); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 13.4 (CH_3), 54.2 (OCH_3), 114.4 (CH), 128.7 (C), 130.2 (CH), 131.1 (C), 137.3 (CH), 158.8 (CH=N), 163.5 (C), 168.4 (C=N); MS (EI) m/z: 232.7 (M^+).

***N*-(4'-Methoxybenzylidene)-5-methylthiazol-2-amine (3b):** Yield: 86 %, m.p: 90 ^{0}C. Anal. Calcd. for $C_{12}H_{12}N_2OS$: C, 62.04; H, 5.21; N, 12.06. Found: C, 62.00; H, 5.17; N, 12.03. IR (KBr, cm^{-1}): 3076 (C-H aromatic), 1591 (C=C aromatic), 1589 (C=C thiazole) 1580 (CH=N Schiff base), 1526 (C=N thiazole), 1390 (CH_3), 1240 (C-O-C linkage), 835 (C-H thiazole), 674 (C-S-C linkage); ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 2.2 (s, 3H, C<u>H</u>$_3$), 3.9 (s, 3H, OC<u>H</u>$_3$), 7.0-8.3 (m, 5H, Ar <u>H</u> + 1H thiazole), 8.5 (s, 1H, C<u>H</u>=N); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 12.1 (CH_3), 55.3 (OCH_3), 112.3 (CH), 127.3 (C), 132.4 (CH), 133.3 (C), 136.1 (CH), 150.4 (CH=N), 160.3 (C), 165.1 (C=N); MS (EI) m/z: 231.4 (M^+).

***N*-(2'-Chlorobenzylidene)-5-methylthiazol-2-amine (3c):** Yield: 76 %, m.p: 162 ^{0}C. Anal. Calcd. for $C_{11}H_9N_2SCl$: C, 55.81; H, 3.83; N, 11.83. Found: C, 55.83; H, 3.80; N, 11.86. IR (KBr, cm^{-1}): 3090 (C-H aromatic), 1578 (C=C aromatic), 1562 (C=C thiazole) 1546 (CH=N Schiff base), 1530 (C=N thiazole), 1331 (CH_3), 830 (C-H thiazole), 736 (C-Cl), 660 (C-S-C linkage); ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 2.3 (s, 3H, C<u>H</u>$_3$), 6.5-7.9 (m, 5H, Ar <u>H</u> + 1H thiazole), 8.1 (s, 1H, C<u>H</u>=N); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 11.5 (CH_3), 111.4 (CH), 126.1 (C), 131.3 (CH), 135.4 (C), 137.8 (CH), 148.3 (CH=N), 159.2 (C), 162.3 (C=N); MS (EI) m/z: 236.1 (M^+).

***N*-(3'-Chlorobenzylidene)-5-methylthiazol-2-amine (3d):** Yield: 70 %, m.p: 140 ^{0}C. Anal. Calcd. for $C_{11}H_9N_2SCl$: C, 55.81; H, 3.83; N, 11.83. Found: C, 55.79; H, 3.86; N, 11.80. IR (KBr, cm^{-1}): 3087 (C-H aromatic), 1575 (C=C aromatic), 1566 (C=C thiazole) 1540 (CH=N Schiff base), 1539 (C=N thiazole), 1338 (CH_3), 829 (C-H thiazole), 734 (C-Cl), 686 (C-S-C linkage); ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 2.2 (s, 3H, C<u>H</u>$_3$), 6.6-7.9 (m, 5H, Ar <u>H</u> + 1H thiazole), 8.0 (s, 1H, C<u>H</u>=N); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 13.4 (CH_3), 112.7 (CH), 124.3 (C), 129.2 (CH), 132.3 (C), 133.7 (CH), 149.1 (CH=N), 160.4 (C), 163.5 (C=N); MS (EI) m/z: 235.9 (M^+).

***N*-(4'-Chlorobenzylidene)-5-methylthiazol-2-amine (3e):** Yield: 76 %, m.p: 85 ^{0}C. Anal. Calcd. for $C_{11}H_9N_2SCl$: C, 55.81; H, 3.83; N, 11.83. Found: C, 55.82; H, 3.76; N, 11.90. IR (KBr, cm^{-1}): 3082 (C-H aromatic), 1570 (C=C aromatic), 1569 (C=C thiazole) 1543 (CH=N Schiff base), 1535 (C=N thiazole), 1334 (CH_3), 830 (C-H thiazole), 740 (C-Cl), 681 (C-S-C linkage); ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 2.6 (s, 3H, C<u>H</u>$_3$), 6.9-7.5 (m, 5H, Ar <u>H</u> + 1H thiazole), 7.9 (s, 1H, C<u>H</u>=N); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 12.1 (CH_3), 110.4 (CH), 126.6 (C), 130.8 (CH), 133.2 (C), 134.2 (CH), 144.3 (CH=N), 163.2 (C), 164.6 (C=N); MS (EI) m/z: 236.5 (M^+).

***N*-(2',3'-Dichlorobenzylidene)-5-methylthiazol-2-amine (3f):** Yield: 82 %, m.p: 129 ^{0}C. Anal. Calcd. for $C_{11}H_8N_2SCl_2$: C, 48.72; H, 2.97; N, 11.33. Found: C, 48.75; H, 2.95; N, 11.30. IR (KBr, cm^{-1}): 3085 (C-H aromatic), 1575 (C=C aromatic), 1561 (C=C thiazole) 1540 (CH=N Schiff base), 1531 (C=N thiazole), 1389 (CH_3), 829 (C-H thiazole), 738 (C-Cl), 676 (C-S-C linkage); ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 2.5 (s, 3H, C<u>H</u>$_3$), 6.8-7.5 (m, 4H, Ar <u>H</u> + 1H thiazole), 7.8 (s, 1H, C<u>H</u>=N); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 14.5 (CH_3), 112.3 (CH), 128.1 (C), 132.7 (CH), 133.8 (C), 135.4 (CH), 140.1 (CH=N), 160.3 (C), 162.8 (C=N); MS (EI) m/z: 269.2 (M^+).

