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# ANTIOXIDANT AND ANTIBACTERIAL STUDIES OF THIAZOLIDIN-4-ONES CONTAINING BENZO [*b*] THIOPHENE MOIETY

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## ABSTRACT

A novel series of 2-(substituted phenyl)-3-(3-chloro-1-benzo[*b*]thiophene-2-carboxamido)-4-thiazolidinones and 2-(substituted phenyl)-3-(3-chloro-1-benzo[*b*]thiophene-2-carboxamido)-5-carboxymethyl-4-thiazolidinones have been synthesized and evaluated for antimicrobial and antioxidant activities. Initially, 3-chloro-1-benzo[b]thiophene-2-carbonyl chloride (1) was prepared from cinnamic acid in the presence of chlorobenzene and thionyl chloride. This compound (1) was treated with hydrazine hydrate to afford 3-chloro-1-benzo[b]thiophene-2-carbohydrazide [2] which was further reacted with various aromatic aldehydes to yield hydrazones 2(a-h). Further reaction of these hydrazones 2a-h with thioglycollic acid gave 2-(substituted phenyl)-3-(3-chloro-1-benzo[*b*]thiophene-2-carboxamido)-4-thiazolidinones 3a-h. Reaction of the same compounds 2a-h in the presence of thiomalic acid afforded 2-(substituted phenyl)-3-(3-chloro-1-benzo[*b*]thiophene-2-carboxamido)-5-carboxymethyl-4-thiazolidinone 4a-h. The structures of newly synthesized compounds 3a-h and 4a-h have been confirmed by spectroscopic techniques such IR, $^{1}$H NMR, $^{13}$C NMR and elemental analysis. The synthesized compounds were screened for their antimicrobial and antioxidant activities. Compounds 3d and 4a-h showed significant antibacterial activity and compounds 3d, 3h and 4h were found to be the most active antioxidants in the series, and thus represent a new class of promising lead compounds.

