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Synthesis and antibacterial activity of 3-chloro-4-(substituted-phenyl)-azetidinonyl/thiazolidinonyl-4-(3-acetanilido) oxa/thiazoles

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ABSTRACT

Cyclocandensation of 2-[(substitutedbenzylidene)amino]-4-(3-acetanilido)oxazoles **(3a-3j)** and 2-[(substitutedbenzylidene)amino]-4-(3-acetanilido)thiazoles **(7a-7j)** with chloroacetyl chloride give and N-2-[3-chloro-4-(substitutedphenyl)-2-oxoazetidin-1-yl]-4-(3-acetanilido)oxazoles **(4a-4j)** and N-2-[3-chloro-4-(substitutedphenyl)-2-oxoazetidin-1-yl]-4-(3-acetanilido)thiazoles **(8a-8j)** respectively. N-2-[2-(substitutedphenyl)-4-oxo-1-thiazolidinyl]-4-(3-acetanilido)oxazoles **(5a-5j)** and N-2-[2-(substitutedphenyl)-4-oxo-1-thiazolidinyl]-4-(3-acetanilido) oxazoles **(5a-5j)** have been synthesized by reaction of compounds **(3a-3j)** and **(7a-7j)** with thioglycolic acid in presence of anhydrous zinc chloride. All the synthesized compounds were screened for their antibacterial activity and compared with reference drugs ampicillin and ciprofloxacin. The compound was the most potent compound of this series. Structure of all the synthesized compounds have been characterized by elemental (C, H, N) and spectral (IR and ^{1}H NMR) analysis.

KEYWORDS

Azetidinonyloxazole;
Thiazolidinonyloxazole;
Azetidinonylthiazole;
Thiazolidinonylthiazole.

INTRODUCTION

The chemistry of heterocyclic compounds has attracted attention in recent time due to its increasing importance in the field of pharmaceuticals and industries. Substitution pattern in oxazole and thiazole derivatives play a pivotal role in delineating the biological activities like antibacterial[1,2], antifungal[3,4], anti-inflammatory[5,6]. Several scientistes have synthesized several oxazole and thiazole derivatives which posses potent antibacterial activity. Further various derivatives of azetidinone[7] and thiazolidinone[8] have also been reported to possess antibacterial activity. In light of above observations it was thought worthwhile to synthesized some new substituted oxa/thiazole derivatives by incorporation of azetidinone and thiazolidinone moieties with the hope to get better antibacterial agents.