***N*-(2',4'-Dichlorobenzylidene)-5-methylthiazol-2-amine (3g):** Yield: 69 %, m.p: 120 ^{0}C. Anal. Calcd. for $C_{11}H_8N_2SCl_2$: C, 48.72; H, 2.97; N, 11.33. Found: C, 48.68; H, 2.90; N, 11.28. IR (KBr, cm^{-1}): 3084 (C-H aromatic), 1570 (C=C aromatic), 1566 (C=C thiazole) 1546 (CH=N Schiff base), 1539 (C=N thiazole), 1380 (CH_3), 830 (C-H thiazole), 729 (C-Cl), 689 (C-S-C linkage); ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 2.4 (s, 3H, C<u>H</u>$_3$), 7.0-7.5 (m, 4H, Ar <u>H</u> + 1H thiazole), 7.9 (s, 1H, C<u>H</u>=N); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 12.1 (CH_3), 113.2 (CH), 126.7 (C), 131.9 (CH), 134.5 (C), 136.7 (CH), 138.4 (CH=N), 161.2 (C), 164.3 (C=N); MS (EI) m/z: 269.8 (M^+).

***N*-(2'-Thienylidene)-5-methylthiazol-2-amine (3h):** Yield: 7 %, m.p: 118 ^{0}C. Anal. Calcd. for $C_9H_8N_2S_2$: C, 51.89; H, 3.87; N, 13.45. Found: C, 51.85; H, 3.90; N, 13.40. IR (KBr, cm^{-1}): 3080 (C-H aromatic), 1573 (C=C aromatic), 1561 (C=C thiazole) 1540 (CH=N Schiff base), 1538 (C=N thiazole), 1330 (CH_3), 836 (C-H thiazole), 690 (C-S-C linkage); ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 2.3 (s, 3H, C<u>H</u>$_3$), 7.2-7.6 (m, 4H, Ar <u>H</u> + 1H thiazole), 7.8 (s, 1H, C<u>H</u>=N); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 18.2 (CH_3), 108.3 (CH), 123.1 (C), 129.2 (CH), 132.4 (C), 134.5 (CH), 146.0 (CH=N), 162.1 (C), 165.3 (C=N); MS (EI) m/z: 208.9 (M^+).

General procedure for the synthesis of *2*-(substitutedphenyl/2'-thienyl)-3-(5'-methylthiazol-2'-yl)-thiazolidin-4-one (4a-h)

An appropriate *N*-(substitutedbenzylidene/2'-thienylidene)-5-methylthiazol-2-amine **(3a-h)** (0.01 mol) and thioglycolic acid (0.01 mol, 0.69 g) dissolved in toluene (50 ml) was taken into a 250 ml round bottomed flask, joint with Dean-Stark water separator. Reaction mixture was heated under reflux for 8-10 hours. The progress of the reaction was monitored on TLC plate using toluene: methanol (10:7 v/v) eluent as mobile phase. After completion of the reaction, the excess of solvent was removed by distilled off and the resulting mixture was transferred into an evaporating dish to evaporate toluene. Then the fallout product was treated with saturated solution of sodium bicarbonate ($NaHCO_3$) to remove excess thioglycolic acid. Thus the product obtained was recrystallized from methanol to gives 2-(substitutedphenyl/2'-thienyl)-3-(5'-methylthiazol-2'-yl)-thiazolidin-4-one **(4a-h)** derivatives.

2-(2'-Methoxyphenyl)-3-(5'-methylthiazol-2'-yl)-thiazolidin-4-one (4a): Yield: 72 %, m.p: 138 ^{0}C. Anal. Calcd. for $C_{14}H_{14}N_2O_2S_2$: C, 54.88; H, 4.61; N, 9.14. Found: C, 54.92; H, 4.66; N, 9.10. IR (KBr, cm^{-1}): 3082 (C-H aromatic), 2979 (C-H alkane), 1698 (C=O), 1576 (C=C thiazole), 1551 (C=N thiazole), 1394 (CH_3), 1351 (C-N thiazole), 1219 (C-O-C linkage), 818 (C-H thiazole), 674 (C-S-C linkage thiazolidinone and thiazole); ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 2.58 (s, 3H, C<u>H</u>$_3$), 3.90 (s, 3H, OC<u>H</u>$_3$), 4.9 (s, 2H, C<u>H</u>$_2$), 5.9 (s, 1H, C<u>H</u>-Ar), 7.1-8.1 (m, 5H, Ar <u>H</u> + 1H thiazole); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 12.9 (CH_3), 33.5 (CH_2), 67.8 (CH), 113.5 (CH), 115.3 (C), 120.5 (C), 128.5 (CH), 130.8 (CH), 131.5 (C), 133.0 (CH), 156.4 (C), 158.3 (C), 171.3 (C=O); MS (EI) m/z: 306.7 (M^+).

