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Original Article

SYNTHESIS AND BIOLOGICAL EVALUATION OF SUBSTITUTED 3-(BENZOTHIAZOLYL)-1, 3-THIAZOLIDINE-4-ONES

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ABSTRACT

Objective: Present research work is carried out for development of some biological active new heterocyclic moieties.

Methods: The substituted-2-aryl-3-(benzothiazolyl)-1,3-thiazolidine-4-ones have been synthesized by the reaction of substituted-2-aminobenzothiazoles with aromatic aldehydes (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. The newly synthesized compounds were screened for their anti-inflammatory, antiulcer, antitumor, entomological and antibacterial activities.

Results: The results of various biological activities show synthesized compounds would be of better use in drug development to combat bacterial infections and as antifeedant and acaricidal agents in future.

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.

Keywords: Benzothiazole, Thiazolidinone, Anti-inflammatory, Antiulcer, Antitumor, Entomological and Antibacterial activities.

INTRODUCTION

The survey of literature related to benzothiazole and thiazolidinone derivatives reveals 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 antitumor [1, 2], antihistamines [3], analgesics [4], anti-inflammatory [5], schistosomicidal [6], anti HIV [7], antibacterial [8, 9] etc. 2-(4-Aminophenyl) benzothiazole derivatives were extensively studied for their anticancer action [10]. 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 [11]. 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 [12-14], antimicrobial [15-16], anti-diabetic [17], anti-tubercular [18], antifungal [19-21], anti-diarrheal [22], anticonvulsant [23], antihistaminic [24], Ca^{2+} channel blocker [25], cardio protective [26], anti-ischemic [27], cycloxygenase inhibitory [28], hypo-glycemic [29], inhibition of gastric H^+K^+-ATPase [30], CFTR inhibitor [31], anti-platelet activating factor [32], non-peptide thrombin receptor antagonist [33] and tumor necrosis factor-α antagonist activities [34]. 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 [35, 36], we are reporting the synthesis and anti-inflammatory, antiulcer, antitumor, entomological and antibacterial activities of substitutes-3-(benzothiazolyl)-1,3-thiazolidine-4-ones.

MATERIALS AND METHODS

General Procedures

Reagent grade chemicals were used without further purification. All the melting points were taken in open capillaries and are uncorrected. The purity of the synthesized compounds was checked by Thin Layer Chromatographic studies. IR spectra were scanned on FT IR Perkins Elmer (Spectrum RX1) spectrophotometer (δ in cm^{-1}) using a KBr disc. ^{1}H NMR spectral was recorded in DMF/ DMSO with tetramethylsilane (TMS) as the internal standard at 300 MHz on a Bruker DRTX-300 spectrophotometer. The chemical shifts are reported as parts per million (ppm). Fast atom bombardment mass spectra (FABMS) were recorded 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 Procedures for the synthesis of 2-(arylidenimino)-substituted benzothiazoles 1(a-l)

A mixture of 2-amino-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.

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

Yield 65%, m.p. 230-232 ^{0}C. IR (KBr, cm^{-1}): 3069, 1599, 1502, 1172, 1081, 809, 753 and 635 (benzothiazole with aromatic ring), 3070 (Ar-H), 2975 (aliphatic CH), 1630 (C=N), 1549 (Ar-C=C), 538 (C-Br). ^{1}H-NMR ($CDCl_3$ δ, ppm): 7.02-7.52 (m, 8H, Ar-H), 4.80 (s, 1H, N=CH), MS 317 (M+). Anal. Calcd for $C_{14}H_9N_2SBr$: C, 53.01%; H, 2.86%; N, 8.83%. Found: C, 52.07%; H, 2.82%; N, 8.82%.

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

Yield 68%, m.p. 131-133 ^{0}C. IR (KBr, cm^{-1}): 3070, 1598, 1441, 1100, 1075, 806, 733 and 659 (benzothiazole with aromatic ring), 3449 (OH), 3060 (Ar-H), 2973 (aliphatic CH), 1629 (C=N), 1550 (Ar-C=C), 534 (C-Br). ^{1}H-NMR ($CDCl_3$ δ, ppm): 9.12 (s, 1H, OH), 7.01-7.42 (m, 7H, Ar-H), 4.71 (s, 1H, N=CH), MS 333 (M+). Anal. Calcd for $C_{14}H_9N_2OSBr$: C, 50.46%; H, 2.72%; N, 8.41%. Found: C, 50.43%; H, 2.70%; N, 8.38%.

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

Yield 60%, m.p. 122-124 ^{0}C. IR (KBr, cm^{-1}): 3072, 1540, 1470, 1150, 1051, 810, 743 and 640 (benzothiazole with aromatic ring), 3050 (Ar-H), 2978 (aliphatic CH), 1639 (C=N), 1552 (Ar-C=C), 1038 (C-O-C), 540 (C-Br). ^{1}H-NMR ($CDCl_3$ δ, ppm): 7.41-7.77 (m, 7H, Ar-H), 5.19 (s, 1H, N=CH), 3.51 (s, 3H, Ar-O-CH_3), MS 347 (M+). Anal. Calcd for $C_{15}H_{11}N_2OSBr$: C, 51.89%; H, 3.19%; N, 8.07%. Found: C, 51.86%; H, 3.17%; N, 8.05%.

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

Yield 70%, m.p. 252-254 ^{0}C. IR (KBr, cm^{-1}): 3075, 1528, 1475, 1148, 1055, 812, 724 and 630 (benzothiazole with aromatic ring), 3051 (Ar-H), 2973 (aliphatic CH), 1641 (C=N), 1550 (Ar-C=C), 548 (C-Br), 810 (C-Cl). ^{1}H-NMR ($CDCl_3$ δ, ppm): 7.12-7.34 (m, 7H, Ar-H), 5.15 (s, 1H, N=CH), MS 352 (M+). Anal. Calcd for $C_{14}H_8N_2SClBr$: C, 47.82%; H, 2.29%; N, 7.97%. Found: C, 47.83%; H, 2.28%; N, 7.96%.

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

Yield 65%, m.p. 233-235 ^{0}C. IR (KBr, cm^{-1}): 3044, 1588, 1498, 1172, 1100, 771, 676 and 623 (benzothiazole with aromatic ring), 3075 (Ar-H), 2965 (aliphatic CH), 1618 (C=N), 1549 (Ar-C=C), 1510 (NO_2). ^{1}H-NMR ($CDCl_3$ δ, ppm): 7.20-7.70 (m, 8H, Ar-H), 5.11 (s, 1H, N=CH), MS 283 (M+). Anal. Calcd for $C_{14}H_9N_3O_2S$: C, 59.35%; H, 3.20%, N, 14.83%. Found: C, 59.31%; H, 3.17%; N, 14.81%.

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

Yield 67%, m.p. 215-217 ^{0}C. IR (KBr, cm^{-1}): 3090, 1594, 1100, 1176, 1123, 747, 674 and 616 (benzothiazole with aromatic ring), 3415 (OH), 3070 (Ar-H), 2963 (aliphatic CH), 1632 (C=N), 1547 (Ar-C=C), 1512 (NO_2). ^{1}H-NMR ($CDCl_3$ δ, ppm): 8.70 (s, 1H, OH), 7.31-7.63 (m, 7H, Ar-H), 5.17 (s, 1H, N=CH), MS 299 (M+). Anal. Calcd for $C_{14}H_9N_3O_3S$: C, 56.18%; H, 3.03%; N, 14.04%. Found: C, 56.15%; H, 3.00%; N, 14.02%.