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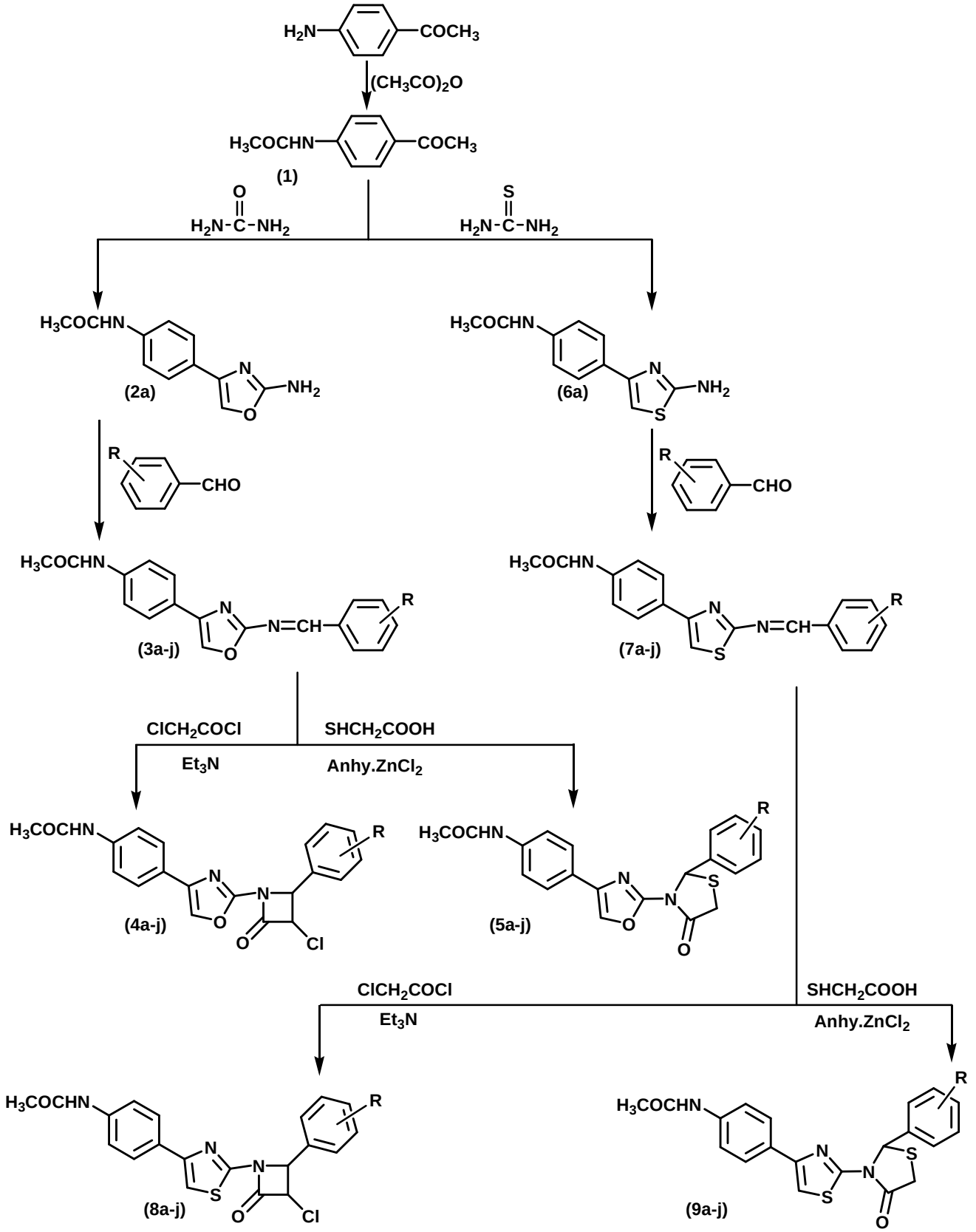
Synthesis routes of oxa/thiazole derivatives are outlined in Scheme 1. Accordingly reaction of m-aminoacetophenone with acetic anhydride afforded m-Acetamidoacetophenone **(1)**. Compound **(1)** converted into 2-Amino-4-(3-acetanilido)oxa/thiazole **(2a)/(6a)** by the reaction of iodine mixture and urea/



R = 4-OCH_3, 4-OH, 4-Cl, 2-Cl, 2-OCH_3, 4-$N(CH_3)_2$, 4-OH & 3-OCH_3, 2,6-Cl, 2,6-Br, 2-OH

Scheme 1

thiourea. 2-[(substitutedbenzylidene)amino]-4-(3-acetanilido)oxa/thiazoles **(3a-3j)/(7a-7j)** on reaction with dry dioxane and triethylamine yielded N-2-[3-chloro-4-(4-methoxyphenyl)-2-oxoazetidin-1-yl]-4-(3-acetanilido)oxazole/thiazoles **(4a-4j)/(8a-8j)**. Compounds **(4a-4j)/(8a-8j)** undergo cycloaddition reaction with thioglycolic acid in presence of anhydrous zinc chloride to furnish N-2-[2-(substitutedphenyl)-4-oxo-1-thiazolidinyl]-4-(3-acetanilido)oxazoles **(5a-5j)/(9a-9j)**.

EXPERIMENTAL

m-Acetamidoacetophenone (1)

A mixture of m-aminoacetophenone (1.0 mole) and acetic anhydride (30mL) was refluxed for 2 h and the reaction mixture was cooled. The solid thus obtained was filtered, dried and recrystallized from ethanol to yield compound 1 96% m.p.: 220°C. IR (KBr) νcm^{-1}: 3295 (NH), 2930 (CH_3), 1750 (C = O), 1675 (C = O, amide), 1621 (C = C aromatic ring). ^1H NMR ($CDCl_3$ + DMSO-d_6) δ in ppm: 7.40-8.20 (m, 4H, Ar-H), 7.26 (s, 1H, NH exchangeable with D_2O), 2.30 (s, 3H, $NHCOCH_3$), 2.10 (s, 3H, $COCH_3$). Anal. Calcd. for $C_{10}H_{11}NO_2$: C, 67.78; H, 6.26; N, 7.90; Found: C, 67.56; H, 6.45; N, 7.86.

