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Synthesis and biological evaluation of 4-thiazolidinone derivatives incorporating benzothiazole moiety

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ABSTRACT

Some 2-aryl-3-(6-substitutedbenzothiazolyl)-1,3-thiazolidine-4-ones have been synthesized by the reaction of substituted-2-aminobenzothiazole with aromatic aldehyde (benzaldehyde, p-chlorobenzaldehyde, anisaldehyde, salicylaldehyde) followed by condensation with mercapto acetic acid. All the synthesized compounds were characterized by elemental analysis, IR spectra, ^{1}H-NMR and Mass spectral studies. These were screened for their entomological (Antifeedant activity, Acaricidal activity, Contact toxicity, Stomach toxicity) and antibacterial activities.

Keywords: Benzothiazole, Thiazolidinone, Entomological and Antibacterial activities.

INTRODUCTION

Nitrogen- and sulfur-containing heterocycles play an important role, not only for life science, but also in many other industrial fields related to special and fine chemistry. The survey of literature related to benzothiazole and thiazolidinone derivatives show that compounds with these nuclei have vast medicinal importance in the field of pharmaceutical chemistry. Benzothiazole derivatives possess a wide spectrum of biological activities such as antimicrobial [1], anti-inflammatory [2], antitubercular [3,4], anticancer [5], fungicidal [6], anti-histamines [7], schistosomicidal [8] etc. 2-(4-Aminophenyl) benzothiazole derivatives were extensively studied for their anticancer action [9].

The chemistry of thiazolidin-4-one ring systems is of considerable interest as it is a core structure in various synthetic pharmaceuticals displaying a broad spectrum of biological activities [10]. Thiazolidin-4-one a saturated form of thiazole with carbonyl group on fourth carbon, has been considered as a magic moiety (wonder nucleus) which posses almost all types of biological activities such as anti-HIV agent [11,13], antidiarrhoeal [14], anticonvulsant [15], antidiabetic [16], antihistaminic [17], anticancer [18], Ca^{2+} channel blocker [19] PAF antagonist [20], cardioprotective [21], anti-ischemic [22], cycloxygenase inhibitory [23], analgesic [24], antimicrobial [25,26], antidiabetic [27], antitubercular [28], antioxidant [29], hypo-glycemic [30], Inhibition of gastric H^+K^+-ATPase [31], CFTR inhibitor [32], anti-platelet activating factor [33], non-peptide thrombin receptor antagonist [34] and tumor necrosis factor-α antagonist activities [35] Also 2-imino-thiazolidin-4-ones have been found to have antifungal activity [36-38].

Looking at the importance of these heterocyclic nuclei, it is thought of interest to accommodate thiazolidin-4-one and 2-aminobenzothiazole moieties in single molecular framework and screen them for their various biological activities. In continuation to our research work on benzothiazole derivatives [39] we are reporting the synthesis and entomological and antibacterial activities of substitutes-3-(benzothiazolyl)-1,3-thiazolidine-4-ones. 2-Amino-6-substitutedbenzothiazoles on reaction with substituted aromatic aldehydes give 2-(arylidenimino)-6-substitutedbenzothiazoles (**1**), which on reaction with mercapto acetic acid gives 2-aryl-3-(6-substituted benzothiazolyl)-1,3-thiazolidine-4-ones (**2**) (Scheme-1). The structures of all the synthesized compounds were established on the basis of spectroscopic and analytical data.

MATERIALS AND METHODS

General Procedures

Reagent grade chemicals were used without further purification. The substrates and solvents were used as received. All the melting points are taken in open capillaries and uncorrected. The purity of the compounds was checked by thin layer chromatography (TLC). Infrared (IR) spectra were obtained on a Fourier transform infrared (FTIR) Perkin Elmer (Spectrum RX1) spectrophotometer (u in cm^{-1}) using KBr discs. ^{1}H-nuclear magnetic resonance (NMR) data were recorded in $CDCl_3$ with tetramethylsilane (TMS) as the internal standard at 300 MHz on a Bruker DRTX-300 spectrophotometer. The chemical shifts are reported in part per million. Fast atom bombardment mass spectra (FABMS) were recorded at room temperature on a Jeol SX-102/DA-6000 mass spectrophotometer/data system using Argon/Xenon (6 kV, 10 mA) as the FAB gas. The accelerating potential was 10 kV. The elemental analysis of compounds was performed on Elementar Vario EL III Carlo Erba-1108 elemental analyzer.

General procedure for synthesis of 2-(Arylidenimino)-6-substituted benzothiazoles 1(a-j)

A mixture of 2-amino-6-substituted benzothiazole (0.01 mole) and aromatic aldehyde (benzaldehyde, p-chlorobenzaldehyde, anisaldehyde, salicylaldehyde) (0.01 mole) was refluxed in absolute ethanol (40 mL) for 3 hrs. The excess solvent was then distilled off and the resulting solid washed with water, dried and recrystallized from ethanol **1 (a-j)**.