2-(4'-Methoxyphenyl)-3-(5'-methylthiazol-2'-yl)-thiazolidin-4-one (4b): Yield: 78 %, m.p: 131 ^{0}C. Anal. Calcd. for $C_{14}H_{14}N_2O_2S_2$: C, 54.88; H, 4.61; N, 9.14. Found: C, 54.85; H, 4.58; N, 9.17. IR (KBr, cm^{-1}): 3080 (C-H aromatic), 2981 (C-H alkane), 1695 (C=O), 1575 (C=C thiazole), 1553 (C=N thiazole), 1390 (CH_3), 1347 (C-N thiazole), 1220 (C-O-C linkage), 820 (C-H thiazole), 670 (C-S-C linkage thiazolidinone and thiazole); ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 2.4 (s, 3H, C<u>H</u>$_3$), 3.8 (s, 3H, OC<u>H</u>$_3$), 4.7 (s, 2H, C<u>H</u>$_2$), 5.5 (s, 1H, C<u>H</u>-Ar), 7.0-8.0 (m, 5H, Ar <u>H</u> + 1H thiazole); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 13.4 (CH_3), 31.2 (CH_2), 65.7 (CH), 111.6 (CH), 113.2 (C), 121.4 (C), 125.3 (CH), 129.7 (CH), 132.0 (C), 134.5 (CH), 154.2 (C), 156.7 (C), 170.2 (C=O); MS (EI) m/z: 306.2 (M^+).

2-(2'-Chlorophenyl)-3-(5'-methylthiazol-2'-yl)-thiazolidin-4-one (4c): Yield: 80 %, m.p: 141 ^{0}C. Anal. Calcd. for $C_{13}H_{11}N_2S_2OCl$: C, 50.23; H, 3.57; N, 9.01. Found: C, 50.20; H, 3.54; N, 9.07. IR (KBr, cm^{-1}): 3082 (C-H aromatic), 2982 (C-H alkane), 1690 (C=O), 1580 (C=C thiazole), 1563 (C=N thiazole), 1384 (CH_3), 1340 (C-N thiazole), 824 (C-H thiazole), 730 (C-Cl), 668 (C-S-C linkage thiazolidinone and thiazole); ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 2.2 (s, 3H, C<u>H</u>$_3$), 4.4 (s, 2H, C<u>H</u>$_2$), 5.2 (s, 1H, C<u>H</u>-Ar), 6.5-8.1 (m, 5H, Ar <u>H</u> + 1H thiazole); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 11.2 (CH_3), 29.8 (CH_2), 64.3 (CH), 112.4 (CH), 114.6 (C), 122.2 (C), 124.1 (CH), 126.8 (CH), 133.3 (C), 135.7 (CH), 155.6 (C), 168.2 (C=O); MS (EI) m/z: 310.0 (M^+).

2-(3'-Chlorophenyl)-3-(5'-methylthiazol-2'-yl)-thiazolidin-4-one (4d): Yield: 71 %, m.p: 177 ^{0}C. Anal. Calcd. for $C_{13}H_{11}N_2S_2OCl$: C, 50.23; H, 3.57; N, 9.01. Found: C, 50.26; H,

3.60; N, 9.04. IR (KBr, cm^{-1}): 3086 (C-H aromatic), 2980 (C-H alkane), 1682 (C=O), 1580 (C=C thiazole), 1569 (C=N thiazole), 1390 (CH_3), 1335 (C-N thiazole), 822 (C-H thiazole), 734 (C-Cl), 660 (C-S-C linkage thiazolidinone and thiazole); ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 2.5 (s, 3H, C<u>H</u>$_3$), 4.6 (s, 2H, C<u>H</u>$_2$), 5.3 (s, 1H, C<u>H</u>-Ar), 6.9-7.9 (m, 5H, Ar <u>H</u> + 1H thiazole); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 13.4 (CH_3), 28.3 (CH_2), 65.4 (CH), 110.2 (CH), 113.5 (C), 123.9 (C), 126.7 (CH), 128.4 (CH), 132.2 (C), 134.6 (CH), 154.3 (C), 167.1 (C=O); MS (EI) m/z: 310.6 (M^+).

2-(4'-Chlorophenyl)-3-(5'-methylthiazol-2'-yl)-thiazolidin-4-one (4e): Yield: 82 %, m.p: 127 ^{0}C. Anal. Calcd. for $C_{13}H_{11}N_2S_2OCl$: C, 50.23; H, 3.57; N, 9.01. Found: C, 50.22; H, 3.66; N, 9.02. IR (KBr, cm^{-1}): 3092 (C-H aromatic), 2976 (C-H alkane), 1680 (C=O), 1585 (C=C thiazole), 1563 (C=N thiazole), 1391 (CH_3), 1330 (C-N thiazole), 818 (C-H thiazole), 736 (C-Cl), 666 (C-S-C linkage thiazolidinone and thiazole); ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 2.2 (s, 3H, C<u>H</u>$_3$), 4.7 (s, 2H, C<u>H</u>$_2$), 5.6 (s, 1H, C<u>H</u>-Ar), 7.0-8.0 (m, 5H, Ar <u>H</u> + 1H thiazole); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 12.6 (CH_3), 29.2 (CH_2), 64.3 (CH), 112.5 (CH), 114.3 (C), 126.1 (C), 127.8 (CH), 129.6 (CH), 131.4 (C), 135.2 (CH), 150.4 (C), 168.9 (C=O); MS (EI) m/z: 309.9 (M^+).