2-Amino-4-(3-acetanilido)oxazole (2a)

A mixture of iodine (0.3 mole) and urea (0.6 mole) was triturated and the reaction mixture transfered into a conical flask containing m-acetamidoacetophenone **(1)** (0.3 mole), and heated for 8 h. The solid obtained was washed with diethyl ether, after and then it was washed with sodium thiosulphate. Finally, the reaction mixture was poured in ice water. The solid thus obtained was filtered, washed with water, dried and recrytallized from acetone/hexane to yield compound **(2a)** (94%) m.p.: 190°C; IR (KBr) νcm^{-1}: 3340 (NH_2), 3291 (NH), 1671 (C = O, amide), 1620 (C = C of aromatic ring), 1070 (C-O-C of oxazole). ^1H NMR ($CDCl_3$ + DMSO-d_6) δ in ppm: 9.00 (s, 2H, NH_2 exchangeable with D_2O), 7.40-8.24 (m, 4H, Ar-H), 7.27 (s, 1H, NH exchangeable with D_2O), 6.95 (s, 1H, CH at C_5 of oxazole), 2.34 (s, 3H, $NHCOCH_3$). Anal. Calcd. for $C_{11}H_{11}N_3O_2$: C, 60.82; H, 5.10; N, 19.34; Found: C, 60.65; H, 5.30; N, 19.58.

2-[(substitutedbenzylidene)amino]-4-(3-acetanilido)oxazoles (3a-3j)

A mixture of compound 2-Amino-4-(3-acetanilido) oxazole **(2a)** (0.5mole) and 4-methoxy benzaldehyde (0.5 mole) in 40ml of ethanol along with glacial acetic acid (2-3 drops) was refluxed for 12 h. The reaction mixture was cooled. The solid obtained was filtered, washed with water, dried and recrystallized from appropriate solvents to furnish compounds **(3a-3j)**.

2-[(4-methoxybenzylidene)amino]-4-(3-acetanilido)oxazole (3a)

Yield (93%) (Methanol) m.p.: 221°C; IR (KBr) νcm^{-1}: 3292 (NH), 2925 (CH_3), 1671 (C = O, amide), 1660 (N = C), 1620 (C = C of aromatic ring), 1507 (C-N), 1225 (OCH_3), 1070 (C-O-C of oxazole). ^1H NMR ($CDCl_3$ + DMSO-d_6) δ in ppm: 8.87 (s, 1H, N = CH), 7.41-8.21 (m, 8H, Ar-H), 7.26 (s, 1H, NH exchangeable with D_2O), 6.96 (s, 1H, CH at C_5 of oxazole), 3.37 (s, 3H, OCH_3), 2.15 (s, 3H, $NHCOCH_3$). Anal. Calcd. for $C_{19}H_{17}N_3O_3$: C, 68.05; H, 5.11; N, 12.53; Found: C, 68.25; H, 5.08; N, 12.67.

2-[(4-hydroxybenzylidene)amino]-4-(3-acetanilido)oxazole (3b)

Yield (92%) (Ethanol) m.p.: 223°C; IR (KBr) νcm^{-1}: 3425 (OH), 3291 (NH), 1670 (C = O, amide), 1662 (N = C), 1624 (C = C of aromatic ring), 1510 (C-N), 1074 (C-O-C of oxazole). ^1H NMR ($CDCl_3$ + DMSO-d_6) δ in ppm: 11.01 (s, 1H, OH exchangeable with D_2O), 8.86 (s, 1H, N = CH), 7.42-8.23 (m, 8H, Ar-H), 7.24 (s, 1H, NH exchangeable with D_2O), 6.95 (s, 1H, CH at C_5 of oxazole), 2.17 (s, 3H, $NHCOCH_3$). Anal. Calcd. for $C_{18}H_{15}N_3O_3$: C, 67.28; H, 4.71; N, 13.08; Found: C, 67.30; H, 4.83; N, 13.20.