Spectral and microanalysis data for compounds 1(a-j)

2-(Benzylidenoimino)-6-methoxybenzothiazole (1a)

Yield: 68 %. m.p. 140-142 ^{0}C. IR (KBr, cm^{-1}): 3015 (Ar-H), 2970 (aliphatic CH), 1618 (C=N), 1569 (Ar-C=C), 1057 (C-O-C). ^{1}H-NMR ($CDCl_3$ δ, ppm): 7.04-7.42 (m, 8H, Ar-H); 5.75 (s, 1H, N=CH); 3.73 (s, 3H, Ar-OCH_3). MS: 268 (M+). Anal. Calcd. For $C_{15}H_{12}N_2OS$: C- 67.14; H, 4.51; N- 10.44; S-11.95%. Found: C- 67.11; H- 4.49; N- 10.42; S- 11.93%.

2-(2'-Hydroxybenzylidenoimino)-6-methoxybenzothiazole (1b)

Yield: 65%. m.p. 130-132 ^{0}C. IR (KBr, cm^{-1}): 3410 (OH), 3023 (Ar-H), 2975 (aliphatic CH), 1607 (C=N), 1573 (Ar-C=C), 1056 (C-O-C). ^{1}H-NMR ($CDCl_3$ δ, ppm): 9.8 (s, 1H, Ar-OH); 7.10-7.51 (m, 7H, Ar-H); 6.01 (s, 1H, N=CH); 3.75 (s, 3H, Ar-OCH_3). MS: 284 (M+). Anal. Calcd. For $C_{15}H_{12}N_2O_2S$: C- 63.36; H- 4.25; N- 9.85; S- 11.28%. Found: C- 63.32; H- 4.22; N- 9.83; S-11.25%.

2-(4'-Methoxybenzylidenoimino)-6-methoxybenzothiazole (1c)

Yield: 62%. m.p. 124-127 ^{0}C. IR (KBr, cm^{-1}): 3030 (Ar-H), 2970 (aliphatic CH), 1630 (C=N), 1584 (Ar-C=C), 1049 (C-O-C). ^{1}H-NMR ($CDCl_3$ δ, ppm): 7.12-7.80 (m, 7H, Ar-H); 6.03 (s, 1H, N=CH); 3.79 (s, 3H, Ar-OCH_3). MS: 298 (M+). Anal. Calcd. For $C_{16}H_{14}N_2O_2S$: C- 64.41; H- 4.73; N- 9.39; S- 10.75%. Found: C- 64.38; H- 4.71; N- 9.37; S- 10.72%.

2-(4'-Chlorobenzylidenoimino)-6-methoxybenzothiazole (1d)

Yield: 65%. m.p. 130-132 ^{0}C. IR (KBr, cm^{-1}): 3035 (Ar-H), 2975 (aliphatic CH), 1633 (C=N), 1595 (Ar-C=C), 1039 (C-O-C), 815 (C-Cl). ^{1}H-NMR ($CDCl_3$ δ, ppm): 7.01-7.35 (m, 7H, Ar-H); 6.06 (s, 1H, N=CH); 3.76 (s, 3H, Ar-OCH_3). MS: 303 (M+). Anal. Calcd. For $C_{15}H_{11}N_2OSCl$: C- 59.50; H- 3.66; N- 9.25; S- 10.59%. Found: C- 59.47; H-3.64; N- 9.22; S- 10.57%.

2-(Benzylidenoimino)-6-flourobenzothiazole (1e)

Yield: 66%. m.p. 148-150 ^{0}C. IR (KBr, cm^{-1}): 3095 (Ar-H), 2975 (aliphatic CH), 1635 (C=N), 1562 (Ar-C=C), 1005 (C-F), 811 (C-Cl). ^{1}H-NMR ($CDCl_3$ δ, ppm): 7.11-7.52 (m, 8H, Ar-H); 4.90 (s, 1H, N=CH). MS: 256 (M+). Anal. Calcd. For $C_{14}H_9N_2SF$: C- 65.61; H- 3.54; N- 10.93; S- 12.51%. Found: C- 65.59; H- 3.52; N- 10.90; S- 12.48%.

2-(2'-Hydroxybenzylidenoimino)-6-flourobenzothiazole (1f)

Yield: 60%. m.p. 141-145 ^{0}C. IR (KBr, cm^{-1}): 3415 (OH), 3080 (Ar-H), 2965 (aliphatic CH), 1615 (C=N), 1580 (Ar-C=C), 1005 (C-F), 810 (C-Cl). ^{1}H-NMR ($CDCl_3$ δ, ppm): 9.54 (s, 1H, Ar-OH); 7.01-7.32 (m, 7H, Ar-H); 4.92 (s, 1H, N=CH). MS: 272 (M+). Anal. Calcd. For $C_{14}H_9N_2OSF$: C- 61.75; H- 3.33; N- 10.24; S- 11.78%. Found: C- 61.72; H- 3.30; N- 10.20; S- 11.75%.