**KEYWORDS:** Antioxidant, Antibacterial, Thiazolidin-4-one, Benzo[*b*]thiophene.

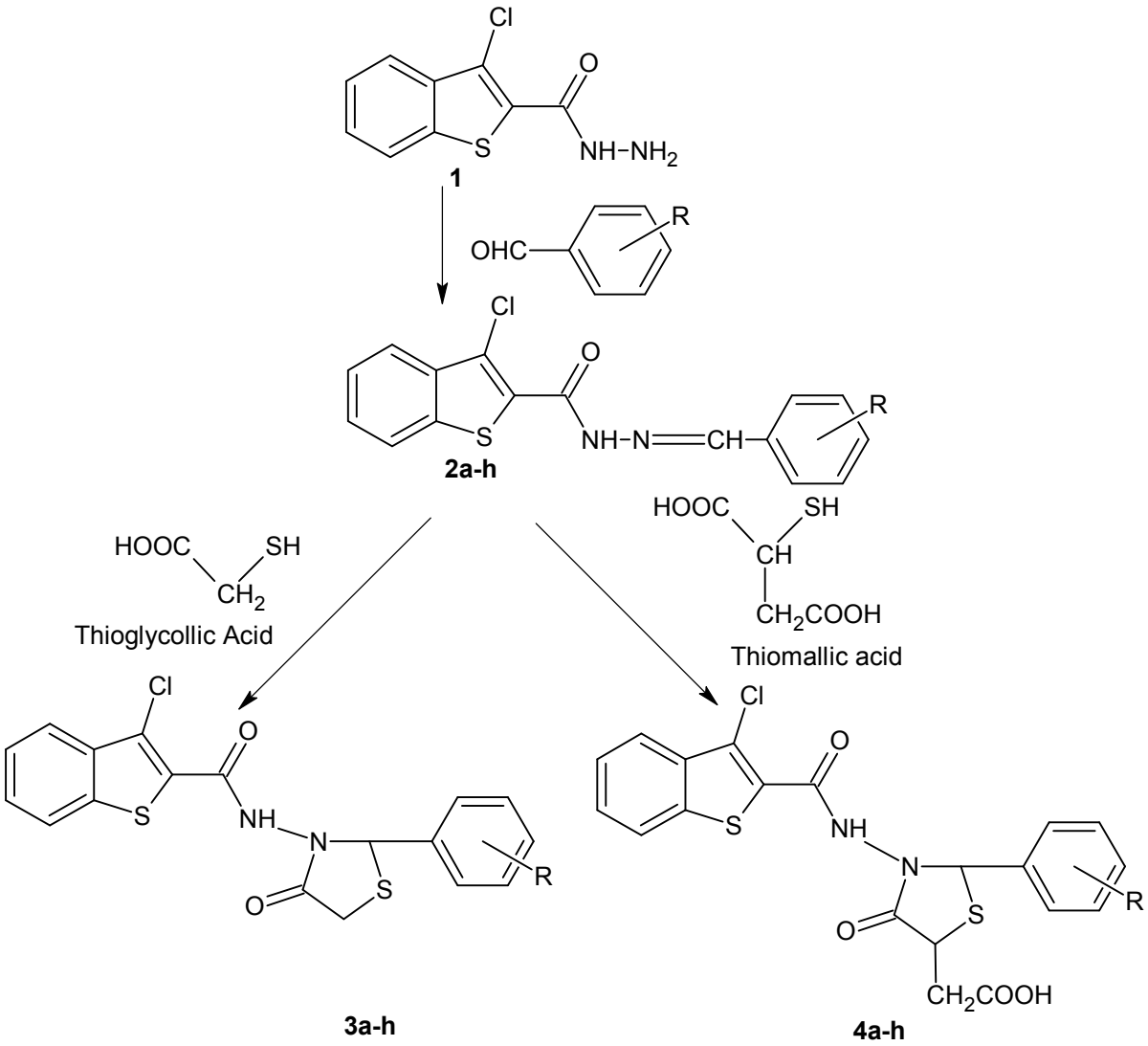
## INTRODUCTION

In recent years, there has been an increasing interest in molecular oxygen derived free radicals such as superoxide ($O_2^*$), hydroxyl ($OH^*$), and peroxyl ($ROO^*$) radicals, and hydrogen peroxide ($H_2O_2$) which are products of normal aerobic metabolic process. Free radicals have been implicated in a variety of human diseases, ranging from atherosclerosis, to cancer, to neurodegenerative disorders[1,2] These molecules are unstable and highly reactive and can

damage cells by chemical chain reactions such as lipid peroxidation. On the other hand, all living organisms contain antioxidant enzymes systems and the major action of antioxidant enzymes systems/antioxidants in the cell is to prevent damage due to free radicals. In addition, reactive oxygen species are produced by different mechanisms such as cytochrome P 450s (CYPs). CYPs are a superfamily of enzymes involved in the oxidation of numerous xenobiotics. For example, CYP1A1/2 transforms polycylic aromatic hydrocarbons to their ultimate mutagenic or carcinogenic metabolites. Moreover, CYP1A1/2, which catalyzes ethoxyresorufin *O*-deethylase (EROD) activity, is effective in producing reactive oxygen species[3].

The treatment of infectious disease still remains an important and challenging problem due to combination of factors including emergence of new infectious diseases and the increasing number of multi-drug resistant microbial pathogens evolved with particular relevance to Gram positive bacteria[4].

It was found that 4-thiazolidinone ring system which is a core structure in various synthetic pharmaceuticals display a broad spectrum of biological activity, including antimicrobial[5-7], antioxidant[8], anticonvulsant[9], diuretic[10], anti-inflammatory[11], anticancer[12], antiHIV[13], antitubercular[14], hypnotic[15] and follicle stimulating hormone receptor agonist[16] activities. In view of the above mentioned findings and as continuation of our effort[17], to identify new candidates that may be value designing new, potent, selective and less toxic antibacterial agents, we report in the present work the synthesis of some new 4-thiazolidinone derivatives bearing benzo[*b*]thiophene nucleus. As part of our ongoing studies in developing new antimicrobials[18], we report the synthesis of new class of structurally novel 4-thiazolidinone derivatives incorporated with two known bioactive nuclei thiazolidin-4-one and benzo[*b*]thiophene.