2-[(4-chlorobenzylidene)amino]-4-(3-acetanilido)oxazole (3c)

Yield (91%) (Acetone) m.p.: 224°C; IR (KBr) νcm^{-1}: 3296 (NH), 1675 (C = O, amide), 1665 (N = C), 1628 (C = C of aromatic ring), 1511 (C-N), 1079 (C-O-C of oxazole), 760 (C-Cl). ^1H NMR ($CDCl_3$ + DMSO-d_6) δ in ppm: 8.87 (s, 1H, N = CH), 7.41-8.22 (m, 8H, Ar-H), 7.25 (s, 1H, NH exchangeable with D_2O), 6.97 (s, 1H, CH at C_5 of oxazole), 2.16 (s, 3H, $NHCOCH_3$). Anal. Calcd. for $C_{18}H_{14}ClN_3O_2$: C, 63.63; H, 4.15; N,

12.37; Found: C, 63.84; H, 4.34; N, 12.57.

2-[(2-chlorobenzylidene)amino]-4-(3-acetanilido)oxazole (3d)

Yield (90%) (Petroleum ether) m.p.: 227°C; IR (KBr) νcm^{-1}: 3290 (NH), 1672 (C = O, amide), 1664 (N = C), 1623 (C = C of aromatic ring), 1511 (C-N), 1076 (C-O-C of oxazole), 763 (C-Cl). ^1H NMR ($CDCl_3$ + DMSO-d_6) δ in ppm: 8.86 (s, 1H, N = CH), 7.40-8.20 (m, 8H, Ar-H), 7.28 (s, 1H, NH exchangeable with D_2O), 6.98 (s, 1H, CH at C_5 of oxazole), 2.00 (s, 3H, $COCH_3$). Anal. Calcd. for $C_{18}H_{14}ClN_3O_2$: C, 63.63; H, 4.15; N, 12.37; Found: C, 63.94; H, 4.36; N, 12.68.

2-[(2-methoxybenzylidene)amino]-4-(3-acetanilido)oxazole (3e)

Yield (89%) (Ethanol) m.p.: 229°C; IR (KBr) νcm^{-1}: 3292 (NH), 1675 (C = O, amide), 1667 (N = C), 1624 (C = C of aromatic ring), 1513 (C-N), 1229 (OCH_3), 1077 (C-O-C of oxazole). ^1H NMR ($CDCl_3$ + DMSO-d_6) δ in ppm: 8.87 (s, 1H, N = CH), 7.41-8.21 (m, 8H, Ar-H), 7.26 (s, 1H, NH exchangeable with D_2O), 6.98 (s, 1H, CH at C_5 of oxazole), 3.34 (s, 3H, OCH_3), 2.01 (s, 3H, $NHCOCH_3$). Anal. Calcd. for $C_{19}H_{17}N_3O_3$: C, 68.05; H, 5.11; N, 12.53; Found: C, 68.26; H, 5.32; N, 12.74.

2-[(4-(dimethylamino)benzylidene)amino]-4-(3-acetani- lido)oxazole (3f)

Yield (87%) (Methanol) m.p.: 230°C; IR (KBr) νcm^{-1}: 3294 (NH), 1679 (C = O, amide), 1669 (N = C), 1620 (C = C of aromatic ring), 1512 (C-N), 1079 (C-O-C of oxazole). ^1H NMR ($CDCl_3$ + DMSO-d_6) δ in ppm: 8.85 (s, 1H, N = CH), 7.40-8.20 (m, 8H, Ar-H), 7.27 (s, 1H, NH exchangeable with D_2O), 6.96 (s, 1H, CH at C_5 of oxazole), 2.89 (s, 6H, $N(CH_3)_2$), 2.17 (s, 3H, $NHCOCH_3$). Anal. Calcd. for $C_{20}H_{20}N_4O_2$: C, 68.95; H, 5.79; N, 16.08; Found: C, 68.88; H, 5.80; N, 16.11.

2-[(4-hydroxy-3-methoxybenzylidene)amino]-4-(3-acetanilido)oxazole (3g)

Yield (86%) (Acetone) m.p.: 234°C; IR (KBr) νcm^{-1}: 3451 (OH), 3293 (NH), 1674 (C = O,amide), 1669 (N = C), 1625 (C = C of aromatic ring), 1509 (C-N), 1075 (C-O-C of oxazole). ^1H NMR ($CDCl_3$ + DMSO-d_6) δ in ppm: 11.02 (s, 1H, OH exchangeable with D_2O), 8.88 (s, 1H, N = CH), 7.43-8.23 (m, 7H, Ar-H), 7.28 (s, 1H, NH exchangeable with D_2O), 6.98 (s, 1H, CH at C_5 of oxazole), 3.34 (s, 3H, OCH_3), 2.16 (s, 3H, $NHCOCH_3$). Anal. Calcd. for $C_{19}H_{17}N_3O_4$: C, 64.95; H, 4.88; N, 11.96; Found: C, 64.74; H, 4.49; N, 11.75.