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

Yield 65%, m.p. 183-185 ^{0}C. IR (KBr, cm^{-1}): 3090, 1528, 1502, 1148, 1085, 810, 724 and 624 (benzothiazole with aromatic ring), 3070 (Ar-H), 2963 (aliphatic CH), 1618 (C=N), 1539 (Ar-C=C), 1510 (NO_2), 1054 (C-O-C). ^{1}H-NMR ($CDCl_3$ δ, ppm): 7.15-7.40 (m, 7H, Ar-H), 5.25 (s, 1H, N=CH), 3.79 (s, 3H, Ar-O-CH_3), MS 313 (M+). Anal. Calcd for $C_{15}H_{11}N_3O_3S$: C, 57.50%; H, 3.54%; N, 13.41%. Found: C, 57.48%; H, 3.51%; N, 13.38%.

2-(4'-Chlorobenzylidenoimino)-6-nitrobenzothiazole (1h)

Yield 70%, m.p. 202-204 ^{0}C. IR (KBr, cm^{-1}): 3080, 1538, 1510, 1140, 1080, 806, 725 and 620 (benzothiazole with aromatic ring), 3069 (Ar-H), 2965 (aliphatic CH), 1623 (C=N), 1542 (Ar-C=C), 1524 (NO_2), 807 (C-Cl). ^{1}H-NMR ($CDCl_3$ δ, ppm): 7.21-7.77 (m, 7H, Ar-H), 5.19 (s, 1H, N=CH), MS 318 (M+). Anal. Calcd for $C_{14}H_8N_3O_2SCl$: C, 52.92%.; H, 2.54%; N, 13.22%. Found: C, 52.90%; H, 2.52%; N, 13.20%.

2-(Benzylidenoimino)-4-methylbenzothiazole (1i)

Yield 64%, m.p. 119-121 ^{0}C. IR (KBr, cm^{-1}): 3077, 1601, 1455, 1163, 1081, 840, 735 and 658 (benzothiazole with aromatic ring), 3028 (Ar-H), 2980 (aliphatic CH), 1616 (C=N), 1458 (Ar-C=C). ^{1}H-NMR ($CDCl_3$ δ, ppm): 7.51-7.72 (m, 8H, Ar-H), 5.16 (s, 1H, N=CH), 2.32 (s, 3H, Ar-CH_3), MS 252 (M+). Anal. Calcd for $C_{15}H_{11}N_2S$: C, 71.40%; H, 4.79%; N, 11.10%. Found: C, 71.38%; H, 4.77%; N, 11.07%.

2-(2'-Hydroxybenzylidenoimino)-4-methylbenzothiazole (1j)

Yield 66%, m.p. 93-95 ^{0}C. IR (KBr, cm^{-1}): 3090, 1610, 1454, 1162, 1102, 832, 718 and 655 (benzothiazole with aromatic ring), 3415 (OH), 3030 (Ar-H), 2984 (aliphatic CH), 1618 (C=N), 1550 (Ar-C=C). ^{1}H-NMR ($CDCl_3$ δ, ppm): 9.26 (s, 1H.OH), 7.00 -7.29 (m, 7H, Ar-H), 5.23 (s, 1H, N=CH), 2.41 (s, 3H, Ar-CH_3), MS 268 (M+). Anal. Calcd for $C_{15}H_{12}N_2OS$: C, 67.14%; H, 4.51%; N, 10.44%. Found: C, 67.11%; H, 4.48%; N, 10.41%.

2-(4'-Methoxybenzylidenoimino)-4-methylbenzothiazole (1k)

Yield 68%, m.p. 89-91 ^{0}C. IR (KBr, cm^{-1}): 3087, 1603, 1462, 1156, 1073, 841, 728 and 683 (benzothiazole with aromatic ring), 3021 (Ar-H), 2983 (aliphatic CH), 1620 (C=N), 1546 (Ar-C=C), 1049 (C-O-C). ^{1}H-NMR ($CDCl_3$ δ, ppm): 7.21-7.85 (m, 7H, Ar-H), 5.16 (s, 1H, N=CH), 3.65 (s, 3H, Ar-OCH_3), 2.52 (s, 3H, Ar-CH_3), MS 282 (M+). Anal. Calcd for $C_{16}H_{14}N_2OS$: C, 68.06%; H, 5.00%; N, 9.92%. Found: C, 68.00%; H, 4.97%; N, 9.89%.

2-(4'-Chlorobenzylidenoimino)-4-methylbenzothiazole (1l)

Yield 70%, m.p. 115-117 ^{0}C. IR (KBr, cm^{-1}): 3085, 1605, 1465, 1160, 1080, 845, 724 and 680 (benzothiazole with aromatic ring), 3038 (Ar-H), 2989 (aliphatic CH), 1618 (C=N), 1549 (Ar-C=C), 817 (C-Cl). ^{1}H-NMR ($CDCl_3$ δ, ppm): 7.01- 7.56 (m, 7H, Ar-H), 5.15 (s, 1H, N=CH), 2.50 (s, 3H, Ar-CH_3), MS 287 (M+). Anal. Calcd for $C_{15}H_{11}N_2SCl$: C, 62.82%; H, 3.87%; N, 9.77. Found: C, 62.76%; H, 3.85%, N, 9.74%.

2.3 Preparation of 2-aryl-3-(4/6-substituted benzothiazolyl) -1, 3- thiazolidine- 4-ones 2(a-l)

A mixture of **1**(**a-l**) (0.01 mole) and mercapto acetic acid (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.

3-(6-Bromo-1,3-benzothiazol-2-yl)-2-phenyl-1,3-thiazolidin-4-one (2a)

Yield 45%, m.p. 151-153 ^{0}C. IR (KBr, cm^{-1}): 3070, 1598, 1505, 1170, 1083, 810, 750 and 633 (benzothiazole with aromatic ring), 3081 (Ar-CH), 2972 (N-CH-S); 2958 (CH_2-S), 1700 (cyclic C=O), 1580 (Ar-C=C), 548 (C-Br), 710 (C-S-C). ^{1}H-NMR ($CDCl_3$ δ, ppm): 7.10- 7.62 (m, 8H, Ar-H), 3.71 (s, 2H, S-CH_2), 3.21 (s, 1H, N-CH-Ar), MS 391 (M+). Anal. Calcd for $C_{16}H_{11}N_2OS_2Br$: C, 49.11%; H, 2.83%; N, 7.16%. Found: C, 49.08%; H, 2.80%; N, 7.14%.

3-(6-Bromo-1,3-benzothiazol-2-yl)-2-(2-hydroxyphenyl)-1,3-thiazolidin-4-one (2b)

Yield 47%, m.p. 136-138 ^{0}C. IR (KBr, cm^{-1}): 3075, 1595, 1445, 1110, 1073, 809, 738 and 649 (benzothiazole with aromatic ring), 3405 (OH), 3076 (Ar-CH), 2981 (N-CH-S); 2965 (CH_2-S), 1698 (cyclic C=O), 1582 (Ar-C=C), 549 (C-Br), 715 (C-S-C). ^{1}H-NMR ($CDCl_3$ δ, ppm): 8.62 (s, 1H, OH), 6.95-7.31 (m, 7H, Ar-H), 3.77 (s, 2H, S-CH_2), 3.20 (s, 1H, N-CH-Ar), MS 407 (M+). Anal. Calcd for $C_{16}H_{11}N_2O_2S_2Br$: C, 47.18%; H, 2.72%; N, 6.88%. Found: C, 47.13%; H- 2.70%; N- 6.86%.