2-(4'-Methoxybenzylidenoimino)-6-flourobenzothiazole (1g)

Yield: 62%. m.p. 118-123 ^{0}C. IR (KBr, cm^{-1}): 3088 (Ar-H), 2977 (aliphatic CH), 1612 (C=N), 1585 (Ar-C=C), 1046 (C-O-C), 1008 (C-F), 815 (C-Cl). ^{1}H-NMR ($CDCl_3$ δ, ppm): 7.14-7.51 (m, 7H, Ar-H); 4.98 (s, 1H, N=CH); 3.45 (s, 3H, Ar-OCH_3). MS: 286 (M+). Anal. Calcd. For $C_{15}H_{11}N_2OSF$: C- 62.92; H- 3.87, N- 10.78; S- 11.28%. Found: C- 62.90; H- 3.85; N- 10.7; S- 11.25%.

2-(4'-Chlorobenzylidenoimino)-6-flourobenzothiazole (1h)
Yield: 60%. m.p. 142-145 ^{0}C. IR (Ker, cm^{-1}): 3090 (Ar-H), 2980 (aliphatic CH), 1610 (C=N), 1585 (Ar-C=C), 1005 (C-F), 812 (C-Cl). ^{1}H-NMR ($CDCl_3$ δ, pap): 7.09-7.35 (m, 7H, Ar-H); 4.85 (s, 1H, N=CH). MS: 290 (M+). Anal. Calcd. For $C_{14}H_8N_2SFCl$: C- 57.83; H- 2.77; N- 9.64; S- 11.30%. Found: C- 57.80; H- 2.75; N- 9.61; S- 11.29%.

2-(4'-Methoxybenzylidenoimino)-6-carboxylicbenzothiazole (1i)
2-{[(*Z*)-(4-methoxyphenyl)methylidene]amino}-1,3-benzothiazole-6-carboxylic acid
Yield: 55%. m.p. 245-247 ^{0}C. IR (KBr, cm^{-1}): 3090 (Ar-H), 2980 (aliphatic CH), 1610 (C=N), 1595 (Ar-C=C), 1045 (C-O-C). ^{1}H-NMR ($CDCl_3$ δ, ppm): 10.98 (s, 1H, COOH); 7.09-7.35 (m, 8H, Ar-H); 4.85 (s, 1H, N=CH). MS: 312 (M+). Anal. Calcd. For $C_{16}H_{12}N_2O_3S$: C- 61.53; H- 3.8; N- 8.97; S- 10.27%. Found: C- 61.50; H-3.84; N- 8.95; S- 10.25%.

2-(4'-Chlorobenzylidenoimino)-6-carboxylicbenzothiazole (1j)
2-{[(*Z*)-(4-chlorophenyl)methylidene]amino}-1,3-benzothiazole-6-carboxylic acid
Yield: 60%. m.p. 260-263 ^{0}C. IR (KBr, cm^{-1}): 3095 (Ar-H), 2975 (aliphatic CH), 1610 (C=N), 1598(Ar-C=C), 812 (C-Cl). ^{1}H-NMR ($CDCl_3$ δ, ppm): 11.01 (s, 1H, COOH); 7.09-7.35 (m, 8H, Ar-H); 4.85 (s, 1H, N=CH). MS: 317 (M+). Anal. Calcd. For $C_{15}H_9N_2O_2SCl$: C- 56.88; H- 2.86; N- 8.84; S- 10.12%. Found: C- 56.84; H- 2.84; N- 8.82; S- 10.10%.

Preparation of 2-aryl 3-(6-substituted benzothiazolyl)-1,3-thiazolidine- 4-ones 2(a-j)
A mixture of **1(a-j)** (0.01 mole) and mercapto aceticacid (0.012 mole) in DMF (25 mL) containing a pinch of anhydrous $ZnCl_2$ was refluxed for 8 hrs. The reaction mixture was then cooled and poured into ice-cold water. The resulting solid was filtered, washed several times with water and then crystallized from DMF to give **2(a-j)** Scheme-1.

Spectral and microanalysis data for compounds 2(a-j)
3-(6-Methoxy-1,3-benzothiazol-2-yl)-2-phenyl-1,3-thiazolidin-4-one (2a)
Yield: 55%. m.p. 195-198 ^{0}C. IR (KBr, cm^{-1}): 3076 (Ar-CH), 2970 (N-CH-S), 2930 (CH_2-S), 1698 (cyclic C=O), 1576 (Ar-C=C), 1055 (C-O-C), 710 (C-S-C). ^{1}H-NMR ($CDCl_3$ δ, ppm): 7.01-7.38 (m, 8H, Ar-H); 3.45 (s, 2H, S-CH_2); 3.24 (s, 1H, N-CH-Ar); 3.75 (s, 3H, Ar-OCH_3). MS: 342 (M+). Anal. Calcd. For $C_{17}H_{14}N_2S_2O_2$: C- 59.63; H- 4.12; N-8.18; S- 18.73%. Found: C- 59.60; H- 4.10; N- 8.16; S,- 18.71%.