2-(2',3'-Dichlorophenyl)-3-(5'-methylthiazol-2'-yl)-thiazolidin-4-one (4f): Yield: 82 %, m.p: 193 ^{0}C. Anal. Calcd. for $C_{13}H_{10}N_2S_2Cl_2O$: C, 45.22; H, 2.92; N, 8.11. Found: C, 45.18; H, 2.90; N, 8.15. IR (KBr, cm^{-1}): 3086 (C-H aromatic), 2964 (C-H alkane), 1674 (C=O), 1590 (C=C thiazole), 1560 (C=N thiazole), 1395 (CH_3), 1336 (C-N thiazole), 812 (C-H thiazole), 731 (C-Cl), 664 (C-S-C linkage thiazolidinone and thiazole); ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.9 (s, 3H, C<u>H</u>$_3$), 4.9 (s, 2H, C<u>H</u>$_2$), 5.9 (s, 1H, C<u>H</u>-Ar), 6.8-7.6 (m, 4H, Ar <u>H</u> + 1H thiazole); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 11.2 (CH_3), 27.4 (CH_2), 63.1 (CH), 110.7 (CH), 112.4 (C), 120.2 (C), 124.6 (CH), 127.5 (CH), 132.3 (C), 133.4 (C), 146.2 (C), 172.3 (C=O); MS (EI) m/z: 345.8 (M^+).

2-(2',4'-Dichlorophenyl)-3-(5'-methylthiazol-2'-yl)-thiazolidin-4-one (4g): Yield: 71 %, m.p: 147 ^{0}C. Anal. Calcd. for $C_{13}H_{10}N_2S_2Cl_2O$: C, 45.22; H, 2.92; N, 8.11. Found: C, 45.26; H, 2.95; N, 8.08. IR (KBr, cm^{-1}): 3097 (C-H aromatic), 2986 (C-H alkane), 1684 (C=O), 1585 (C=C thiazole), 1556 (C=N thiazole), 1396 (CH_3), 1331 (C-N thiazole), 810 (C-H thiazole), 736 (C-Cl), 669 (C-S-C linkage thiazolidinone and thiazole); ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 2.6 (s, 3H, C<u>H</u>$_3$), 4.3 (s, 2H, C<u>H</u>$_2$), 5.5 (s, 1H, C<u>H</u>-Ar), 6.9-7.6 (m, 4H, Ar <u>H</u> + 1H thiazole); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 12.4 (CH_3), 28.3 (CH_2), 66.2 (CH), 112.1 (CH), 114.1 (C), 122.6 (C), 125.7 (CH), 128.2 (CH), 133.4 (C), 135.3 (C), 140.1 (C), 169.2 (C=O); MS (EI) m/z: 345.0 (M^+).

2-(2'-Thiophenyl)-3-(5'-methylthiazol-2'-yl)-thiazolidin-4-one (4h): Yield: 71 %, m.p: 110 ^{0}C. Anal. Calcd. for $C_{11}H_{10}N_2S_3O$: C, 46.78; H, 3.57; N, 9.92. Found: C, 46.80; H, 3.60; N, 9.90. IR (KBr, cm^{-1}): 3095 (C-H aromatic), 2992 (C-H alkane), 1682 (C=O), 1580 (C=C thiazole), 1559 (C=N thiazole), 1392 (CH_3), 1338 (C-N thiazole), 812 (C-H thiazole), 739 (C-Cl), 679 (C-S-C linkage thiazolidinone and thiazole); ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 2.0 (s, 3H, C<u>H</u>$_3$), 4.1 (s, 2H, C<u>H</u>$_2$), 5.3 (s, 1H, C<u>H</u>-Ar), 6.8-7.4 (m, 3H, Ar <u>H</u> + 1H thiazole); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 14.5 (CH_3), 32.6 (CH_2), 68.9 (CH), 114.3 (CH), 116.7 (C), 120.2 (C), 123.9 (CH), 127.5 (CH), 136.1 (C), 140.5 (C), 165.3 (C=O); MS (EI) m/z: 282.9 (M^+).

General procedure for the synthesis of *2*-(substitutedphenyl/2'-thienyl)-5-methyl-3-(5'-methylthiazol-2'-yl)-thiazolidin-4-one (5a-h)

An equimolar mixture of *N*-(substitutedbenzylidene/2'-thienylidene)-5-methylthiazol-2-amine **(3a-h)** and thiolactic acid (0.01 mol, 0.88 g) dissolved in toluene (50 ml) were taken into a 250 ml round bottomed flask, attached with Dean-Stark water separator. The reaction mixture was heated under reflux for 8-10 hours. The progress of the reaction was monitored on TLC plate using toluene: methanol (10:6 v/v) eluent as mobile phase. After completion of the

reaction, the excess of solvent was removed by distilled off and the resulting mixture was transferred into evaporating dish to evaporate toluene. Then the fallout product was treated with saturated solution of sodium bicarbonate ($NaHCO_3$) to remove excess thiolactic acid. Thus the product obtained was recrystallized from methanol to gives *2*-(substitutedphenyl/2'-thienyl)-5-methyl-3-(5'-methylthiazol-2'-yl)-thiazolidin-4-one **(5a-h)** derivatives.