R: **a**= H, **b**= 4-F, **c**= 3-$OCH_3$, **d**= 2-Cl, **e**= 4-$OCH_3$, **f**= 3-$NO_2$, **g**= 4-Cl, **h**= 3-$OCH_3$, 4-OH

Scheme 1

## MATERIAL AND METHODS

All chemicals were of laboratory grade and obtained from Merck, Mumbai. Melting points were determined on a Veego VMP-1 capillary melting point apparatus in open capillaries and are uncorrected. The purity of the compounds was ascertained by thin layer chromatography on silica gel G in various solvent systems using iodine vapors as detecting agents. IR spectra were recorded on a JASCO FT/IR-410 spectrometer in potassium bromide pellets and are expressed in $cm^{-1}$. $^1H$ NMR spectra was recorded on Brucker 400 MHz spectrophotometers using tetramethylsilane as internal standard. Chemical shifts are expressed in δ (ppm). Mass spectra were recorded on JEOL 5x102/DA-6000.

**Synthesis of 3-chlorobenzo[*b*]thiophene-2-carbonyl chloride (1)**

3-Chloro-benzo[*b*]thiophene-2-carbonyl chloride was prepared from cinnamic acid in the presence of chlorobenzene and thionyl chloride according to reported procedure [19].

**Synthesis of 3-chloro-2-hydrazinocarbonylbenzo[*b*]thiophene (2)**

The carbonyl chloride (2.31 g, 0.01 mol) **(1)** was dissolved in ethanol (50 mL) and to this hydrazine hydrate (85%, 3 mL) was added, and the mixture was heated under reflux for 4 h. The reaction mixture was evaporated under reduced pressure and the crude product was purified by crystallization from ethanol. The purity of the hydrazide was established by single spot on thin layer chromatography (TLC) plates using methanol: carbon tetrachloride (8:2, v/v) as solvent system. Yield 63%, m.p. 179-181$^{O}$C [20].

**Synthesis of 2-(substituted phenyl)-3-(3-chloro-1-benzo[b]thiophene-2-carboxamido)-4-thiazolidinone[21]3a – h**

A mixture of compounds **2a-h** (0.01 mol) and thioglycollic acid (0.92 g, 0.01 mol) in dioxane (15 ml) was refluxed for 24 h. The reaction mixture was triturated with sodium bicarbonate solution (10%). The neutral solid resulted was poured onto crushed ice. The separated product was filtered off, washed with water, dried and crystallized from methanol. The purity of all the compounds was established by single spot on the TLC plates. The solvent system used was methanol : carbontetrachloride (7:3).

**Compound 3a**: IR (KBr, ν cm$^{-1}$): 3165 (NH), 1722 (C=O), 727 (C-S-C); $^{1}$H NMR (DMSO-d$_6$) δ ppm: 3.36, 3.73 (dd, 2H, thiazolidin-4-one C$_5$-H), 6.23 (s, 1H, thiazolidin-4-one C$_2$-H), 7.20-7.84 (m, 9H, Ar-H), 8.86 (s, 1H, NH); mass (%): (MH)$^+$ 390, 315, 210, 211, 178

**Compound 3b**: IR (KBr, ν cm$^{-1}$): 3168 (NH), 1717 (C=O), 729 (C-S-C); $^{1}$H NMR (DMSO-d$_6$) δ ppm: 3.38, 3.68 (dd, 2H, thiazolidin-4-one C$_5$-H), 6.28 (s, 1H, thiazolidin-4-one C$_2$-H), 7.16-7.88 (m, 8H, Ar-H), 8.86 (s, 1H, NH); mass (%): (MH)$^+$ 409, 333, 196, 178

**Compound 3c**: IR (KBr, ν cm$^{-1}$): 3166 (NH), 1718 (C=O), 727 (C-S-C); $^{1}$H NMR (DMSO-d$_6$) δ ppm: 3.35, 3.65 (dd, 2H, thiazolidin-4-one C$_5$-H), 3.78 (s, 3H, Ar-OCH$_3$), 6.38 (s, 1H, thiazolidin-4-one C$_2$-H), 7.20-7.84 (m, 8H, Ar-H), 8.73 (s, 1H, NH); mass (%): (MH)$^+$ 420, 345, 218, 134.