3-(6-Methoxy-1,3-benzothiazol-2-yl)-2-(2-hydroxyphenyl)-1,3-thiazolidin-4-one (2b)
Yield: 50%. m.p. 129-132^{0}C. IR (KBr, cm^{-1}): 3400 (OH), 3070 (Ar-CH), 2965 (N-CH-S), 2922 (CH_2-S), 1700 (cyclic C=O), 1585 (Ar-C=C), 1052 (C-O-C), 720 (C-S-C). ^{1}H-NMR ($CDCl_3$ δ, ppm): 9.8 (s, 1H, Ar-OH); 7.01-7.33 (m, 7H, Ar-H); 3.42 (s, 2H, S-CH_2); 3.19 (s, 1H, N-CH-Ar); 3.77 (s, 3H, Ar-OCH_3). MS: 358 (M+). Anal. Calcd. For $C_{17}H_{14}N_2O_3S_2$: C- 56.96; H- 3.94; N- 7.82; S- 17.89%. Found: C-56.92; H- 3.91; N- 7.80; S- 17.87%.

3-(6-Methoxy-1,3-benzothiazol-2-yl)-2-(4-methoxyphenyl)-1,3-thiazolidin-4-one (2c)
Yield: 52%. m.p. 142-145^{0}C. IR (KBr, cm^{-1}): 3068 (Ar-CH), 2933 (N-CH-S), 2922 (CH_2-S), 1705 (cyclic C=O), 1605 (Ar-C=C), 1059 (C-O-C), 695 (C-S-C). ^{1}H-NMR ($CDCl_3$ δ, ppm): 7.11-7.43 (m, 7H, Ar-H); 3.80 (s, 3H, Ar-OCH_3); 3.42(s, 2H, S-CH_2); 3.21 (s, 1H, N-CH-Ar).

MS: 372 (M+). Anal. Calcd. For $C_{18}H_{16}N_2O_3S_2$: C- 58.04; H- 4.33; N- 7.52; S-17.22%. Found: C- 58.00; H- 4.31; N- 7.50; S- 17.19%.

3-(6-Methoxy-1,3-benzothiazol-2-yl)-2-(4-chloroyphenyl)-1,3-thiazolidin-4-one (2d)
Yield: 54%. m.p. 139-142 ^{0}C. IR (KBr, cm^{-1}): 3090 (Ar-CH), 2965 (N-CH-S), 2920 (CH_2-S), 1712 (cyclic C=O), 1625 (Ar-C=C), 1041 (C-O-C), 819 (C-Cl), 725 (C-S-C). ^{1}H-NMR ($CDCl_3$ δ, ppm): 7.11-7.47 (m, 7H, Ar-H); 3.45 (s, 2H, S- CH_2); 3.20 (s, 1H, N-CH-Ar); 3.76 (s, 3H, Ar-OCH_3). MS: 377 (M+). Anal. Calcd. For $C_{17}H_{13}N_2S_2O_2Cl$: C- 54.18; H-3.48; N- 7.43; S-17.02%. Found: C- 54.14; H- 3.45; N- 7.41; S- 17.00%.

3-(6-Flouro-1,3-benzothiazol-2-yl) -2-phenyl-1,3-thiazolidin-4-one (2e)
Yield: 55%. m.p. 180-183^{0}C. IR (KBr, cm^{-1}): 3081 (Ar-CH), 2980 (N-CH-S), 2962 (CH_2-S), 1719 (cyclic C=O), 1598 (Ar-C=C), 1008 (C-F), 810 (C-Cl), 730 (C-S-C). ^{1}H-NMR ($CDCl_3$ δ, ppm): 7.25- 7.52 (m, 8H, Ar-H); 3.57 (s, 2H, S-CH_2); 3.23 (s, 1H, N-CH-Ar). MS: 330 (M+). Anal. Calcd. For $C_{16}H_{11}N_2OS_2F$: C- 58.16; H- 3.36; N- 8.48; S- 19.41%. Found: C- 58.12; H- 3.33; N- 8.46; S- 19.40%.

3-(6-Flouro-1,3-benzothiazol-2-yl)-2-(2-hydroxyphenyl)-1,3-thiazolidin-4-one (2f)
Yield: 53%. m.p. 165-168 ^{0}C. IR (KBr, cm^{-1}): 3410 (OH), 3090 (Ar-CH), 2972 (N-CH-S), 2955 (CH_2-S), 1715 (cyclic C=O), 1630 (Ar C=C), 1005 (C-F), 811 (C-Cl), 720 (C-S-C). ^{1}H-NMR ($CDCl_3$ δ, ppm): 9.50 (s, 1H, OH); 7.01-7.43 (m, 7H, Ar-H); 3.54 (s, 2H, S- CH_2); 3.20 (s, 1H, N-CH-Ar). MS: 346 (M+). Anal. Calcd. For $C_{16}H_{11}N_2O_2S_2F$: C- 55.48; H- 3.20; N- 8.09; S-18.51%. Found: C- 55.45; H- 3.17; N- 8.07; S-18.50%.