2-[(2,6-dichlorobenzylidene)amino]-4-(3-acetanilido)oxazole (3h)

Yield (85%) (Ethanol) m.p.: 236°C; IR (KBr) νcm^{-1}: 3291 (NH), 1676 (C = O, amide), 1666 (N = C), 1628 (C = C of aromatic ring), 1507 (C-N), 1070 (C-O-C of oxazole), 762 (C-Cl). ^1H NMR ($CDCl_3$ + DMSO-d_6) δ in ppm: 8.86 (s, 1H, N = CH), 7.42-8.22 (m, 7H, Ar-H), 7.27 (s, 1H, NH exchangeable with D_2O), 6.97 (s, 1H, CH at C_5 of oxazole), 2.14 (s, 3H, $NHCOCH_3$). Anal. Calcd. for $C_{18}H_{13}Cl_2N_3O_2$: C, 57.77; H, 3.50;N, 11.23; Found: C, 57.98; H, 3.45; N, 11.45.

2-[(2,6-dibromobenzylidene)amino]-4-(3-acetanilido)oxazole (3i)

Yield (85%) (Methanol) m.p.: 240°C; IR (KBr) νcm^{-1}: 3294 (NH), 1672 (C = O, amide), 1670 (N = C), 1626 (C = C of aromatic ring), 1510 (C-N), 1074 (C-O-C of oxazole). ^1H NMR ($CDCl_3$ + DMSO-d_6) δ in ppm: 8.87 (s, 1H, N = CH), 7.40-8.41 (m, 7H, Ar-H), 7.26 (s, 1H, NH exchangeable with D_2O), 6.95 (s, 1H, CH at C_5 of oxazole), 2.15 (s, 3H, $NHCOCH_3$). Anal. Calcd. for $C_{18}H_{13}Br_2N_3O_2$: C, 46.68; H, 2.83; N, 9.07; Found: C, 46.99; H, 2.56; N, 9.40.

2-[(2-hydroxybenzylidene)amino]-4-(3-acetanilido)oxazole (3j)

Yield (82%) (DMF-water) m.p.: 243°C; IR (KBr) νcm^{-1}: 3455 (OH), 3295 (NH), 1674 (C = O, amide), 1669 (N = C), 1625 (C = C of aromatic ring), 1509 (C-N), 1070 (C-O-C of oxazole). ^1H NMR ($CDCl_3$ + DMSO-d_6) δ in ppm: 11.01 (s, 1H, OH exchangeable with D_2O), 8.86 (s, 1H, N = CH), 7.41-8.23 (m, 8H, Ar-H), 7.26 (s, 1H, NH exchangeable with D_2O), 6.96 (s, 1H, CH at C_5 of thiazole), 2.18 (s, 3H, $NHCOCH_3$). Anal. Calcd. for $C_{18}H_{15}N_3O_3$: C, 67.28; H, 4.71; N, 13.08; Found: C, 67.55; H, 4.95; N, 13.34.

N-2-[3-chloro-4-(substitutedphenyl)-2-oxoazetidin-1-yl]-4-(3-acetanilido)oxazoles (4a-4j)

A mixture of 2-[(substitutedbenzylidene)amino]-4-

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(3-acetanilido)oxazoles **(3a-3j)** (0.3 mole), dry dioxane (5ml) and triethylamine (0.6 mole) were taking in a conical flask. The reactions were stirred on an ice bath and when the temperature dropped below 5°C, then choroacetylchloride (0.015 mole) was added drop wise with stirring. After completion of addition the stirring was continued for 10 h at room temperature. The reaction mixtures were then kept a side for 52 h. Finally, the reaction masses were added to ice cold water to obtain the final product. It was filtered, washed with water, dried and recrystallized from appropriate solvents to yield compounds **(4a-4j)**.