2-(2'-Methoxyphenyl)-5-methyl-3-(5'-methylthiazol-2'-yl)-thiazolidin-4-one (5a): Yield: 75 %, m.p: 132 ^{0}C. Anal. Calcd. for $C_{15}H_{16}N_2S_2O_2$: C, 56.23; H, 5.03; N, 8.74. Found: C, 56.27; H, 5.08; N, 8.79. IR (KBr, cm^{-1}): 3089 (C-H aromatic), 2992 (C-H alkane), 1674 (C=O), 1580 (C=C thiazole), 1569 (C=N thiazole), 1385 (CH_3 thiazolidinone and thiazole), 1349 (C-N thiazole), 1240 (C-O-C linkage), 803 (C-H thiazole), 669 (C-S-C linkage thiazolidinone and thiazole); ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 2.6 (s, 3H, C<u>H</u>$_3$), 3.4 (s, 3H, OC<u>H</u>$_3$), 4.0 (q, 1H, C<u>H</u>-CH$_3$), 5.7 (s, 1H, C<u>H</u>-Ar), 7.0-8.0 (m, 5H, Ar <u>H</u> + 1H thiazole); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 12.7 (CH_3), 40.9 (CH), 64.1 (CH), 111.4 (CH), 116.4 (C), 118.2 (C), 121.2 (CH), 127.9 (CH), 128.4 (CH), 130.0 (C), 132.6 (CH), 152.2 (C), 160.5 (C), 168.8 (C=O); MS (EI) m/z: 320.1 (M^+).

2-(4'-Methoxyphenyl)-5-methyl-3-(5'-methylthiazol-2'-yl)-thiazolidin-4-one (5b): Yield: 81 %, m.p: 99 ^{0}C. Anal. Calcd. for $C_{15}H_{16}N_2S_2O_2$: C, 56.23; H, 5.03; N, 8.74. Found: C, 56.20; H, 5.00; N, 8.70. IR (KBr, cm^{-1}): 3080 (C-H aromatic), 2995 (C-H alkane), 1671 (C=O), 1582 (C=C thiazole), 1565 (C=N thiazole), 1381 (CH_3 thiazolidinone and thiazole), 1342 (C-N thiazole), 1238 (C-O-C linkage), 812 (C-H thiazole), 690 (C-S-C linkage thiazolidinone and thiazole); ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 2.2 (s, 3H, C<u>H</u>$_3$), 3.9 (s, 3H, OC<u>H</u>$_3$), 4.2 (q, 1H, C<u>H</u>-CH$_3$), 5.5 (s, 1H, C<u>H</u>-Ar), 6.9-7.6 (m, 5H, Ar <u>H</u> + 1H thiazole); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 13.4 (CH_3), 38.2 (CH), 66.7 (CH), 110.2 (CH), 112.3 (C), 116.1 (C), 122.4 (CH), 125.3 (CH), 127.9 (CH), 129.7 (C), 132.4 (CH), 150.2 (C), 159.7 (C), 164.2 (C=O); MS (EI) m/z: 320.6 (M^+).

2-(2'-Chlorophenyl)-5-methyl-3-(5'-methylthiazol-2'-yl)-thiazolidin-4-one (5c): Yield: 68 %, m.p: 130 ^{0}C. Anal. Calcd. for $C_{14}H_{13}N_2S_2OCl$: C, 51.76; H, 4.03; N, 8.62. Found: C, 51.70; H, 4.06; N, 8.58. IR (KBr, cm^{-1}): 3096 (C-H aromatic), 2990 (C-H alkane), 1670 (C=O), 1585 (C=C thiazole), 1560 (C=N thiazole), 1390 (CH_3 thiazolidinone and thiazole), 1338 (C-N thiazole), 816 (C-H thiazole), 696 (C-S-C linkage thiazolidinone and thiazole); ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 2.5 (s, 3H, C<u>H</u>$_3$), 4.3 (q, 1H, C<u>H</u>-CH$_3$), 5.9 (s, 1H, C<u>H</u>-Ar), 7.0-7.8 (m, 5H, Ar <u>H</u> + 1H thiazole); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 10.1 (CH_3), 36.4 (CH), 69.2 (CH), 108.7 (CH), 110.2 (C), 113.6 (C), 123.9 (CH), 126.7 (CH), 128.2 (CH), 130.2 (C), 133.2 (CH), 148.1 (C), 153.4 (C), 166.2 (C=O); MS (EI) m/z: 324.1 (M^+).

2-(3'-Chlorophenyl)-5-methyl-3-(5'-methylthiazol-2'-yl)-thiazolidin-4-one (5d): Yield: 73 %, m.p: 132 ^{0}C. Anal. Calcd. for $C_{14}H_{13}N_2S_2OCl$: C, 51.76; H, 4.03; N, 8.62. Found: C, 51.74; H, 4.00; N, 8.60. IR (KBr, cm^{-1}): 3100 (C-H aromatic), 2980 (C-H alkane), 1664 (C=O), 1572 (C=C thiazole), 1559 (C=N thiazole), 1396 (CH_3 thiazolidinone and thiazole), 1330 (C-N thiazole), 810 (C-H thiazole), 690 (C-S-C linkage thiazolidinone and thiazole); ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 2.1 (s, 3H, C<u>H</u>$_3$), 4.2 (q, 1H, C<u>H</u>-CH$_3$), 6.2 (s, 1H, C<u>H</u>-Ar), 6.5-7.2 (m, 5H, Ar <u>H</u> + 1H thiazole); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 13.2 (CH_3), 34.5 (CH), 67.3 (CH), 110.3 (CH), 112.5 (C), 114.4 (C), 122.2 (CH), 125.7 (CH), 129.1 (CH), 132.3 (C), 134.6 (CH), 140.5 (C), 152.3 (C), 169.1 (C=O); MS (EI) m/z: 324.9 (M^+).