3-(6-Flouro-1,3-benzothiazol-2-yl)-2-(4-methoxyphenyl)-1,3-thiazolidin-4-one (2g)
Yield: 50%. m.p. 140-142 ^{0}C. IR (KBr, cm^{-1}): 3084 (Ar-CH), 2975 (N-CH-S), 2960 (CH_2-S), 1712 (cyclic C=O), 1610 (Ar C=C), 1025 (C-O-C), 1005 (C-F), 730 (C-S-C), 810 (C-Cl). ^{1}H-NMR ($CDCl_3$ δ, ppm): 6.99- 7.29 (m, 7H, Ar-H); 3.45(s, 2H, S-CH_2); 3.52 (s, 3H, Ar-OCH_3); 3.21 (s, 1H, N-CH-Ar). MS: 360 (M+). Anal. Calcd. For $C_{17}H_{13}N_2O_2S_2F$: C- 56.55; H- 3.64; N-7.77; S- 17.79%. Found: C- 56.51; H- 3.62; N- 7.74; S- 17.76%.

3-(6-Flouro-1,3-benzothiazol-2-yl)-2-(4-chloroyphenyl)-1,3-thiazolidin-4-one (2h)
Yield: 52%. m.p. 152-155 ^{0}C. IR (KBr, cm^{-1}): 3080 (Ar-CH), 2974 (N-CH-S), 2962 (CH_2-S), 1715 (cyclic C=O), 1600 (Ar-C=C), 1002 (C-F) 815 (C-Cl), 740 (C-S-C). ^{1}H-NMR ($CDCl_3$ δ, ppm): 7.15- 7.37 (m, 7H, Ar-H); 3.50 (s, 2H, S-CH_2); 3.23 (s, 1H, N-CH-Ar). MS: 365 (M+). Anal. Calcd. For $C_{16}H_{10}N_2OS_2FCl$: C- 52.67; H- 2.76; N- 7.68; S- 17.58%. Found: C- 52.64; H- 2.73; N- 7.65; S- 17.56%.

3-(6-Carboxylic-1,3-benzothiazol-2-yl)-2-(4-methoxyphenyl)-1,3-thiazolidin-4-one (2i)
(2-[2-(4-methoxyphenyl)-4-oxo-1,3-thiazolidin-3-yl]-1,3-benzothiazole-6-carboxylic acid)
Yield: 48%. m.p. 255-258^{0}C. IR (KBr, cm^{-1}): 3080 (Ar-CH), 2974 (N-CH-S), 2960 (CH_2-S), 1705 (cyclic C=O), 1580 (Ar-C=C), 690 (C-S-C). ^{1}H-NMR ($CDCl_3$ δ, ppm): 11.01 (s, 1H, COOH); 7.15- 7.37 (m, 7H, Ar-H); 3.50 (s, 2H, S-CH_2); 3.23 (s, 1H, N-CH-Ar); 3.57 (s, 3H, Ar-OCH_3). MS: 386 (M+). Anal. Calcd. For $C_{18}H_{14}N_2O_4S_2$: C- 55.94; H- 3.65; N- 7.25; S- 16.59%. Found: C- 55.90; H- 3.61; N-7.23; S- 16.56%.

3-(6-Carboxylic-1,3-benzothiazol-2-yl)-2-(4-chloroyphenyl)-1,3-thiazolidin-4-one (2j)
(2-[2-(4-chlorophenyl)-4-oxo-1,3-thiazolidin-3-yl]-1,3-benzothiazole-6-carboxylic acid)
Yield: 50%. m.p. 275-278 ^{0}C. IR (KBr, cm^{-1}): 3085 (Ar-CH), 2978 (N-CH-S), 2960 (CH_2-S), 1715 (cyclic C=O), 1610 (Ar-C=C), 815 (C-Cl), 725 (C-S-C). ^{1}H-NMR ($CDCl_3$ δ, ppm): 7.17-7.46 (m, 7H, Ar-H); 3.52 (s, 2H, S-CH_2); 3.33 (s, 1H, N-CH-Ar). MS: 391 (M+). Anal. Calcd. For $C_{17}H_{11}N_2O_3S_2Cl$: C- 52.24; H- 2.84; N- 7.17; S- 16.91%. Found: C- 52.20; H- 2.82; N- 7.14; S- 16.89%.

Antibacterial activity
All the synthesized compounds were tested against gram positive bacteria *Staphylococcus aureus* and *Micrococcus luteus* and gram negative bacteria *Escherichia coli*, and *Klebsiellia species* using paper disc method. Muller Hinton Agar (Hi-Media Pvt. Ltd. Mumbai, India) was used to culture the test bacteria. The microbial culture were grown at 37 ^{0}C for 8 hours and then appropriately diluted with sterile 0.8% saline solution. The concentration of test drugs was kept 200 µg/mL and 100 µg/mL in DMF. Standard drugs Streptomycin and Ceftazidime were used for comparison. The antimicrobial activity was evaluated by measuring the zones of growth inhibition around disc of test organism (Table 1).

Antifeedant activity
The antifeedant activity of these compounds was carried out by leaf dip method [40,41], using fourth instars larvae of Spodoptera litura. The leaf discs of about 25 cm^2 were prepared and dipped for thirty seconds in various test compounds. The leaf discs were air-dried to evaporate the excess acetone and offered for feeding. The insects were allowed to feed for 24 hrs. After 24 hrs leaf area uneaten was measured by using leaf area meter. The difference between leaf area provided and the leaf area uneaten is taken as amount of leaf area consumed. The feeding inhibition was calculated and used for calculation of effective concentration (EC_{50}/ LD_{50}) using Maximum Likelihood Programmer (MLP 3.01). The results of antifeedant activity are summarized in (Table 2).