**Compound 3d**: IR (KBr, ν cm$^{-1}$): 3178 (NH), 1721 (C=O), 721 (C-S-C); $^{1}$H NMR (DMSO-d$_6$) δ ppm: 3.38, 3.68 (dd, 2H, thiazolidin-4-one C$_5$-H), 6.28 (s, 1H, thiazolidin-4-one C$_2$-H), 7.12-7.80 (m, 8H, Ar-H), 8.86 (s, 1H, NH); mass (%): (MH+2)$^+$ 425, 349, 212, 78.

**Compound 3e:** IR (KBr, ν $cm^{-1}$): 3158 (NH), 1717 (C=O), 728 (C-S-C); $^1$H NMR (DMSO-$d_6$) δ ppm: 3.38, 3.65 (dd, 2H, thiazolidin-4-one $C_5$-H), 3.74 (s, 3H, Ar-$OCH_3$), 6.38 (s, 1H, thiazolidin-4-one $C_2$-H), 7.11-8.12 (m, 8H, Ar-H), 8.76 (s, 1H, NH); mass (%): $(MH)^+$ 420, 345, 218, 211, 78

**Compound 3f**: IR (KBr, ν $cm^{-1}$): 3165 (NH), 1722 (C=O), 727 (C-S-C); $^1$H NMR (DMSO-$d_6$) δ ppm: 3.36, 3.73 (dd, 2H, thiazolidin-4-one $C_5$-H), 6.23 (s, 1H, thiazolidin-4-one $C_2$-H), 7.10-7.88 (m, 8H, Ar-H), 8.89 (s, 1H, NH); mass (%): $(MH)^+$ 435, 360, 223, 134

**Compound 3g:** IR (KBr, ν $cm^{-1}$): 3168 (NH), 1726 (C=O), 728 (C-S-C); $^1$H NMR (DMSO-$d_6$) δ ppm: 3.38, 3.68 (dd, 2H, thiazolidin-4-one $C_5$-H), 6.28 (s, 1H, thiazolidin-4-one $C_2$-H), 7.20-7.94 (m, 8H, Ar-H), 8.86 (s, 1H, NH); mass (%): $(MH+2)^+$ 425, 349, 212, 78

**Compound 3h:** IR (KBr, ν $cm^{-1}$): 3166 (NH), 1711 (C=O), 717 (C-S-C); $^1$H NMR (DMSO-$d_6$) δ ppm: 3.33, 3.65 (dd, 2H, thiazolidin-4-one $C_5$-H), 3.78 (s, 3H, Ar-$OCH_3$), 6.38 (s, 1H, thiazolidin-4-one $C_2$-H), 7.10-7.84 (m, 7H, Ar-H), 8.74 (s, 1H, NH), 9.30 (s, 1H, NH); mass (%): $(MH)^+$ 436, 362, 225, 134.

**Synthesis of 2-(substituted phenyl)-3-(3-chloro-1-benzo[b]thiophene-2-carboxamido)-5-carboxymethyl-4-thiazolidinone[21]4a – h**

A mixture of compounds **2a-h** (0.01 mol) and thiomallic acid (1.52 g, 0.01 mol) in dioxane (15 ml) was refluxed for 24 h. The reaction mixture was dissolved in sodium bicarbonate solution (10%). The neutral solid resulted was poured onto crushed ice. The separated product was filtered off, washed with water, dried and crystallized from methanol. The purity of all the compounds was established by single spot on the TLC plates. The solvent system used was methanol:carbontetrachloride (7:3).