2-(4'-Chlorophenyl)-5-methyl-3-(5'-methylthiazol-2'-yl)-thiazolidin-4-one (5e): Yield: 83 %, m.p: 123 ^{0}C. Anal. Calcd. for $C_{14}H_{13}N_2S_2OCl$: C, 51.76; H, 4.03; N, 8.62. Found: C, 51.70; H, 4.10; N, 8.68. IR (KBr, cm^{-1}): 3093 (C-H aromatic), 2976 (C-H alkane), 1662 (C=O), 1569 (C=C thiazole), 1554 (C=N thiazole), 1392 (CH_3 thiazolidinone and thiazole), 1343 (C-N thiazole), 823 (C-H thiazole), 687 (C-S-C linkage thiazolidinone and thiazole); ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.9 (s, 3H, C<u>H</u>$_3$), 4.8 (q, 1H, C<u>H</u>-CH$_3$), 6.0 (s, 1H, C<u>H</u>-Ar), 6.9-

7.6 (m, 5H, Ar H + 1H thiazole); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 14.5 (CH_3), 32.1 (CH), 68.2 (CH), 112.1 (CH), 114.4 (C), 116.3 (C), 126.2 (CH), 129.7 (CH), 130.2 (CH), 133.5 (C), 135.0 (CH), 138.2 (C), 151.0 (C), 170.3 (C=O); MS (EI) m/z: 323.8 (M^+).

2-(2',3'-Dichlorophenyl)-5-methyl-3-(5'-methylthiazol-2'-yl)-thiazolidin-4-one (5f): Yield: 83 %, m.p: 159 ^{0}C. Anal. Calcd. for $C_{14}H_{12}N_2S_2Cl_2O$: C, 46.80; H, 3.37; N, 7.80. Found: C, 46.83; H, 3.34; N, 7.85. IR (KBr, cm^{-1}): 3079 (C-H aromatic), 2965 (C-H alkane), 1626 (C=O), 1546 (C=C thiazole), 1535 (C=N thiazole), 1330 (CH_3 thiazolidinone and thiazole), 1323 (C-N thiazole), 816 (C-H thiazole), 690 (C-S-C linkage thiazolidinone and thiazole); ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.5 (s, 3H, C$\underline{H}_3$), 4.6 (q, 1H, C$\underline{H}$-CH_3), 5.6 (s, 1H, C$\underline{H}$-Ar), 7.0-7.7 (m, 4H, Ar H + 1H thiazole); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 13.1 (CH_3), 31.3 (CH), 67.2 (CH), 110.4 (CH), 112.5 (C), 114.0 (C), 123.7 (CH), 126.6 (CH), 131.9 (CH), 135.2 (C), 136.9 (C), 137.1 (C), 148.5 (C), 168.2 (C=O); MS (EI) m/z: 360.2 (M^+).

2-(2',4'-Dichlorophenyl)-5-methyl-3-(5'-methylthiazol-2'-yl)-thiazolidin-4-one (5g): Yield: 76 %, m.p: 69 ^{0}C. Anal. Calcd. for $C_{14}H_{12}N_2S_2Cl_2O$: C, 46.80; H, 3.37; N, 7.80. Found: C, 46.76; H, 3.40; N, 7.83. IR (KBr, cm^{-1}): 3082 (C-H aromatic), 2968 (C-H alkane), 1629 (C=O), 1550 (C=C thiazole), 1540 (C=N thiazole), 1339 (CH_3 thiazolidinone and thiazole), 1324 (C-N thiazole), 810 (C-H thiazole), 689 (C-S-C linkage thiazolidinone and thiazole); ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.9 (s, 3H, C$\underline{H}_3$), 4.4 (q, 1H, C$\underline{H}$-CH_3), 5.3 (s, 1H, C$\underline{H}$-Ar), 6.9-7.6 (m, 4H, Ar H + 1H thiazole); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 15.9 (CH_3), 36.2 (CH), 69.1 (CH), 112.4 (CH), 113.2 (C), 115.9 (C), 126.0 (CH), 128.8 (CH), 130.4 (CH), 139.2 (C), 141.8 (C), 142.3 (C), 144.6 (C), 167.6 (C=O); MS (EI) m/z: 359.6 (M^+).

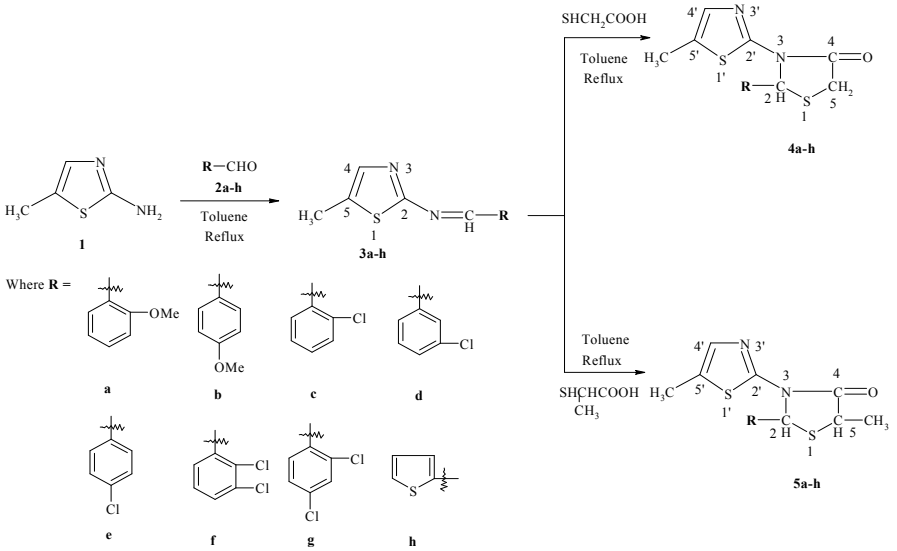
2-(2'-Thiophenyl)-5-methyl-3-(5'-methylthiazol-2'-yl)-thiazolidin-4-one (5h): Yield: 76 %, m.p: 93 ^{0}C. Anal. Calcd. for $C_{12}H_{12}S_3N_2O$: C, 48.62; H, 4.08; N, 9.45. Found: C, 48.64; H, 4.12; N, 9.40. IR (KBr, cm^{-1}): 3091 (C-H aromatic), 2996 (C-H alkane), 1645 (C=O), 1565 (C=C thiazole), 1543 (C=N thiazole), 1340 (CH_3 thiazolidinone and thiazole), 1320 (C-N thiazole), 819 (C-H thiazole), 692 (C-S-C linkage thiazolidinone and thiazole); ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 2.3 (s, 3H, C$\underline{H}_3$), 4.0 (q, 1H, C$\underline{H}$-CH_3), 5.1 (s, 1H, C$\underline{H}$-Ar), 7.0-7.5 (m, 4H, Ar H + 1H thiazole); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 14.3 (CH_3), 35.1 (CH), 70.4 (CH), 113.2 (CH), 116.7 (C), 124.5 (CH), 129.2 (CH), 132.7 (CH), 134.3 (C), 139.0 (C), 140.2 (C), 141.9 (C), 173.8 (C=O); MS (EI) m/z: 296.6 (M^+).