3-(6-Bromo-1,3-benzothiazol-2-yl)-2-(4-methoxyphenyl)-1,3-thiazolidin-4-one (2c)

Yield 43%, m.p. 187-189 ^{0}C. IR (KBr, cm^{-1}): 3072, 1580, 1470, 1150, 1055, 810, 743 and 640 (benzothiazole with aromatic ring), 3084 (Ar-CH), 2976 (N-CH-S), 2962 (CH_2-S), 1696 (cyclic C=O), 1576 (Ar C=C), 1035 (C-O-C), 547 (C-Br), 705 (C-S-C). ^{1}H-NMR ($CDCl_3$ δ, ppm): 6.99- 7.29 (m, 7H, Ar-H), 3.72 (s, 2H, S-CH_2), 3.69 (s, 3H, Ar-OCH_3), 3.27 (s, 1H, N-CH-Ar), MS 421 (M+). Anal. Calcd for $C_{17}H_{13}N_2O_2S_2Br$: C, 48.46%; H, 3.11%; N, 6.65%. Found: C, 48.42%; H, 3.09%; N- 6.62%.

3-(6-Bromo-1,3-benzothiazol-2-yl)-2-(4-chloroyphenyl)-1,3-thiazolidin-4-one (2d)

Yield 53%, m.p. 131-133 ^{0}C. IR (KBr, cm^{-1}): 3075, 1578, 1475, 1149, 1055, 812, 728 and 635 (benzothiazole with aromatic ring), 3080 (Ar-CH), 2978 (N-CH-S); 2960 (CH_2-S), 1698 (cyclic C=O), 1580 (Ar-C=C), 548 (C-Br), 720 (C-S-C). ^{1}H-NMR ($CDCl_3$ δ, ppm): 7.01- 7.70 (m, 7H, Ar-H), 3.79 (s, 2H,S- CH_2), 3.29 (s, 1H, N-CH-Ar), MS 426 (M+). Anal. Calcd for $C_{16}H_{11}N_2OS_2ClBr$: C, 45.14%; H, 2.37%; N, 6.58%. Found: C, 45.10%; H, 2.35%; N, 6.56%.

3-(6-Nitro-1,3-benzothiazol-2-yl) -2-phenyl-1,3-thiazolidin-4-one (2e)

Yield 50%, m.p. 212-214 ^{0}C. IR (KBr, cm^{-1}): 3045, 1585, 1490, 1174, 1105, 773, 670 and 625 (benzothiazole with aromatic ring), 3076 (Ar-CH), 2980 (N-CH-S); 2962 (CH_2-S), 1704 (cyclic C=O), 1572 (Ar-C=C), 1536 (NO_2), 730 (C-S-C). ^{1}H-NMR ($CDCl_3$ δ, ppm): 7.15-7.48 (m, 8H, Ar-H), 3.57 (s, 2H, S-CH_2), 3.24 (s, 1H, N-CH-Ar), MS 357 (M+). Anal. Calcd for $C_{16}H_{11}N_3O_3S_2$: C, 53.77%; H, 3.10%; N, 11.76%. Found: C, 53.74%; H, 3.07%; N- 11.73%.

3-(6-Nitro-1,3-benzothiazol-2-yl)-2-(2-hydroxyphenyl)-1,3-thiazolidin-4-one (2f)

Yield 53%, m.p. 188-190 ^{0}C. IR (KBr, cm^{-1}): 3090, 1590, 1109, 1176, 1120, 749, 674 and 618 (benzothiazole with aromatic ring), 3410 (OH), 3072 (Ar-CH), 2985 (N-CH-S), 2960 (CH_2-S), 1699 (cyclic C=O), 1574 (Ar-C=C), 1533 (NO_2), 700 (C-S-C). ^{1}H-NMR ($CDCl_3$ δ, ppm): 8.80 (s, 1H, Ar-OH), 7.01- 7.62 (m, 7H, Ar-H), 3.52 (s, 2H, S-CH_2), 3.37 (s, 1H, N-CH-Ar), MS 373 (M+). Anal. Calcd for $C_{16}H_{11}N_3O_4S_2$: C, 51.46%; H, 2.97%; N, 11.25%. Found: C, 51.44%; H, 2.94%; N, 11.22%.

3-(6-Nitro-1,3-benzothiazol-2-yl)-2-(4-methoxyphenyl)-1,3-thiazolidin-4-one (2g)

Yield 48%, m.p. 182-184 ^{0}C. IR (KBr, cm^{-1}): 3087, 1525, 1500, 1150, 1086, 812, 728 and 628 (benzothiazole with aromatic ring), 3075 (Ar-CH), 2978 (N-CH-S), 2962 (CH_2-S), 1495 (Ar-C=C), 1705 (cyclic C=O), 1530 (NO_2), 1027 (C-O-C), 698 (C-S-C). ^{1}H-NMR ($CDCl_3$ δ, ppm): 7.11- 7.71 (m, 7H, Ar-H), 3.49 (s, 2H, S-CH_2), 3.71 (s, 3H, Ar-OCH_3), 3.21 (s, 1H, N-CH-Ar), MS 387 (M+). Anal. Calcd for $C_{17}H_{13}N_3O_4S_2$: C, 52.70%; H, 3.38%; N, 10.85%. Found: C, 52.68%; H, 3.36%; N, 10.83%.

3-(6-Nitro-1,3-benzothiazol-2-yl)-2-(4-chloroyphenyl)-1,3-thiazolidin-4-one (2h)

Yield 53%, m.p. 197-199 ^{0}C. IR (KBr, cm^{-1}): 3077, 1534, 1511, 1142, 1082, 809, 729 and 625 (benzothiazole with aromatic ring), 3070 (Ar-CH), 2980 (N-CH-S), 2963 (CH_2-S), 1577 (Ar C=C), 1711 (cyclic C=O), 1531 (NO_2), 816 (C-Cl), 715 (C-S-C). ^{1}H-NMR ($CDCl_3$ δ, ppm): 7.01- 7.51 (m, 7H, Ar-H), 3.58 (s, 2H, S-CH_2), 3.26 (s, 1H, N-CH-Ar), MS 391 (M+). Anal. Calcd for $C_{16}H_{10}N_3O_3S_2Cl$: C, 49.04%; H, 2.57%; N, 10.72%. Found: C, 49.01%; H, 2.55%; N, 10.70%.

3-(4-Methyl-1,3-benzothiazol-2-yl)-2-phenyl-1,3-thiazolidin-4-one (2i)

Yield 48%, m.p. 130-132 ^{0}C. IR (KBr, cm^{-1}): 3079, 1605, 1457, 1160, 1080, 842, 733 and 655 (benzothiazole with aromatic ring), 3079 (Ar-CH), 2970 (N-CH-S), 2965 (CH_2-S), 1698 (cyclic C=O), 1582 (Ar-C=C), 725 (C-S-C). ^{1}H-NMR ($CDCl_3$ δ, ppm): 7.10- 7.39 (m, 8H, Ar-H), 3.52 (s, 2H, S-CH_2), 3.24 (s, 1H, N-CH-Ar), 2.42 (s, 3H, Ar-CH_3), MS 326 (M+). Anal. Calcd for $C_{17}H_{14}N_20S_2$: C, 62.55%; H, 4.32%; N, 8.58%. Found: C, 62.51%; H, 4.28%, N, 8.55%.