**Compound 4a:** IR (KBr, ν $cm^{-1}$): 3645 (OH), 3165 (NH), 1711 (C=O), 727 (C-S-C); $^1$H NMR (DMSO-$d_6$) δ ppm: 2.38 (dd, 1H, $CH_A$-COO), 2.62 (dd, 1H, $CH_B$-COO), 4.34 (dd, 1H, thiazolidin-4-one $C_5$-H), 6.51 (s, 1H, thiazolidin-4-one $C_2$-H), 6.68-7.83 (m, 9H, Ar-H), 8.73 (s, 1H, NH), 9.30 (s, 1H, COOH); mass (%): $(MH)^+$ 448, 315, 270, 211

**Compound 4b**: IR (KBr, ν $cm^{-1}$): 3648 (OH), 3168 (NH), 1707 (C=O), 729 (C-S-C); $^1$H NMR (DMSO-$d_6$) δ ppm: 2.42 (dd, 1H, $CH_A$-COO), 2.57 (dd, 1H, $CH_B$-COO), 4.38 (dd, 1H, thiazolidin-4-one $C_5$-H), 6.54 (s, 1H, thiazolidin-4-one $C_2$-H), 6.98-7.85 (m, 8H, Ar-H), 8.73 (s, 1H, NH), 9.40 (s, 1H, COOH); mass (%): $(MH)^+$ 467, 417, 333, 78

**Compound 4c:** IR (KBr, ν $cm^{-1}$): 3625 (OH), 3158 (NH), 1721 (C=O), 721 (C-S-C); $^1$H NMR (DMSO-$d_6$) δ ppm: 2.43 (dd, 1H, $CH_A$-COO), 2.60 (dd, 1H, $CH_B$-COO), 3.75 (s, 3H, Ar-$OCH_3$), 4.32 (dd, 1H, thiazolidin-4-one $C_5$-H), 6.54 (s, 1H, thiazolidin-4-one $C_2$-H), 6.72-7.82 (m, 8H, Ar-H), 8.74 (s, 1H, NH), 9.32 (s, 1H, COOH); mass (%): $(MH)^+$ 478, 343, 211, 78.

**Compound 4d:** IR (KBr, ν $cm^{-1}$): 3612 (OH), 3148 (NH), 1715 (C=O), 724 (C-S-C); $^1$H NMR (DMSO-$d_6$) δ ppm: 2.42 (dd, 1H, $CH_A$-COO), 2.58 (dd, 1H, $CH_B$-COO), 4.38 (dd, 1H, thiazolidin-4-one $C_5$-H), 6.51 (s, 1H, thiazolidin-4-one $C_2$-H), 6.68-7.85 (m, 8H, Ar-H), 8.73 (s, 1H, NH), 9.40 (s, 1H, COOH); mass (%): $(MH+2)^+$ 483, 433, 350, 270, 211.

**Compound 4e**: IR (KBr, ν $cm^{-1}$): 3625 (OH), 3155 (NH), 1717 (C=O), 727 (C-S-C); $^1$H NMR (DMSO-$d_6$) δ ppm: 2.43 (dd, 1H, $CH_A$-COO), 2.60 (dd, 1H, $CH_B$-COO), 3.75 (s, 3H, Ar-$OCH_3$), 4.32 (dd, 1H, thiazolidin-4-one $C_5$-H), 6.58 (s, 1H, thiazolidin-4-one $C_2$-H), 6.72-7.83 (m, 8H, Ar-H), 8.73 (s, 1H, NH), 9.36 (s, 1H, COOH); mass (%): $(MH)^+$ 478, 343, 211, 78.

**Compound 4f:** IR (KBr, ν $cm^{-1}$): 3628 (OH), 3165 (NH), 1711 (C=O), 727 (C-S-C); $^1$H NMR (DMSO-$d_6$) δ ppm: 2.43 (dd, 1H, $CH_A$-COO), 2.57 (dd, 1H, $CH_B$-COO), 4.42 (dd, 1H, thiazolidin-4-one $C_5$-H), 6.51 (s, 1H, thiazolidin-4-one $C_2$-H), 6.68-7.80 (m, 8H, Ar-H), 8.71 (s, 1H, NH), 9.30 (s, 1H, COOH); mass (%): $(MH)^+$ 493, 444, 360, 211, 78.

**Compound 4g**: IR (KBr, ν $cm^{-1}$): 3632 (OH), 3168 (NH), 1721 (C=O), 728 (C-S-C); $^1$H NMR (DMSO-$d_6$) δ ppm: 2.42 (dd, 1H, $CH_A$-COO), 2.58 (dd, 1H, $CH_B$-COO), 4.38 (dd, 1H, thiazolidin-4-one $C_5$-H), 6.51 (s, 1H, thiazolidin-4-one $C_2$-H), 6.98-7.85 (m, 8H, Ar-H), 8.73 (s, 1H, NH), 9.38 (s, 1H, COOH); mass (%): $(MH+2)^+$ 483, 433, 350, 270, 211.