N-2-[3-chloro-4-(4-methoxyphenyl)-2-oxoazetidin-1-yl]-4-(3-acetanilido)oxazole (4a)

Yield(81%) (Ethanol) m.p.: 255°C; IR (KBr) νcm^{-1}: 3296 (NH), 1679 (C = O, amide), 1669 (N = C), 1627 (C = C of aromatic ring), 1594 (C = O, cyclized), 1506 (C-N), 1371 (N-C), 1228 (OCH_3), 1072 (C-O-C of oxazole), 760 (C-Cl). ^{1}H NMR ($CDCl_3$ + DMSO-d_6) δ in ppm : 7.40-8.20 (m, 8H, Ar-H), 7.27 (s, 1H, NH exchangeable with D_2O), 6.97 (s, 1H, CH at C_5 of oxazole), 6.75 (d, 1H, N-CH of oxoazetidine), 3.75 (d, 1H, CH-Cl), 3.38 (s, 3H, OCH_3), 2.16 (s, 3H, $NHCOCH_3$). Anal. Calcd. for $C_{21}H_{18}ClN_3O_4$: C, 61.24; H, 4.41; N, 10.20; Found: C, 61.65; H, 4.56; N, 10.45.

N-2-[3-chloro-4-(4-hydroxyphenyl)-2-oxoazetidin-1-yl]-4-(3-acetanilido)oxazole (4b)

Yield (80%) (Methanol) m.p.: 257°C; IR (KBr) νcm^{-1}: 3452 (OH), 3296 (NH), 1676 (C = O, amide), 1667 (N = C), 1627 (C = C of aromatic ring), 1594 (C = O, cyclized), 1507 (C-N), 1373 (N-C), 1078 (C-O-C of oxazole), 760 (C-Cl). ^{1}H NMR ($CDCl_3$ + DMSO-d_6) δ in ppm: 11.03 (s, 1H, OH exchangeable with D_2O), 7.42-8.21 (m, 8H, Ar-H), 7.26 (s, 1H, NH exchangeable with D_2O), 6.97 (s, 1H, CH at C_5 of oxazole), 6.76 (d, 1H, N-CH of oxoazetidine), 3.75 (d, 1H, CH-Cl), 2.17 (s, 3H, $NHCOCH_3$). Anal. Calcd. for $C_{20}H_{16}Cl\ N_3O_4$: C, 60.38; H, 4.05; N, 10.56; Found: C, 60.67; H, 4.36; N, 10.87.

N-2-[3-chloro-4-(4-chlorophenyl)-2-oxoazetidin-1-yl]-4-(3-acetanilido)oxazole (4c)

Yield (79%) (Petroleum ether) m.p.: 260°C; IR (KBr) νcm^{-1}: 3295 (NH), 1677 (C = O, amide), 1662 (N = C), 1624 (C = C of aromatic ring), 1593 (C = O, cyclized), 1506 (C-N), 1371 (N-C), 1079 (C-O-C of oxazole), 761 (C-Cl). ^{1}H NMR ($CDCl_3$ + DMSO-d_6) δ in ppm: 7.40-8.20 (m, 8H, Ar-H), 7.27 (s, 1H, NH exchangeable with D_2O), 6.96 (s, 1H, CH at C_5 of oxazole), 6.78 (d, 1H, N-CH of oxoazitidine), 3.75 (d, 1H, CH-Cl), 2.16 (s, 3H, $NHCOCH_3$). Anal. Calcd. for $C_{20}H_{15}Cl_2\ N_3O_3$: C, 57.71; H, 3.63; N, 10.09; Found: C, 57.89; H, 3.95; N, 10.26.

N-2-[3-chloro-4-(2-chlorophenyl)-2-oxoazetidin-1-yl]-4-(3-acetanilido)oxazole (4d)

Yield (78%) (Ethanol) m.p.: 263°C; IR (KBr) νcm^{-1}: 3293 (NH), 1674 (C = O, amide), 1669 (N = C), 1625 (C = C of aromatic ring), 1595 (C = O, cyclized), 1508 (C-N), 1371 (N-C), 1075 (C-O-C of oxazole), 760 (C-Cl). ^{1}H NMR ($CDCl_3$ + DMSO-d_6) δ in ppm : 7.42-8.23 (m, 8H, Ar-H), 7.26 (s, 1H, NH exchangeable with D_2O), 6.98 (s, 1H, CH at C_5 of oxazole), 6.74 (d, 1H, N-CH of oxoazetidine), 3.77 (d, 1H, CH-Cl), 2.17 (s, 3H, $NHCOCH_3$). Anal. Calcd. for $C_{20}H_{15}Cl_2\ N_3O_3$: C, 57.71; H, 3.63; N, 10.09; Found: C, 57.89; H, 3.95; N, 10.26.