3-(4-Methyl-1,3-benzothiazol-2-yl)-2-(2-hydroxyphenyl)-1,3-thiazolidin-4-one (2j)

Yield 47%, m.p. 98-100 ^{0}C. IR (KBr, cm^{-1}): 3090, 1612, 1455, 1162, 1105, 835, 720 and 659 (benzothiazole with aromatic ring), 3409 (OH), 3065 (Ar-CH), 2970 (N-CH-S), 2959 (CH_2-S), 1700 (cyclic C=O), 1577 (Ar-C=C), 720 (C-S-C). ^{1}H-NMR ($CDCl_3$ δ, ppm): 7.02- 7.42 (m, 7H, Ar-H), 3.70 (s, 2H, S-CH_2), 3.30 (s, 1H, N-CH-Ar), 2.49 (s, 3H, Ar-CH_3), MS 342 (M+). Anal. Calcd for $C_{17}H_{14}N_2O_2S_2$: C, 59.63%; H, 4.12%; N, 8.18%. Found: C, 59.61%; H, 4.10%; N, 8.17%.

3-(4-Methyl-1,3-benzothiazol-2-yl)-2-(4-methoxyphenyl)-1,3-thiazolidin-4-one (2k)

Yield 47%, m.p. 94-96 ^{0}C. IR (KBr, cm^{-1}): 3089, 1609, 1460, 1158, 1075, 840, 730 and 680 (benzothiazole with aromatic ring), 3071 (Ar-CH), 2972 (N-CH-S), 2963 (CH_2-S), 1709 (cyclic C=O), 1565 (Ar-C=C), 1025 (C-O-C), 730 (C-S-C). ^{1}H-NMR ($CDCl_3$ δ, ppm): 6.95- 7.26 (m, 7H, Ar-H), 3.68 (s, 2H, S-CH_2), 3.79 (s, 3H, Ar-OCH_3), 3.25 (s, 1H, N-CH-Ar), 2.54 (s, 3H, Ar-CH_3), MS 356 (M+). Anal. Calcd for $C_{18}H_{16}N_2O_2S_2$: C, 60.65%; H, 4.52%; N, 7.86%. Found: C, 60.63%; H, 4.50%; N, 7.83%.

3-(4-Methyl-1,3-benzothiazol-2-yl)-2-(4-chloroyphenyl)-1,3-thiazolidin-4-one (2l)

Yield 44%, m.p. 110-112 ^{0}C. IR (KBr, cm^{-1}): 3087, 1610, 1467, 1162, 1080, 845, 726 and 683 (benzothiazole with aromatic ring), 3068 (Ar-CH), 2976 (N-CH-S), 2961 (CH_2-S), 1578 (Ar-C=C), 1705 (cyclic C=O), 811 (C-Cl), 715 (C-S-C). ^{1}H-NMR ($CDCl_3$ δ, ppm): 6.99- 7.42 (m, 7H, Ar-H), 3.45 (s, 2H, S-CH_2), 3.29 (s, 1H, N-CH-Ar), 2.63 (s, 3H, Ar-CH_3), MS 361 (M+). Anal. Calcd for $C_{17}H_{13}N_2OS_2Cl$: C, 56.58%; H, 3.63%; N, 7.76%. Found: C, 56.56%; H, 3.64%; N, 7.73%.

Antibacterial activity

All the synthesized compounds were tested against gram positive bacteria *Staphylococcus aureus* and *Micrococcus luteus* and gram negative bacteria *Escherichia coli* and *Klebsiella species* using paper disc method [37]. 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).

Anti-inflammatory activity

Animals for Experiments

Adult Swiss albino mice (25-30 gm) and Albino wistar rat (125-150 gm) were procured from Animal House Facility of Hygia Institutes of Pharmaceutical Education and Research, Lucknow. These animals were maintained under standard condition and provided pelleted diet and sterile water ad libitum and kept in 12-12 hrs light-dark cycle. All the animal experiments were performed by following the approval of study protocols by the Institutional Animal Ethical Committee (DOPJH/417/IAEC08).

The anti-inflammatory activity (% inhibition) of the test samples was evaluated *in-vivo* using carrageenan-induced paw edema bioassay method in rats [38]. The % inhibition values were determined for each samples using phenyl butanone as a reference standard drug. The freshly prepared suspension of carrageenan (0.2 mL, 1.0% in 0.9% saline) was injected subcutaneously into the planter aponeurosis of the hind paw of the rats of both genders (male/ female) of about 120-140 g of body weight. One group of five rats was kept as a control and the animals of other group of five each were penetrated with the test compounds given orally 30 min before the carrageenan injection. The paw volume was measured by a water plethysmometer socrel at the time of treatment and then at an interval of one hour for four hours. The mean increase of paw volume at each time interval was compared with that of control groups and % anti-inflammatory values was calculated as given below.

% anti-inflammatory = (1-DT/DC) X 100

Here, DT= volume of paw edema in drug treated, DC= volume of paw edema in drug control. The results of anti-inflammatory activity are summarized in (Table 2).

Antiulcer activity

Aspirin (ASP) Induced Ulcers

Aspirin in dose of 200mg/ kg (20mg/ml) was administered to the animals on the day of the experiment and ulcers were scored after four hrs. The animals were sacrificed and the stomach was then excised and cut along the greater curvature, washed carefully with 5 ml of 0.9% NaCl and ulcers were scored by a person unaware by the experimental protocol in the glandular portion of the stomach. Ulcer index was calculated by adding the total number of ulcers/ stomach and total severity of ulcers/stomach. The pooled group ulcer score was then calculated by reported method.

Ethanol (EtOH) induced Ulcers

The gastric ulcers were induced in rats by administering ethanol (1mL/ 200 gm/kg for 1 hr) and the animals were sacrificed by cervical dislocation and the stomach was incised along the greater curvature and examined for ulcers. The ulcer index was scored, based upon the product of length and width of the ulcers present in the glandular portion of the stomach (mm^2/ rats). The results of antiulcer activity are summarized in (Table 3).

Antitumor activity

This method was carried out to estimate the effect of test compound on the growth of tumor cells. The human breast cancer cells lines (MCF-7) were employed. The human breast cancer cell line (MCF-7)

and mammary cancer cell line (EVSA-7),were co-incubated with the test compounds at 1 µg/mL doses for 96 hrs and the cell growth count was measured by MTT assay [39-41]. 17-Estradiol and culture medium was kept as positive and negative control, respectively. The cell proliferation activity was carried out to estimate the effect of test compounds on the growth of tumor cells *in vitro*. A measurement of cell viability and proliferation forms the basis for this *in vitro* assay. The basic principle involved in this assay depends upon the reduction of tetrazoleum salt. The yellow colored tetrazoleum MTT, [3-(4, 5-dimethylthiazol-2-yl)-2, 5,-diphenyltetrazoleumbromide] is reduced by metabolically active cells in part by the action of dehydrogenase enzymes to generate reducing equivalents such as NADH and NADPH. The resulting intra cellular purple colour zones was solubilized and quantified by spectrophotometer method. The MTT was dissolved in PBS (Phosphate Buffer Saline) at a concentration of 5 mg/mL. Then 50 µL of the MTT solution was added to each of the 96 well culture plates, containing the 100 µL culture along with test compound and incubated at 37^{o}C for 4 hrs. The medium was then removed carefully without disturbing the purple colored crystals. Then, 50 mL of dimethylsulfoxide (DMSO) was added to each well and mixed thoroughly to dissolve the crystals. The plates were then read on ELISA plate reader at a wavelength of 570 nm. The readings were presented as optical density/cell count. The results of antitumor activity are summarized in (Table 4).

Entomological activity

The newly synthesized compounds were also screened out for their entomological activity (Antifeedant, Acaricidal, Contact toxicity and Stomach toxicity) against *Spodoptera litura* (an insect which damages the Indian agriculture crops) and *Tetranychus urticae* of mites (damage house goods) respectively.