Results and discussion

Chemistry

The synthesis of the target **(3a-h), (4a-h)** and **(5a-h)** compounds were carried out as outlined in **Scheme 1**. The structures of all synthesised compounds were inferred from their analytical and spectral data. As an example, in the IR spectrum of compound **3a**, characteristic is the CH=N stretching vibration, which appear as an intense band at 1583 cm^{-1}. The absence of characteristic band of NH_2 group of thiazole moiety at 3300-3400 cm^{-1} confirms the formation of the proposed Schiff base. The structural element characteristic for the 2-amino-5-methylthiazole nucleus, namely; the stretching vibration band for the C=N, C-S-C linkage and CH_3 stretching observed at 1523, 680 and 1394 cm^{-1} respectively. Several bands appeared at 1599 and 3073 cm^{-1} are due to the stretching of C=C and C-H vibrations of aromatic ring. The ^{1}H NMR spectrum of compound **3a** did not only show the absence of NH_2 protons of thiazole unit as singlet signal at δ 3-4 ppm but exerted a singlet at higher field at δ 9.7 ppm for -CH=N- proton of the imine group. There was emphasized signal as singlet for the methyl group protons at δ 2.4 ppm which confirmed the thiazole nucleus. The aromatic protons for the substituted benzene ring and methoxy group protons are found in the region at δ 7.2-7.9 and 3.4 ppm as multiplet and singlet signal respectively. Finally, the ^{13}C NMR spectrum of the product **3a** was recorded in $CDCl_3$ and the spectral signals were in good agreement with

the proposed structure. The chemical shifts for the carbon atoms of azomethine group are observed at δ 158.8 ppm, while the carbon atoms from the thiazole nucleus exerted at δ 13.4, 137.3 and 168.4 ppm respectively.The signals for aromatic carbons appeared between δ 114.4-163.5 ppm in the ^{13}C spectrum.



Scheme 1. Systematic path for the synthesis of **(3a-h)**, **(4a-h)** and **(5a-h)**

The title compounds 2,3-disubstituted-4-thiazolidinones **(4a-h)** and 2,3-disubstituted-5-methyl-4-thiazolidinones **(5a-h)** were obtained by the attack of Sulphur nucleophile on imine carbon followed by intramolecular cyclization with elimination of water. The IR spectra of the synthesised compound **4a** and **5a** shows the strong absorption band at 1698 and 674 cm^{-1} for **4a** and at 1674 and 669 cm^{-1} for **5a** confirms the presence of cyclic amido C=O group and C-S-C linkage of 4-thiazolidinone unit. There was no absorption in the region of 1605-1621 cm^{-1} which signifying the disappearance of azomethine group in this structure. Moreover the compound **5a**, showed a strong absorption band at 1394 cm^{-1} due to the presence of the CH_3 group attached on the C-5 position of thiazolidine ring which confirmed the cyclocondensation of Schiff base. A broad stretching band for the C=N functionality and CH_3 group of thiazole ring is observed at between 1495-1635 cm^{-1} and 1300-1400 cm^{-1} respectively. The ^1H NMR spectrum of compound **4a** clearly indicated the presence of the active methylene group in the thiazolidine ring by exhibiting a signal as singlet at δ 4.9 ppm while compound **5a** displayed diagnostic peaks at δ 5.7 and 4.0 ppm as singlet and quartet for the Ar-CH and CH_3-CH proton for the thiazolidine ring system. The presence of the methyl group proton of the thiazolidine ring by exhibiting a signal as doublet at δ 2.6 ppm also supported the cyclised product **5a**. The disappearance of the N=CH proton between δ 9-10 ppm and the appearance of a methine proton of C-2 at δ 5.7-5.9 ppm as singlet also supported presence of thiazolidine ring. The other remaining aromatic protons appeared as a multiplet signal at δ 7.0-8.2 ppm along with singlet at δ 3.4-3.9 ppm corresponding to the methoxy group protons. Finally, the ^{13}C NMR spectra of the cyclised product **4a** and **5a** were recorded in $CDCl_3$ and the spectral signals were in good agreement with the proposed structure. In the ^{13}C NMR spectrum of compound **4a**, the shielded signal at δ 12.9 and 33.5 ppm were assigned to the methyl group of thiazole ring and methylene carbon of thiazolidine ring whereas in the^{13}C NMR spectrum of compound **5a**, the characterisation signal at δ 12.7

ppm for methyl carbon along with the peaks at δ 40.9 and 64.1 ppm for ring carbons. The most deshielded signal that appeared at δ 168-173 ppm was assigned to the carbonyl group of thiazolidine unit. The signals for aromatic carbons appeared between at δ 111.0-160.5 ppm in the ^{13}C spectrum. Further, mass spectra of all the title compounds showed molecular ion peak M^+ corresponding to their exact mass which is in agreement with its proposed structure. The obtained elemental analysis values are in good agreement with theoretical data.