N-2-[3-chloro-4-(2-methoxyphenyl)-2-oxoazetidin-1-yl]-4-(3-acetanilido)oxazole (4e)

Yield (76%) (Acetone) m.p.: 267°C; IR (KBr) νcm^{-1}: 3295 (NH), 1675 (C = O, amide), 1668 (N = C), 1628 (C = C of aromatic ring), 1594 (C = O, cyclized), 1509 (C-N), 1370 (N-C), 1228 (OCH_3), 1073 (C-O-C of oxazole), 761 (C-Cl). ^{1}H NMR ($CDCl_3$ + DMSO-d_6) δ in ppm: 7.41-8.21 (m, 8H, Ar-H), 7.26 (s, 1H, NH exchangeable with D_2O), 6.98 (s, 1H, CH at C_5 of oxazole), 6.75 (d, 1H, N-CH of oxoazetidine), 3.78 (d, 1H, CH-Cl), 3.38 (s, 3H, OCH_3), 2.16 (s, 3H, $NHCOCH_3$). Anal. Calcd. for $C_{21}H_{18}Cl\ N_3O_4$: C, 61.24; H, 4.41; N, 10.20; Found: C, 61.65; H, 4.56; N, 10.45.

N-2-[3-chloro-4-(4-(dimethylamino)phenyl)-2-oxoazetidin-1-yl]-4-(3-acetanilido)oxazole (4f)

Yield (75%) (Ethanol) m.p.: 270°C; IR (KBr) νcm^{-1}: 3294 (NH), 1674 (C = O, amide), 1665 (N = C), 1626 (C = C of aromatic ring), 1595 (C = O, cyclized), 1506 (C-N), 1376 (N-C), 1076 (C-O-C of oxazole) 763 (C-Cl). ^{1}H NMR ($CDCl_3$ + DMSO-d_6) δ in ppm : 7.40-8.20 (m, 8H, Ar-H), 7.27 (s, 1H,

NH exchangeable with D_2O), 6.97 (s, 1H, CH at C_5 of oxazole), 6.76 (d, 1H, N-CH of oxoazetidine), 3.78 (s, 1H, CH-Cl), 2.87 (s, 6H, $N(CH_3)_2$), 2.16 (s, 3H, $NHCOCH_3$). Anal. Calcd. for $C_{22}H_{21}Cl\ N_4O_3$: C, 62.19; H, 4.98; N, 13.19; Found: C, 62.35; H, 4.85; N, 13.34.

N-2-[3-chloro-4-(4-hydroxy-3-methoxyphenyl)-2-oxoazetidin-1-yl]-4-(3-acetanilido)oxazole (4g)

Yield (73%) (Methanol) m.p.: 274°C; IR (KBr) νcm^{-1}: 3453 (OH), 3296 (NH), 1676 (C = O, amide), 1668 (N = C), 1623 (C = C of aromatic ring), 1596 (C = O, cyclized), 1507 (C-N), 1373 (N-C), 1227 (OCH_3), 1074 (C-O-C of oxazole), 762 (C-Cl). ^1H NMR ($CDCl_3$ + DMSO-d_6) δ in ppm: 11.02 (s, 1H, OH exchangeable with D_2O), 7.42-8.22 (m, 7H, Ar-H), 7.27 (s, 1H, NH exchangeable with D_2O), 6.98 (s, 1H, CH at C_5 of oxazole), 6.75 (d, 1H, N-CH of oxoazetidine), 3.76 (d, 1H, CH-Cl), 3.37 (s, 3H, OCH_3), 2.17 (s, 3H, $NHCOCH_3$). Anal. Calcd. for $C_{21}H_{18}Cl\ N_3O_5$: C, 58.95; H, 4.24; N, 9.82; Found: C, 58.74; H, 4.56; N, 9.95.