Antifeedant activity

The antifeedant activity of these compounds was carried out by leaf dip method [42] using fourth instars larvae of *Spodoptera litura*, an insect responsible for the damage of Indian agricultural crops. Ten larvae were used for each replication and three replications were maintained for each concentration. The given compounds were dissolved in acetone and different concentrations were prepared *viz.* 0.06%, 0.12%, 0.25%, 0.50% and 1.00%. The leaf discs of about 25 cm^2 were prepared and dipped for thirty seconds in various concentrations of the test compounds. Now the leaf discs were air-dried to evaporate the excess acetone and the leaf discs were 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 differences 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 (LC_{50}/LD_{50}) using Maximum Likelihood Programmer (MLP 3.01).The results of antifeedant activity are summarized in (Table 5).

Acaricidal activity

The acaricidal activity of these compounds was also carried out by leaf dip method [42]. Leaf discs of Mulberry (5 cm^2 diameter) were dipped in different compounds for 30 seconds. The leaf discs were air dried to evaporate the excess 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 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 6).

Contact toxicity

The contact toxicity of these compounds, were carried out by topical application method [43] against larvae of *Spodoptera litura* which is harmful for Indian crops. First the given compounds were dissolved in acetone and different concentrations were prepared *viz*., 0.06%, 0.12%, 0.25%, 0.50%, and 1.00%. Now each concentration was applied on the dorsal surface of the larvae of insect. About 10 µl of each concentration was applied on each larva. Some of the larvae of insect were treated by acetone alone, works as control. Now 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 7).

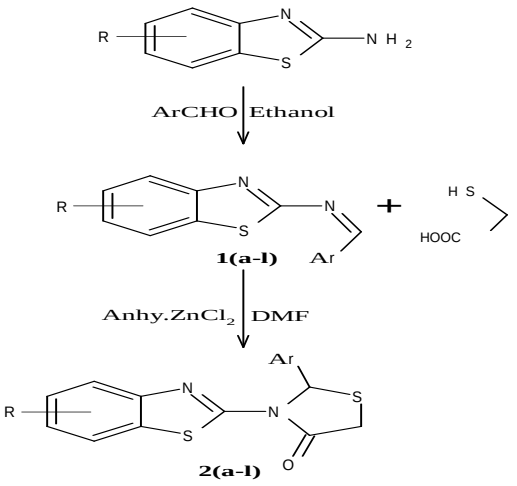
Stomach toxicity

The stomach toxicity of these compounds was carried out by leaf dip method [42]. 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 concentration. The given compounds were dissolved in acetone and different concentrations were prepared *viz*. 0.06%, 0.12%, 0.25%, 0.50%, and 1.00%. The leaf disc were prepared out of caster leaf and dipped in various concentrations of the test compounds for thirty seconds. Now 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 was used for calculation of LC_{50}/LD_{50} using Maximum Likelihood Programmer (MLP 3.01). The results of stomach toxicity are summarized in (Table 8).

RESULTS AND DISCUSSIONS

2-Amino-4/6-substitutedbenzothiazoles on reaction with substituted aromatic aldehydes give 2-(arylidenimino)-4/6-substituted benzothiazoles (**1**), which on reaction with mercapto acetic acid provide 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 and H) found for all the condensed products were in close agreement with the calculated values. Disappearance of NH_2 peaks in IR spectra of compound supports the formation of **1**(**a-l**) by the condensation of substituted-2-aminobenzothiazoles with aromatic aldehydes. The IR spectra of compounds **2**(**a-l**) display two characteristic bands at 1720-1680 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



R = 6-Br, 6-NO_2, 4- CH_3; Ar:= C_6H_5, *o*-C_6H_4OH, *p*- $C_6H_4OCH_3$, *p*- C_6H_4Cl

The antibacterial activity of all the synthesized compounds were tested *in-vitro* against pathogenic *Escherichia coli, Klebsiella species*, *Micrococcus luteus* and *Staphylococcus aureus* and the results were compared with standard drugs (Streptomycin and Ceftazidime). In case of *Escherichia coli* compounds **2h** and **2l** exhibit higher activity at 200 µg/mL. While **1e, 1g, 1h, 1i** and **1k** show moderate activity and compounds **2(a-l)** show good activities. In case of *Klebsiella* compound **2d** shows good activity and rest of the compounds show

moderate activity. In case of *Staphylococcus aureus* compound 2k shows good activity while other compounds 1d, 1e, 1i, 2a, 2d, 2e, 2h and 2l show moderate activity *while* rest of the compounds possess less activity. In case of *Micrococcus*

Scheme1. Synthesis of 2-aryl-3-(4/6-substituted benzo thiazolyl)-1,3-thia zolidine-4-ones

luteus compound **2i** shows good activity than the rest of the compounds. The presence of nitro and methyl groups, in **2h** and **2l**, play an important role in activity, while in compound **2k** presence of a methyl group, along with methoxy group, justify the activity. It may be found that the nitro group present on the phenyl ring generally forms complexes with metaloenzymes, particularly those which are responsible in basic physiology such as cytochrome oxidase. These compounds may react with the peptidoglycan layer of the bacterial cell wall and damage it by penetrating in such a manner that the phenyl ring gets entered inside the cell by puncturing it, followed by bacterial cell death [44]. Sometimes these compounds when present in low concentrations may cause bacteriostatic conditions which slow down the growth of bacteria (Table 1).

Table 1: The zone of inhibition of the synthesized compound as well as standard drugs tested for antibacterial activity

Compounds	R	Ar	*E. coli*		*K. species.*		*S.aureus*		*M. luteus*	
			200	100	200	100	200	100	200	100
1a	Br	C_6H_5	++	+	+	---	++	+	+++	+
1b	Br	*o*-C_6H_4OH	++	---	++	+	++	---	++	+
1c	Br	*p*- $C_6H_4OCH_3$	++	+	+	---	++	---	++	+
1d	Br	*p*- C_6H_4Cl	++	++	++	++	+++	++	+++	++
1e	NO_2	C_6H_5	+++	+	+++	++	+++	++	+++	+
1f	NO_2	*o*-C_6H_4OH	++	+	++	+	++	+	++	+
1g	NO_2	*p*- $C_6H_4OCH_3$	+++	++	+++	+	++	++	++	+
1h	NO_2	*p*- C_6H_4Cl	+++	++	++	+	++	+	++	+
1i	4-CH_3	C_6H_5	+++	++	+++	++	+++	++	+++	+
1j	4-CH_3	*p*-C_6H_4OH	++	+	++	+	++	+	++	+
1k	4-CH_3	*p*- $C_6H_4OCH_3$	+++	+	++	++	++	+	++	+
1l	4-CH_3	*p*- C_6H_4Cl	++	++	++	+	++	+	++	++
2a	Br	C_6H_5	+++	++	+++	+	+++	++	+++	++
2b	Br	*o*-C_6H_4OH	+++	++	++	+	++	++	++	++
2c	Br	*p*- $C_6H_4OCH_3$	+++	++	++	+	++	+	+++	++
2d	Br	*p*- C_6H_4Cl	+++	+++	++++	+++	+++	++	+++	++
2e	NO_2	C_6H_5	+++	+++	+++	+++	+++	++	+++	+++
2f	NO_2	*o*-C_6H_4OH	+++	++	+++	++	++	++	++	++
2g	NO_2	*p*- $C_6H_4OCH_3$	+++	++	+++	++	++	++	+++	++
2h	NO_2	*p*- C_6H_4Cl	++++	+++	+++	++	+++	++	+++	++
2i	4-CH_3	C_6H_5	+++	++	++	++	++	++	+++	++
2j	4-CH_3	*o*-C_6H_4OH	+++	++	++	++	++	+	++	++
2k	4-CH_3	*p*- $C_6H_4OCH_3$	+++	+++	+++	+++	++++	++	+++	++
2l	4-CH_3	*p*- C_6H_4Cl	++++	+++	+++	++	+++	+++	++++	++
DMF			--		--		--		--	
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

Anti-inflammatory activity

All the newly synthesized compounds and reference drug phenylbutazone have been examined for their anti-inflammatory activity. The pharmacological results of synthesized compounds have been reported in (Table 2). All the compounds have shown anti-inflammatory activity ranging from 20.4- 27.4% at the dose of 50 mg/kg body weight.