**Compound 4h**: IR (KBr, ν $cm^{-1}$): 3645 (OH), 3162 (NH), 1717 (C=O), 729 (C-S-C); $^1$H NMR (DMSO-$d_6$) δ ppm: 2.43 (dd, 1H, $CH_A$-COO), 2.62 (dd, 1H, $CH_B$-COO), 3.78 (s, 3H, Ar-$OCH_3$), 4.32 (dd, 1H, thiazolidin-4-one $C_5$-H), 6.54 (s, 1H, thiazolidin-4-one $C_2$-H), 6.68-7.48 (m, 7H, Ar-H), 8.76 (s, 1H, NH), 9.10 (s, 1H, Ar-OH), 9.40 (s, 1H, COOH); mass (%): $(MH)^+$ 494, 445, 361, 270, 211.

**Biological activity**

**Evaluation of *in vitro* antibacterial activity**

The newly synthesized compounds **3a-h** and 4**a-h** were screened for their antibacterial activity against *Staphylococcus aureus* (NCIM 5021) and *Bacillus subtilis* (NCIM 2010) by disc diffusion method[22-23]. A standard inoculums (1-2 x $10^7$ c.f.u./ml 0.5 McFarland standards) was introduced on to the surface of sterile agar plates, and a sterile cotton swab was used for even

distribution of the inoculum. The discs measuring 6.25 mm in diameter were prepared from Whatman no. 1 filter paper and sterilized by dry heat at 140°C for 1 h. The sterile discs previously soaked in a known concentration of the test compounds were placed in nutrient agar medium. Solvent and growth controls were kept. The plates were inverted and incubated for 24 h at 37 °C. Ciprofloxacin was used as a standard drug. Inhibition zones were measured and compared with the controls. The bacterial zones of inhibition values are given in Table 1.

**Evaluation of *in vitro* antioxidant activity using DPPH assay method [24]**

1.5 ml methanolic solution of the synthesized compounds (0.2 mM) was added to 1.5 ml (0.2mM) solution of DPPH radical in methanol (final concentration of DPPH and synthesized compounds was 0.1mM). The mixture was shaken vigorously and allowed to stand for 30 min. After this, the absorbance at 517 nm was determined and the percentage of scavenging activity was calculated using the formula shown below. Ascorbic acid was used as the reference compound. All tests and analyses were undertaken on three replicates and the results were averaged. The results are given in Table 1.

Scavenging activity (%) = {[(Ab+As) - Am]/Ab} x100%;

Ab: absorbance of 0.1mM methanolic solution of DPPH at 517nm.

As: absorbance of 0.1 mM methanolic solution of test compound at 517nm.

Am: absorbance of methanolic mixture of the drug and DPPH at 517nm.

**RESULTS AND DISCUSSION**

In this study sixteen new compounds incorporated with scaffold 4-thiazolidinone has been synthesized and their antibacterial and antioxidant activities were evaluated. At the first stage 3-chloro-1-benzo[b]thiophene-2-carbohydrazide **1** was prepared by the standard method available in the literature. Imine formation of 3-chloro-1-benzo[b]thiophene-2-carbohydrazide and aromatic aldehydes was prepared. Imine compounds **2a-h** were reacted with thioglycollic acid and thiomalic acid to give 2-(substitutedphenyl)-3-(3-chloro-1-benzo[b]thiophene-2-carboxamido)-4-thiazolidino-nes and 2-(substituted phenyl)-3-(3-chloro-1-benzo[b]thiophene-2-carboxamido)-5-carboxymethyl-4-thiazolidinones derivatives, respectively.

The results of antibacterial screening showed compounds **3c, 3e, 4a, 4b, 4f, 4g** and **4h** to be moderately active and **3d, 4c, 4d** and **4e** to be significantly active against *Staphylococcus aureus* at 250 mcg/disc. Compounds **3c** and **3e** were found to be moderately active and **3d** and **4(a-h)** to be significantly active against Bacillus *subtilis* at 250 mcg/disc concentration. Rest of the compounds did not show antibacterial activity.