***In vitro* antimicrobial activity**

All the synthesized compounds were screened for their antimicrobial activity by using agar cup-plate method[26]. The investigation of antibacterial screening data revels **(Table 1)** that all the screened compounds exerted good inhibition against all pathogenic species. Under identical conditions, the standard antibiotics showed zones of inhibition ampicilin 15-23 mm and amoxicillin 18-23 mm against bacterial strains. From the experimental data it has been observed that in case of Gram positive bacteria, compounds **4b** and **5f** were found to be active against *S. aureus*. Compounds **3c**, **3d**, **3f**, **5f** and **5g** were found to be active against *B. subtilis* compared to ampicillin and amoxicillin. In case of Gram negative bacteria, compounds **3d** and **3h** were found to be active compared to ampicillin. Compounds **5h** were found to be active against *S. paratyphi-B*. All the remaining compounds were found to be moderately or less active against the all pathogenic bacterial strains. None of the compounds showed promising antifungal activity against *C. albicans*.

***In vitro* antitubercular activity**

Antitubercular activity of the compounds was carried out at Tuberculosis Antimicrobial Acquisition Co-ordinating Facility at single concentration 6.25 µg/ml against *Mycobacterium tuberculosis $H_{37}Rv$* in BACTEC 12B medium using the Microplate Alamar Blue Assay[27] method. The observed result **(Table 1)** showed that, compounds **4b**, **4d**, **4e**, **5b**, **5d** and **5e** showed 60-80% inhibition. While the compounds **3a**, **3c**, **3d**, **3f**, **3g**, **3h**, **4a**, **4c**, **4f**, **4g**, **4h**, **5a**, **5c**, **5f** and **5g** exerted moderate activity against *Mycobacterium Tuberculosis $H_{37}Rv$* compared to isoniazid (99% inhibition) and rifampicin (98% inhibition).

***In vitro* anticancer activity**

The title compounds were evaluated for anticancer activity in drug-screening programme at the National Cancer Institute, USA[28]. Total eight compounds **(4a-h)** are selected and evaluated in the three-cell line, NCI-H460 (Lung), MCF7 (Breast) and SF-268 (CNS) at 10^{-4}M concentration one dose primary anticancer assay. Results for each compound were reported as the percent of growth of the treated cells when compared to the untreated control cells. All the compounds which reduced the growth of any one of the cell lines to 32% or less were passed on for evaluation in the full panel of 60 human cancer cell lines and considered active. All the compounds exerted moderately active against all panel of cancer cell line. The results of this screening are presented in **Table 1**.

Table 1. *In vitro* antimicrobial, antitubercular and anticancer activity data of the compounds **(3a-h)**, **(4a-h)**, and **(5a-h)**

Entry	Antibacterial				Antitubercular	Anticancer		
	Zone of inhibition in diameter (mm)				% Inhibition	Growth Percentage		
	S. a	*B. s*	*E. c*	*S. p*	*M. Tuberculosis H_{37} Rv*	MCF-7	NCl-H460	SF-268
3a	-	10	-	-	0	-	-	-
3b	-	13	-	-	0	-	-	-
3c	14	18	10	-	0	-	-	-
3d	-	18	15	-	0	-	-	-
3e	-	11	-	-	0	-	-	-
3f	13	18	-	-	06	-	-	-
3g	12	13	-	-	0	-	-	-
3h	-	10	16	-	0	-	-	-
4a	-	12	-	-	0	95	85	108
4b	16	13	10	-	69	88	86	82
4c	-	14	-	-	12	130	118	117
4d	12	13	-	-	61	124	121	108
4e	-	14	-	-	65	119	112	101
4f	11	14	09	-	08	88	94	84
4g	13	11	10	-	23	80	97	123
4h	11	11	10	-	05	75	106	113
5a	12	12	-	-	09	-	-	-
5b	-	14	13	-	79	-	-	-
5c	12	10	10	-	38	-	-	-
5d	-	13	-	-	78	-	-	-
5e	14	10	12	-	81	-	-	-
5f	16	23	-	-	0	-	-	-
5g	-	15	-	-	36	-	-	-
5h	12	11	18	18	0	-	-	-

- Indicate no zone of inhibition

Conclusion

In the present paper, eight Schiff bases and sixteen 4-thiazolidinone type compounds with 2-amino-5-methylthiazole fragment were synthesised with the aim of discovering innovative structure leads serving as potent antimicrobial and antitubercular and anticancer agents. The screening results revealed that all the compounds exhibited moderate to excellent activities against all the pathogenic strains. Upon varying the substitution on aryl ring appended to the Schiff bases and 4-thiazolidinones ring, the activities changed drastically. Among the twenty four newly synthesised compounds, analogues **3c**, **4b**, **4f**, **4g**, **4h**, **5c**, **5e**, **5f**, and **5h** possessing electron withdrawing group such as methoxy, chloro at the meta or para position or thienyl ring were identified as the most potent antibacterial agents. Compound **5b**, **5d** and **5e** displayed excellent anti tubercular activity. Some of the compounds exerted considerable anticancer activity.

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