The results obtained clearly show that compounds **2b, 2h** and **2l** exhibit moderate activity. Carrageenan induced paw edema is a biphasic response. The first phase was mediated through the release of Histamine, serotonin & Kinin, where as the second phase is related to the release of prostaglandin and slow reacting substances which peak at 4 hour. The synthesized compounds produced significant inhibition of Carrageenan induced paw edema.

Table 2: Anti-inflammatory activity (% Inhibition) of 2-aryl-3-(-6-substituted benzothiazolyl)-1,3-thiazolidine-4-ones

S.No.	Compounds	% Inhibition (50 mg/kg body weight)
1	2b	22.2
2	2h	20.4
3	2l	24.7
4	Phenyl butanone	38.9

Antiulcer activity

All the synthesized compounds and reference drug ranitidine have been examined for their antiulcer activity. The pharmacological results of synthesized compounds have been reported in (Table 3).

The entire synthesized compounds show good activity as compared with standard drug (ranitidine). Compounds **2b, 2h** and **2l** have shown good activity in Aspirin Induced Ulcer (ASP). In case of Ethanol Induced ulcer compound **2l** shows moderate activity.

Antitumor activity

MTT assay method was carried out to estimate the effect of test compound on the growth of tumor cells. The human breast cancer cells lines (MCF-7) were employed. The human breast cancer cell line (MCF-7) and mammary cancer cell line (EVSA-7), their results are summarized in (Table 4) respectively. Compounds **2b** and **2h** exhibit good result against human breast cancer cells lines (MCF-7) and compounds **2b** and **2h** show good results against mammary cancer cell line (EVSA-7).

Entomological activity

Antifeedant activity: The antifeedant activity of the newly synthesized compounds was tested by a leaf dip method against larvae of *Spodoptera litura*. The results clearly indicate that the compounds **2a, 2e** and **2l** show higher antifeedant activity and compounds **2b, 2h, 2i** and **2k** show moderate activity against larvae of *Spodoptera litura* while the rest of the compounds exhibit lower activity as seen by their LC_{50}/LD_{50} results.

The results clearly show that the presence of methyl, nitro and bromo groups on the aromatic ring enhance the activity. The presence of methoxy, chloro and hydroxy group as on the aryl side ring also plays an important role in activity.

It may be found that these compounds may cause a spasm condition in insects by interacting with the active site of the enzyme responsible for nervous breakdown in insects (Table 5).

Table 3: Antiulcer (Gastro protective) activity of 2-aryl-3-(-6-substituted benzothiazolyl)-1,3-thiazolidine-4-ones

S.No.	Compounds	Aspirin Induced		Ethanol Induced	
		Ulcer Index (mm^2/rat)	Protective Ratio (%)	Ulcer Index (mm^2/rat)	Protective Ratio (%)
1	2b	7.1±0.54	61.21	19.7±5.2	18.17
2	2h	7.2±0.56	61.70	19.6±5.2	31.20
3	2l	7.2±0.56	61.70	19.6±5.3	33.72
4	Ranitidine	7.6±0.53	58.46	10.3±3.3	57.43
5	Aspirin	18.3±1.6	-	-	-
6	Ethanol	-	-	24.2±6.5	-

Table 4: Antitumor activity of 2-aryl-3-(-6-substituted benzothiazolyl)-1,3-thiazolidine-4-ones

S. No	Compounds	Cell No. x 10^4 (MCF-7)	Cell No. x 10^4 (EVSA-7)
1	2b	9.24 ± 0.72	9.66±0.90
2	2h	9.22±0.72	9.62±0.88
3	2l	11.89±1.12	10.68±1.08
4	Negative Control	10.21±1.01	10.23±1.03
5	Positive Control	40.26±3.23	42.24±4.22

MCF-7- Human breast adinocarcinoma cell line (breast cancer), EVSA-7- Mammary cancer cell line, Negative Control: Culture medium only, Positive Control: 17- β estradiol

Table 5: Antifeedant activity of 2-aryl-3-(-6-substituted benzothiazolyl)-1,3-thiazolidine-4-ones

Compounds	Fiducial Limits	Slop +	Chi. Sq. (3)	LC_{50}/LD_{50} At 24 hrs.
2a	0.30–0.48	1.25±0.14	3.48 (3)	0.37
2b	0.43–0.87	1.03±0.14	0.34 (3)	0.58
2c	0.84–2.34	1.06±0.15	0.70 (3)	1.24
2d	0.62–1.46	1.05±0.46	1.03 (3)	0.87
2e	0.30–0.47	1.28±0.14	3.42 (3)	0.39
2f	0.72–2.41	0.93±0.14	0.22 (3)	1.13
2g	0.83–2.33	1.08±0.15	0.79 (3)	1.24
2h	0.62–1.42	1.06±0.14	1.07 (3)	0.86
2i	0.43–0.87	1.03±0.14	0.34 (3)	0.58
2j	0.84–2.34	1.06±0.15	0.70 (3)	1.24
2k	0.43–0.87	1.03±0.14	0.34 (3)	0.58
2l	0.30–0.47	1.28±0.14	3.42 (3)	0.39

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

Compounds	Fiducial Limits	Slop +	Chi. Sq. (3)	LC_{50}/LD_{50} At 24 hrs.
2a	0.10–0.23	0.88±0.08	2.14 (3)	0.07
2b	0.08–0.23	0.65±0.07	6.12 (3)	0.13
2c	0.12–0.26	0.89±0.8	8.52 (3)	0.17
2d	0.05–0.10	0.97±0.8	13.22 (3)	0.07
2e	0.05–0.10	0.78±0.06	4.64 (3)	0.06
2f	0.07–0.22	0.76±0.06	5.63 (3)	0.14
2g	0.05–0.09	1.16±0.09	12.67 (3)	0.07
2h	0.04–0.09	0.69±0.06	4.64 (3)	0.05
2i	0.08–0.23	0.65±0.07	6.12 (3)	0.13
2j	0.36–1.89	0.64±0.08	3.57 (3)	0.70
2k	0.16–0.37	0.09±0.09	8.28 (3)	0.23
2l	0.08–0.20	0.75±0.7	5.53 (3)	0.12

Contact toxicity

The contact toxicity of these compounds was carried out by topical application method against larvae of *Spodoptera litura.* The results clearly indicate that the compounds **2c, 2h** and **2l** show good activity and compounds **2d, 2e, 2g** and **2i** show moderate activity and the rest of the compounds show lower to moderate activity against the mites (Table 7).

Stomach toxicity

The stomach toxicity of these compounds was carried out by leaf dip method using fourth instars larvae of *Spodoptera litura.* The results clearly indicate that the compounds **2b** and **2l** show good stomach toxicity against the larvae of the insect and compounds **2c, 2d, 2e, 2g, 2h, 2j** and **2k** exhibit moderate activity against the mites (Table 8).