Among the compounds from the thiazolidin-4-one series: **3d** and **3h** showed good antioxidant activity. Among the compounds from the carboxymethyl-4-thiazolidinone series, **4h** exhibited good antioxidant activity. The activity exhibited by the compound **3d** was the highest. The structures of the compounds were confirmed by spectral methods (IR, $^1$H NMR, MS and elemental analysis). In the IR spectra, bands in the 3308-3133 cm$^{-1}$ and 1722-1684 cm$^{-1}$ region accounts for N-H and C=O stretching of the compounds **3a-h** and **4a-h**. In the $^1$H NMR spectra of compounds **3a-h** and **4a-h**, lack of the CH=N signal at 7.78-8.83 ppm, provided confirmatory evidence for ring closure from Imine compounds **2a-h**. $C_5$-H signals of **3a-h** were observed at δ 3.33-3.38 ppm and δ 3.65-3.73 ppm as double doublets due to chiral center at $C_2$. Similarly compounds **4a-h** exhibited $C_5$-$CH_2COOH$ as two doublets in the δ 2.38-2.62 ppm and $C_5$-H as double doublets in the δ 4.32-4.42 ppm region. MS of all compounds displayed the molecular ion which confirmed their molecular weights. Molecular ions are base peak for most of the compounds. The characterization data of 4-thiazolidinones and 5-carboxymethyl-4-thiazolidinones **3a-h** and **4a-h** are given in Table-2.

**Table 1: [a]Zone of inhibition (mm) and scavenging activity (%) of compounds 3a-h and 4a-h**

| Comp. | *Staphylococcus aureus* | *Bacillus subtilis* | Scavenging activity (%) |
|---|---|---|---|
| **3a** | - | - | 32 |
| **3b** | - | - | 13 |
| **3c** | 14.3±0.3 | 16.0±0.5 | 16 |
| **3d** | 18.3±0.3 | 20.3±0.3 | 95 |
| **3e** | 12.6±0.3 | 16.6±0.8 | 26 |
| **3f** | - | - | 20 |
| **3g** | - | - | 30 |
| **3h** | - | - | 90 |
| **4a** | 13.0±0.5 | 19.3±0.3 | 13 |
| **4b** | 14.3±0.3 | 17.3±0.3 | 17 |
| **4c** | 17.0±0.5 | 21.0±0.6 | 21 |
| **4d** | 18.6±0.8 | 21.6±0.3 | 14 |
| **4e** | 18.0±1.1 | 16.3±0.3 | 18 |
| **4f** | 13.6±0.8 | 17.3±0.3 | 15 |
| **4g** | 15.3±0.3 | 21.0±0.6 | 49 |
| **4h** | 12.6±0.6 | 18.3±0.3 | 91 |
| **[b]Std** | 30.0±1.7 | 33.7±1.2 | - |
| **[c]Std** | - | - | 96 |

[a]Data are means of three different experiments; [b]Ciprofloxacin is used as standard; [c]Ascorbic acid is used as standard; - Indicated compounds are inactive