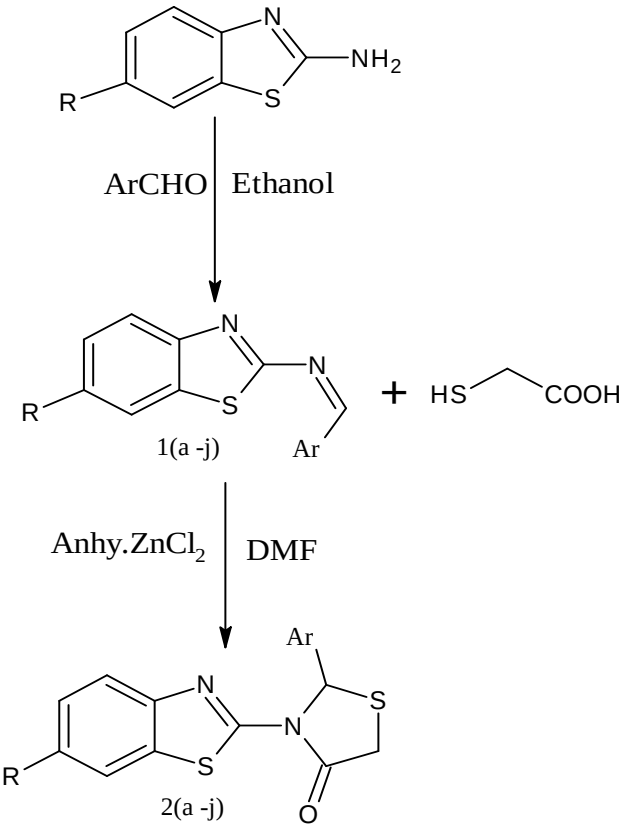
Acaricidal activity
The acaricidal activity of these compounds was carried out by leaf dip method [40, 41], Leaf discs of Mulberry (5 cm^2 diameter) were dipped in different compounds for 30 seconds to remove the excess of acetone and placed over wet cotton in Petri plate. The adult female mites were released on treated leaf discs and mortality data were recorded after 24 hours. Mites (*Tetranychus urticae*) released on leaf treated only with acetone and tween 20 emulsifier served as control. The mortality data were used for calculation of LC_{50}/ LD_{50} using Maximum Likelihood Programmer (MLP 3.01). The results of acaricidal activity are summarized in (Table 3).

Contact toxicity
The contact toxicity of these compounds was carried out by topical application method [42, 43], against larvae of *Spodoptera litura*, which is harmful for Indian crops. First the given compounds were dissolved in acetone than each compound was applied on the dorsal surface of the larvae. About 10 µL concentration of each compound was applied on each larva. Some of the larvae of insect were treated by acetone alone, works as control. The mortality data was recorded after 24 hrs, and the treated mortality was corrected with control morality. These corrected mortality data

was used for calculation of LC_{50}/ LD_{50} using Maximum Likelihood Programmer (MLP 3.01). The results of contact toxicity are summarized in (Table 4).

Stomach toxicity

The stomach toxicity of these compounds was carried out by leaf dip method [40, 41]. In this method we used fourth instar larvae of *Spodoptera litura* of an insect which is responsible for the damage of Indian agricultural crops. Ten larvae were used for each replication and three replications were maintained for each compound. The given compounds were dissolved in acetone. The leaf disc were prepared out of caster leaf and dipped in solutions of the test compounds for thirty seconds. The leaf discs were air dried to evaporate the excess acetone. (The leaf discs dipped only in acetone served as control). The mortality data was recorded after 24 hrs, and the treatment mortality was corrected with control mortality. These mortality data were used for calculation of LC_{50}/LD_{50} using Maximum Likelihood Programmer (MLP 3.01). The results of stomach toxicity are summarized in (Table 5).



R= OCH_3, F, COOH, *Ar= C_6H_5, o-C_6H_4OH, p-$C_6H_4OCH_3$, p-C_6H_4Cl*

(Scheme-1):- Synthesis of 2-aryl 3-(-6-substituted benzothiazolyl)-1,3-thiazolidine- 4-ones

RESULTS AND DISCUSSION

Chemistry

2-Amino-6-substituted benzothiazole on reaction with substituted aromatic aldehyde gives 2-(arylidenimino)-6-substituted benzothiazole **(1)**. The compound on reaction with mercapto acetic acid gives 2-aryl-3-(substituted benzothiazolyl)-1,3-thiazolidine-4-ones **(2)** (Scheme-1). The

structures of all the synthesized compounds were established on the basis of spectroscopic and analytical data. The elemental analysis (C, N, H and S) found for all the condensed products were in close agreement with the calculated values. Disappearance of NH_2 peaks in IR spectra of compound **1(a-j)** supports the formation of **1(a-j)** by the condensation of substituted-2-aminobenzothiazoles with aromatic aldehydes. The IR spectra of compounds **2(a-j)** display two characteristic bands at 1720-1680 cm^{-1} and 2990- 2860 cm^{-1} due to C=O and CH_2 stretching respectively. The molecular ion peaks are in agreement with the molecular weight of the synthesized compounds.