Table 7: Contact toxicity of 2-aryl-3-(-6-substituted benzothiazolyl)-1,3-thiazolidine-4-ones

Compounds	Fiducial Limits	Slop +	Chi. Sq. (3)	LC_{50}/LD_{50} At 24 hrs.
2a	1.33–3.99	1.42±0.20	2.38 (3)	2.01
2b	1.61–9.30	1.07±0.17	0.67 (3)	2.83
2c	0.28–0.40	1.96±0.16	4.39 (3)	0.33
2d	0.56–1.05	1.32±0.15	0.63 (3)	0.73
2e	0.56–1.05	1.32±0.15	0.63 (3)	0.73
2f	1.87–12.07	1.09±0.19	1.63 (3)	3.52
2g	0.43–0.75	1.63±0.16	2.94 (3)	0.58
2h	0.39–0.59	1.67±0.15	5.62 (3)	0.46
2i	0.74–1.32	1.62±0.18	3.24 (3)	0.94
2j	1.57–9.32	1.07±0.17	0.72 (3)	2.83
2k	1.61–9.30	1.07±0.17	0.67 (3)	2.83
2l	0.41–0.61	1.63±0.15	1.84 (3)	0.49

Table 8: Stomach toxicity of 2-aryl-3-(-6-substituted benzothiazolyl)-1,3-thiazolidine-4-ones

Compounds	Fiducial Limits	Slop +	Chi. Sq. (3)	LC_{50}/LD_{50} At 24 hrs.
2a	0.86–1.99	1.28±0.16	0.80 (3)	1.20
2b	0.49–0.77	1.57±0.16	2.79 (3)	0.60
2c	0.54–0.90	1.49±0.16	3.39 (3)	0.68
2d	0.57–1.05	1.32±0.15	0.63 (3)	0.74
2e	0.55–0.97	1.32±0.15	0.69 (3)	0.73
2f	0.85–1.82	1.22±0.16	0.72 (3)	1.12
2g	0.56–0.97	1.33±0.15	0.63 (3)	0.75
2h	0.55–0.90	1.48±0.16	3.37 (3)	0.67
2i	0.85–1.82	1.22±0.16	0.72 (3)	1.12
2j	0.74–1.32	1.62±0.18	3.24 (3)	0.94
2k	0.54–0.90	1.49±0.16	3.39 (3)	0.68
2l	0.49–0.77	1.57±0.16	2.79 (3)	0.60

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 Table1 indicate that among the synthesized compounds **2d, 2e, 2h, 2k, 2l** possessed good antibacterial activity. However, the activities of the tested compounds are much less than those of standard antibacterial agents used. These compounds also show potent antiulcer, anti-inflammatory, antitumor activity, 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 future.

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REFERENCES

1. Yoshida M, Hayakawa, Hayashi N, Agatsuma T, Oda Y, Tanzawa F, Iwasaki S, Koyama K, Furukawa H, Kurakata S, Sugano Y. Synthesis and biological evaluation of benzothiazole derivatives as potent antitumor agents. Bioorg. Med. Chem. 2005; 15 (14): 3328-32.
2. Suvarna K, Swain SP, Gandhi AM. Synthesis and evaluation of novel benzothiazole derivatives against human cervical cancer cell lines. Indian J. Pharm. Sci. 2007; 69 (1): 46-50.
3. Giorgioni G, Accorroni B, Stefano AD, Marucci G, Siniscalchi A, Claudi F. Benzimidazole, benzoxazole and benzothiazole derivatives as 5HT2B receptor ligands, synthesis and preliminary pharmacological evaluation. Med. Chem. Res. 2005; 14 (2): 57-73.
4. Kaur H, Kumar S, Singh I, Saxena KK, Kumar A. Synthesis, characterization and biological activity of various substituted benzothiazole derivatives. Digest J. Nanomaterials and Biostructures 2010; 5 (1): 67-76.
5. Paramashivappa R, Phani KP, Rao PVS, Rao S. Design, synthesis and biological evaluation of benzimidazole/benzothiazole and benzoxazole derivatives as cyclooxygenase inhibitors. Bioorg. Med. Chem. Lett. 2003; 13 (4): 657-60.
6. Mahran MA, William S, Ramzy F, Sembel AM. Synthesis and in vitro evaluation of new benzothiazole derivatives as schistosomicidal agents. Molecules 2007; 12: 622-33.
7. Nagarajan SR, De CGA, Getman DP, Lu HF, Sikorski, Walker JL. Discovery of novel benzothiazolesulfonamides as potent inhibitors of HIV-1 protease. Bioorg. Med. Chem. Lett. 2003; 11 (22): 4769-77.
8. Pareek, PK, Mithlesh, Kriplani P, Tiwari R, Ojha KG. Rapid synthesis and biological activities of some new benzothiazol-2-ylhexahydro-S- triazine derivatives. Phosphorus, Sulfur, and Silicon 2010; 185 (7): 1338-1345.
9. Mithlesh, Pareek PK, Kant R, Shukla SK, Ojha KG, Rapid synthesis and biological evaluation of 1,4-dihydropyridine

derivatives containing a benzothiazolyl moiety. Cent. Eur. J. Chem. 2010, 8 (1), 163-173.