**Table 2: Characterization data of compounds 3a-h and 4a-h**

| Comp. | R | Mol. formula | M.p[° C] | Yield[%] | Analysis(%)found(calc.) | | |
|---|---|---|---|---|---|---|---|
| | | | | | C | H | N |
| **3a** | H | $C_{18}H_{13}ClN_2O_2S_2$ | 180-182 | 56 | 55.28(55.39) | 3.41(3.37) | 7.21(7.20) |
| **3b** | 4-F | $C_{18}H_{12}ClFN_2O_2S_2$ | 198-200 | 66 | 53.15(53.13) | 2.92(2.97) | 6.84(6.88) |
| **3c** | 3-$OCH_3$ | $C_{19}H_{15}ClN_2O_3S_2$ | 161-163 | 60 | 54.44(54.47) | 3.58(3.61) | 6.71(6.69) |
| **3d** | 2-Cl | $C_{18}H_{12}Cl_2N_2O_2S_2$ | 203-205 | 62 | 51.12(51.07) | 2.81(2.86) | 6.59(6.62) |
| **3e** | 4-$OCH_3$ | $C_{19}H_{15}ClN_2O_3S_2$ | 193-195 | 58 | 54.46(54.47) | 3.56(3.61) | 6.73(6.69) |
| **3f** | 3-$NO_2$ | $C_{18}H_{12}ClN_3O_4S_2$ | 231-233 | 65 | 49.79(49.83) | 2.71(2.79) | 9.65(9.68) |
| **3g** | 4-Cl | $C_{18}H_{12}Cl_2N_2O_2S_2$ | 208-210 | 55 | 51.11(51.07) | 2.92(2.86) | 6.61(6.62) |
| **3h** | 3-$OCH_3$, 4-OH | $C_{19}H_{15}ClN_2O_4S_2$ | 198-200 | 62 | 52.41(52.47) | 3.52(3.48) | 6.42(6.44) |
| **4a** | H | $C_{20}H_{15}ClN_2O_4S_2$ | 166-168 | 58 | 53.78(53.75) | 3.41(3.38) | 6.29(6.27) |
| **4b** | 4-F | $C_{20}H_{14}ClFN_2O_4S_2$ | 176-178 | 65 | 51.71(51.67) | 3.08(3.04) | 6.08(6.03) |
| **4c** | 3-$OCH_3$ | $C_{21}H_{17}ClN_2O_5S_2$ | 151-153 | 55 | 52.84(52.88) | 3.57(3.59) | 5.91(5.87) |
| **4d** | 2-Cl | $C_{20}H_{14}Cl_2N_2O_4S_2$ | 197-199 | 54 | 49.86(49.90) | 2.91(2.93) | 5.78(5.82) |
| **4e** | 4-$OCH_3$ | $C_{21}H_{17}ClN_2O_5S_2$ | 181-183 | 61 | 52.84(52.88) | 3.54(3.59) | 5.92(5.87) |
| **4f** | 3-$NO_2$ | $C_{20}H_{14}ClN_3O_6S_2$ | 214-216 | 68 | 48.76(48.83) | 2.91(2.87) | 8.58(8.54) |
| **4g** | 4-Cl | $C_{20}H_{14}Cl_2N_2O_4S_2$ | 186-188 | 63 | 49.88(49.90) | 2.89(2.93) | 5.81(5.82) |
| **4h** | 3-$OCH_3$, 4-OH | $C_{21}H_{17}ClN_2O_6S_2$ | 171-173 | 65 | 51.21(51.17) | 3.46(3.48) | 5.66(5.68) |

## CONCLUSION

The present work comprises the synthesis of eight 4-thiazolidinone with substituent substituted phenyl ring at $C_2$ of 4-thiazolidinone and eight 5-carboxymethyl-4-thiazolidinone with substitution of substituted phenyl ring at $C_2$ of thiazolidin-4-one. Among **3a-h** thiazolindin-4-ones compound with 2-chloro substituent in the phenyl ring exhibited highest antibacterial activity. From **4a-h** 5-carboxymethyl-4-thiazolidin4ones compound with 2-chloro substituent in the phenyl ring exhibited highest antibacterial activity against *Bacillus subtilis* and *Staphylococcus aureus*.

The outstanding activity of this new class of antibacterial compounds substances deserve further investigation in order find out their mode of action at molecular level, responsible for the activity observed. More extensive study is also warranted to determine additional physicochemical and biological parameters to have a deeper insight into structure-activity relationship and to optimize the effectiveness of this series of molecules. Among, the compounds **3c, 3d, 3e** and **4a-h** showed antibacterial activity indicating that the diverse substitutions were well tolerated on the benzylidene moiety for proper fit at the potential receptor site.

Compound with 2-chloro **3d** and 3-methoxy-4-hydroxy **3h** substituent in the phenyl ring exhibited highest antioxidant activity from **3a-h.** 4-thiazolidinone series and 5-carboxymethyl-4-thiazolidinone bearing 3-methoxy-4-hydroxy **4h** phenyl substitution exhibited enhanced antioxidant activity from the respective series.

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