Antibacterial activity

The antibacterial activity of all the synthesized compounds were tested in-vitro against pathogenic *Escherichia coli, Klebsiellia species, Micrococcus luteus* and *Staphylococcus aureus* and the results were compared with standard drugs (Streptomycin and Ceftazidime). In case of *E. coli* compounds **2e** exhibited higher activity at 200 µg/mL while **2a, 2b, 2c, 2d, 2f, 2g, 2h, 2i** and **2j** showed moderate activity. In case of *K. species* compounds **2c, 2d, 2e, 2f, 2g** and **2h** showed moderate activity. Compound **2d** showed good activity while other compound **2c** exhibited moderate activity in case of *S. aureus* while rest of the compounds possesses less activity. In case of *M. luteus* compounds **2b, 2c, 2d, 2e, 2g** and **2h** showed moderate activity (Table 1).

Table 1. The zone of inhibition in mm of the compound as well as standard drugs tested for antibacterial activity of (1a-2j)

Compounds	R	Ar	*E. coli*		*K species.*		*S.aureus*		*M. luteus*	
			200	100	200	100	200	100	200	100
1a	OCH_3	C_6H_5	+++	+	+++	+	+++	++	++	-
1b	OCH_3	*o*-C_6H_4OH	++	+	+	-	++	+	+	-
1c	OCH_3	*p*-$C_6H_4OCH_3$	++	+	+	-	+	+	-	-
1d	OCH_3	*p*-C_6H_4Cl	+	-	+	-	++	+	++	+
1e	F	C_6H_5	+++	++	+++	++	+++	++	++	++
1f	F	*o*-C_6H_4OH	++	+	+++	++	++	+	++	+
1g	F	*p*-$C_6H_4OCH_3$	++	+	++	++	++	+	++	+
1h	F	*p*-C_6H_4Cl	+++	++	++	++	+++	+	+++	++
1i	COOH	*p*-$C_6H_4OCH_3$	++	+	++	-	+	-	+	-
1j	COOH	*p*-C_6H_4Cl	++	-	++	-	+	-	+	-
2a	OCH_3	C_6H_5	+++	++	++	+	++	+	++	+
2b	OCH_3	*o*-C_6H_4OH	+++	++	++	+	++	+	+++	++
2c	OCH_3	*p*-$C_6H_4OCH_3$	+++	++	+++	++	+++	++	+++	**++**
2d	OCH_3	*p*-C_6H_4Cl	+++	+++	+++	++	++++	+++	+++	**+++**
2e	F	*p*-$C_6H_4OCH_3$	++++	+++	+++	++	++	++	+++	++
2f	F	*p*-C_6H_4Cl	+++	++	+++	++	++	++	++	++
2g	F	C_6H_5	+++	++	+++	++	++	++	+++	++
2h	F	*o*-C_6H_4OH	+++	+++	+++	+++	++	++	+++	++
2i	COOH	*p*-$C_6H_4OCH_3$	+++	+	++	+	++	+	++	+
2j	COOH	*p*-C_6H_4Cl	+++	++	++	+	++	+	++	+
DMF(Blank)			--		--		--		--	
Streptomycin			++++		++++		++++		++++	
Ceftazidime			++++		++++		++++		++++	

Solutions are in µg/mL; Data represent zones of inhibition (mm) as follows: --0 mm,+ 6-8 mm; ++ 9-12mm; +++ 13-19 mm; ++++ 20-26 mm

Antifeedant activity

The antifeedant activity of the newly synthesized compounds was tested by a leaf dip method [40, 41]against larvae of *Spodoptera litura*. The results clearly indicate that the compounds **2c** and **2e** showed higher antifeedant activity against the larvae of the insect. Compounds **2b, 2f, 2g** and **2h** showed moderate activity (Table 2).

Table 2. Antifeedant activity of 2-aryl-3-(-6-substituted benzothiazolyl)-1,3-thiazolidine-4-ones 2(a-j)

Compounds	Fiducial Limits	Slop ±	Chi. Sq. (3)	LC_{50}/LD_{50} At 24 hrs.
2a	0.83–2.33	1.08±0.15	0.79 (3)	1.24
2b	0.30–0.47	1.28±0.14	3.42 (3)	0.39
2c	0.21–0.32	1.31±0.14	5.70 (3)	0.25
2d	0.62–1.46	1.05±0.46	1.03 (3)	0.87
2e	0.21–0.32	1.31±0.14	5.70 (3)	0.25
2f	0.49–0.76	1.52±0.16	2.59 (3)	0.58
2g	0.45–1.09	0.87±0.13	1.71 (3)	0.64
2h	0.33–0.61	1.00±0.13	0.68 (3)	0.43
2i	0.84–2.34	1.06±0.15	0.70 (3)	1.24
2j	0.71–2.21	0.89±0.14	0.20 (3)	1.08

Acaricidal activity

The acaricidal activity of these compounds was performed by the same method, as in the case of antifeedant activity, against *Tetranychus urticae*, a species of mite using acetone as a standard. The results obtained clearly showed that compound **2c, 2d, 2e** and **2f** exhibited the highest acaricidal activity with respect to the other compounds. Rest of the compounds showed moderate activity against the mites (Table 3).