10. Kashiyama E, Hutchinson I, Chua MS, Stinson SF, Philips LR, Kaur G, Sansville EA, Bradshaw TD, Westwell AD, Stevens MFG. Synthesis, metabolic formation, and biological properties of the C- and N-oxidation products of antitumor 2-(4-aminophenyl)benzothiazoles. J. Med. Chem.1999; 42 (20): 4172-84.
11. Vigorita MG, Ottana R, Monforte F, Maccari R, Trovato A, Monforte MT, Taviano MF. Synthesis and antiinflammatory, analgesic activity of 3,3'-(1,2-ethanediyl)-bis[2-aryl-4-thiazolidinone] chiral compounds. Bioorg. Med.Chem. Lett. 2001; 11: 2791-94.
12. Rao A, Chimirri A, Ferro S, Monforte AM, Monfort P, Zappala M. Microwave-assisted synthesis of benzimidazole and thiazolidinone derivatives as HIV-1 RT inhibitors. Arkivoc 2004; 5: 147-155.
13. Murugesan V, Prabhakar YS, Katti SB. CoMFA and CoMSIA studies on thiazolidin-4-one as anti-HIV-1 agents, J. Mol. Graph. Model. 2009; 27 (6): 735-743.
14. Balzarini J, Krzesinsk BO, Maeerin JK, Orzesko A. Synthesis and anti-HIV studies of 2- and 3-adamantyl-substituted thiazolidin-4-ones. Eur. J. Med. Chem. 2009; 44 (1): 303-311.
15. Chavan AA, Pai NR. Synthesis and antimicrobial screening of 5-arylidene-2-imino-4-thiazolidinones. Arkivoc 2007; 16: 148-155.
16. Srivastava T, Gaikwad AK, Wahjuihaq, Sinha S, Katti BS. Synthesis and biological evaluation of 4-thiazolidinone derivatives as potential antimycobacterial agents. Arkivoc 2005; 2: 120-130.
17. Pareek D, Chaudhary M, Pareek PK, Kant R, Ojha KG and Pareek A. Synthesis of some bioactive 4-thiazolidinone derivatives incorporating benzothiazole moiety. Der Chemica Sinica 2010; 1 (3): 22-35.
18. Pareek D, Chaudhary M, Pareek PK, Kant R, Ojha KG, Pareek R and Pareek A. Synthesis and biological evaluation of 4-thiazolidinone derivatives incorporating benzothiazole moiety. Der Pharmacia Sinica 2011; 2 (1): 170-181.
19. Sharma MC, Sahu NK, Kohali DV, Chaturvedi SC, Sharma S. QSAR, synthesis and biological activity studies of some thiazolidinones derivatives. Digest Journal of Nanomaterials and Biostructures 2009; 14 (1): 223-232.
20. Rana PB, Mistry BD, Desai KR. Green chemistry: conventional and microwave induced synthesis of various thiazolidinone derivatives from 3-{[(1E)-(2'-chloro-7'-methoxyquinoline-3'-yl)methylene]amino}-4-(substitutedphenyldiazenyl)phenol and their antimicrobial screening. Arkivoc 2008; 15: 262-279.
21. Patel KD, Mistry BD, Deasi KR. Synthesis and antimicrobial activity of 2-Aryl-3-[3′- (2′′,4′′,6′′-trichlorophenoxymethyl)-5′-mercapto-1′,2′,4′-triazol-4′-yl]-5-substituted-4 thiazolidinones. J. Indian Chem. Soc. 2006; 83: 94-96.
22. Diurno MV, Mazzoni O, Izzo AA, Bolognese A. Synthesis and pharmacological activity of 2-(substituted phenyl)-3-[2 or 3-[(4-substituted phenyl-4-hydroxy)piperidino]ethyl or propyl]-1,3-thiazolidin-4-ones. Farmaco 1997; 52 (4): 237-41.
23. Ergene N, Capan G. Synthesis and anticonvulsant activity of new 4-thiazolidone and 4-thiazoline derivatives. Farmaco 1994; 49 (6): 449-51.
24. Diurno MV, Mazzoni O, Correale G, Monterry IG. Synthesis and structure-activity relationships of 2-(substituted phenyl)-3-[3-(N,N-dimethylamino)propyl]-1,3-thiazolidin-4-ones acting as H1-histamine antagonists. Farmaco 1999; 54 (9): 579-83.
25. Kato T, Ozaki T, Tamura K. Novel calcium antagonists with both calcium overload inhibition and antioxidant activity. 2. Structure-activity relationships of thiazolidinone derivatives. J. Med. Chem.1999; 42 (16): 3134-46.
26. Kato T, Ozaki T, Ohi N. Improved synthetic methods of CP-060S, a novel cardioprotective drug. Tetrahedron Asymmetry 1999; 10: 3963-68.
27. Adachi Y, Suzuki Y, Homma N, Fukazawa M, Tamura K, Nishie I, Kuromaru O. The anti-ischemic effects of CP-060S during pacing-induced ischemia in anesthetized dogs. Eur. J. Pharmacol. 1999; 367: 267-73.
28. Ottana R, Mazzon E, Dugo L, Monforte F, Maccari R, Sautebin L, De Luca G, Vigorita MG, Alcaro S, Ortuso F. Modeling and biological evaluation of 3,3'-(1,2-ethanediyl)bis[2-(4-methoxyphenyl)-thiazolidin-4-one], a new synthetic cyclooxygenase-2 inhibitor, Eur. J. Pharmacol. 2002; 448 (1): 71-80.
29. Jacob N and Kutty GN. Synthesis and hypolipidemic activity of a thiazo-lidinone directive, Indian Drugs 2004; 41(2): 76-79.
30. Chandrappa S, Vinay K, Srikanta BM, AnandaKumar CS, Prasanna DS, Thimmwda NR, Shylaja, Dharmesh M, Rangappa KS. Inhibition of gastric H+, K+-ATPase by novel thiazolidinone derivatives. J. Sulfur Chem. 2010; 31: 189-96.
31. Tonghui M, Thiagarajah JR, Yang H, Sonawane DN, Chiara F, Galietta JV and Verkman AS. Thiazolidinone CFTR inhibitor identified by high-throughput screening blocks cholera toxin–induced intestinal fluid secretion. J. Clin. Invest. 2002; 110: 1651-58.
32. Tanabe Y, Yamamoto H, Murakami M, Yanagi K, Kubota Y, Okumura H, Sanemitsu Y, Suzukamo G. Synthetic study of the highly potent and selective anti-platelet activating factor thiazolidin-4-one agents and related compounds. J. Chem. Soc. Perkin Trans. 1995; 1: 935-47.
33. Kato Y, Kita Y, Nishio M, Hirasawa Y, Ito K, Yamanaka T, Motoyama Y, Seki. In vitro antiplatelet profile of FR171113, a novel non-peptide thrombin receptor antagonist. Eur. J. Pharmacol. 1999; 384: 197-202.
34. Voss ME, Carter PH, Tebben AJ, Scherle PA, Brown GD, Thompson LA, Xu M, Lo YC, Yang-Liu RRQ. Both 5-arylidene-2-thioxodihydropyrimidine-4,6(1H,5H)-diones and 3-thioxo-2,3-dihydro-1H-imidazo[1,5-a]indol-1-ones are light-dependent tumor necrosis factor-alpha antagonists. Bioorg. Med. Chem. Lett. 2003; 13(3): 533-38.
35. Mithlesh, Pareek PK, Chippa H, Kant R, Ojha KG. Microwave synthesis of new biologically important 1,4-dihydropyridines containing benzothiazole moiety. Collection of Czechoslovak Chemical Communications 2010; 75(3): 275-87.
36. Pareek PK, Mithlesh, Pareek D, Chaudhary M, Pareek A, Kant R, Ojha KG. Rapid synthesis of some medicinally important hexahydro-s-triazine derivatives incorporating benzothiazole moiety. Main Group Chemistry 2011; 10: 63-71.
37. Cruickshank R, Duguid JP, Marmion BP, Swam HA. The practical of medical microbiology, 12th ed., Churchill Livingstone: London; 1975; p 544.
38. Winter CA, Risely EA and Nuss GW. Carrageenin-induced edema in hind paws of the rat as an assay for anti-inflammatory drugs. Proc. Soc. Exp. Biol. 1962; 111: 544-47.
39. Mosamann MT. Rapid colorimetric assay for cellular growth and survival: application to proliferation and cytotoxicity assays. J. Immunol. Methods. 1983; 65: 55-63.
40. Wasserman TH, Twentyman P. Use of a colorimetric microtiter (MTT) assay in determining the radiosensitivity of cells from murine solid tumors. Int. J. Radiant. Oncol. Biol. Phys. 1988; 15(3): 699-702.
41. Van-de Loosdrecht AA. A tetrazolium-based colorimetric MTT assay to quantitate human monocyte mediated cytotoxicity against leukemic cells from cell lines and patients with acute myeloid leukemia. J. Immunol. Methods. 1994; 174: 311-20.
42. Shelton AM, Robertson JL, Tang JD. Resistance of diamondback moth (Lepidoptera: Plutellidae) to Bacillus thuringiensis subspecies in the field. J. Econ. Entomol. 1993; 86(9): 697-705.
43. Leonardi MG, Cappelloza S, Ianne P, Cappelloza L, Parenti P, Giordana B. Effects of the topical application of an insect growth regulator (fenoxycarb) on some physiological parameters in the fifth instar larvae of the silkworm Bombyx mori. Compedium of Biochemistry and Physiology 1996; 113(B): 361-65.
44. Kant R, Amresh G, Chandrashekar K, Anil KKS. Synthesis and biological activity on some organoantimony (III) compounds. Phosphorus, Sulfur, Silicon 2008; 183: 1410-19.