Table 3. Acaricidal activity of 2-aryl-3-(-6-substituted benzothiazolyl)-1,3-thiazolidine-4-ones 2(a-j)

Compounds	Fiducial Limits	Slop ±	Chi. Sq. (3)	LC_{50}/LD_{50} At 24 hrs.
2a	0.12–0.26	0.89±0.8	8.52 (3)	0.17
2b	0.08–0.20	0.75±0.7	5.53 (3)	0.12
2c	0.05–0.10	0.97±0.8	13.22 (3)	0.07
2d	0.04–0.09	0.70±0.06	4.61 (3)	0.05
2e	0.04–0.09	0.70±0.06	4.61 (3)	0.05
2f	0.05–0.10	0.97±0.07	13.23 (3)	0.07
2g	0.08–0.23	0.65±0.07	6.12 (3)	0.13
2h	0.10–0.23	0.88±0.08	2.14 (3)	0.15
2i	0.36–1.89	0.64±0.08	3.57 (3)	0.70
2j	0.07–0.22	0.76±0.06	5.63 (3)	0.14

Contact toxicity

The contact toxicity of these compounds was carried out by topical application method [42, 43] against larvae of *Spodoptera litura*. The results clearly indicates that the compounds **2c** and **2j** are showed good activity and compound **2b** and **2d** showed moderate activity and the rest of the compounds showed lower to moderate activity against the mites (Table 4).

Table 4. Contact toxicity of 2-aryl-3-(-6-substituted benzothiazolyl)-1,3-thiazolidine-4-ones 2(a-j)

Compounds	Fiducial Limits	Slop ±	Chi. Sq. (3)	LC_{50}/LD_{50} At 24 hrs.
2a	0.74–1.32	1.62±0.18	3.24 (3)	0.94
2b	0.41–0.61	1.63±0.15	1.84 (3)	0.49
2c	0.29–0.39	1.97±0.16	4.39 (3)	0.34
2d	0.56–1.05	1.32±0.15	0.63 (3)	0.73
2e	1.87–12.08	1.09±0.19	1.60 (3)	3.53
2f	0.72–1.46	1.71±0.18	3.32 (3)	0.97
2g	1.61–9.30	1.07±0.17	0.67 (3)	2.83
2h	1.42–3.89	1.32±0.16	2.37 (3)	2.12
2i	1.57–9.32	1.07±0.17	0.72 (3)	2.83
2j	0.40–0.59	1.66±0.15	5.66 (3)	0.48

Stomach toxicity

The stomach toxicity of these compounds was carried out by leaf dip method [40, 41]. In this method we used fourth instars larvae of *Spodoptera litura.* The results clearly indicate that the compounds **2b** and **2d** showed good stomach toxicity against the larvae of the insect. Compounds **2a, 2c, 2f, 2i** and **2j** exhibited moderate activity and the rest of the compounds showed lower activity against the mites (Table 5).

Table 5. Stomach toxicity of 2-aryl-3-(-6-substituted benzothiazolyl)-1,3-thiazolidine-4-ones 2(a-j)

Compounds	Fiducial Limits	Slop ±	Chi. Sq. (3)	LC_{50}/LD_{50} At 24 hrs.
2a	0.57–1.05	1.32±0.15	0.63 (3)	0.74
2b	0.49–0.77	1.57±0.16	2.79 (3)	0.60
2c	0.55–0.89	1.58±0.16	9.01 (3)	0.68
2d	0.42–0.65	156±0.15	2.33 (3)	0.52
2e	2.49–39.65	0.93±0.18	0.501 (3)	5.88
2f	0.74–1.32	1.62±0.18	3.24 (3)	0.94
2g	1.61–9.39	1.01±0.17	0.69 (3)	2.93
2h	1.33–3.99	1.42±0.20	2.38 (3)	2.01
2i	0.74–1.32	1.62±0.18	3.24 (3)	0.94
2j	0.54–0.90	1.49±0.16	3.39 (3)	0.68

CONCLUSION

All the newly synthesized compounds were screened for antibacterial activity at a concentration of 200 µg/mL and 100 µg/mL using DMF as a control and Streptomycin and Ceftazidime used as standard against gram positive and gram negative bacteria. The data in the Table 2 indicate that among the synthesized compounds **2d** and **2e** possessed good activity. However, the activities of the tested compounds are much less than those of standard antibacterial agents used. These compounds also show potent antifeedant, acaricidal activities. From the results of various biological activities it is clear that these compounds would be of better use in drug development to combat bacterial infections and as antifeedant and acaricidal agents in the future.

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