N-2-[3-chloro-4-(2,6-dichlorophenyl)-2-oxoazetidi-1-yl]-4-(3-acetanilido)oxazole (4h)

Yield (72%) (DMF-water) m.p.: 228°C; IR (KBr) νcm^{-1}: 3292 (NH), 1671 (C = O, amide), 1667 (N = C), 1624 (C = C of aromatic ring), 1596 (C = O, cyclized), 1505 (C-N), 1372 (N-C), 1077 (C-O-C of oxazole), 761 (C-Cl). ^1H NMR ($CDCl_3$ + DMSO-d_6) δ in ppm: 7.40-8.21 (m, 7H, Ar-H,), 7.28 (s, 1H, NH exchangeable with D_2O), 6.98 (s, 1H, CH at C_5 of oxazole), 6.77 (d, 1H, N-CH of oxoazetidine), 3.75 (d, 1H, CH-Cl), 2.17 (s, 3H, $NHCOCH_3$). Anal. Calcd. for $C_{20}H_{14}Cl_3\ N_3O_3$: C, 53.30; H, 3.13; N, 9.32; Found: C, 53.57; H, 3.29; N, 9.50.

N-2-[3-chloro-4-(2,6-dibromophenyl)-2-oxoazetidin-1-yl]-4-(3-acetanilido)oxazole (4i)

Yield (71%) (Ethanol) m.p.: 281°C; IR (KBr) νcm^{-1}: 3193 (NH), 1674 (C = O, amide), 1664 (N = C), 1626 (C = C of aromatic ring), 1594 (C = O, cyclized), 1508 (C-N), 1373 (N-C), 1076 (C-O-C of oxazole), 762 (C-Cl), 612 (C-Br). ^1H NMR ($CDCl_3$ + DMSO-d_6) δ in ppm: 7.42-8.23 (m, 7H, Ar-H), 7.26 (s, 1H, NH exchangeable with D_2O), 6.98 (s, 1H, CH at C_5 of oxazole), 6.69 (d, 1H, N-CH of oxoazetidine), 3.77 (d, 1H, CH-Cl), 2.16 (s, 3H, $NHCOCH_3$). Anal. Calcd. for $C_{20}H_{14}Br_2Cl\ N_3O_3$: C, 44.52; H, 2.62; N, 7.79; Found: C, 44.57; H, 2.79; N, 7.50.

N-2-[3-chloro-4-(2-hydroxyphenyl)-2-oxoazetidin-1-yl]-4-(3-acetanilido)oxazole (4j)

Yield (72%) (Methanol) m.p.: 284°C; IR (KBr) νcm^{-1}: 3452 (OH), 3295 (NH), 1679 (C = O, amide), 1667 (N = C), 1628 (C = C of aromatic ring), 1591 (C = O, cyclized), 1503 (C-N), 1372 (N-C), 1075 (C-O-C of oxazole), 763 (C-Cl). ^1H NMR ($CDCl_3$ + DMSO-d_6) δ in ppm: 11.02 (s, 1H, OH exchangeable with D_2O), 7.40-8.21 (m, 8H, Ar-H), 7.28 (s, 1H, NH exchangeable with D_2O), 6.98 (s, 1H, CH at C_5 of oxazole), 6.76 (d, 1H, N-CH of oxoazitidine), 3.77 (d, 1H, CH-Cl), 2.17 (s, 3H, $NHCOCH_3$). Anal. Calcd. for $C_{20}H_{16}Cl\ N_3O_4$: C, 60.38; H, 4.05; N, 10.56; Found: C, 60.47; H, 4.19; N, 10.70.

N-2-[2-(substitutedphenyl)-4-oxo-1-thiazolidinyl]-4-(3-acetanilido)oxazoles (5a-5j)

To ethanolic solution (60mL) of compounds **(4a-4j)** (0.02 mole) thioglycolic acid (0.04 mole) was added in the presence of anhydrous zinc chloride. The reaction mixtures were refluxed for 10 h. The excess of solvent was distilled off and separated masses were poured in to ice water, filtered and washed with water and recrystallized from appropriate solvents to give compounds **(5a-5j)**.

N-2-[2-(4-methoxyphenyl)-4-oxo-1-thiazolidinyl]-4-(3-acetanilido)oxazole (5a)

Yield (69%) (Ethanol) m.p.: 245°C; IR (KBr) νcm^{-1}: 3298 (NH), 1678 (C = O, amide), 1666 (N = C), 1626 (C = C of aromatic ring), 1598 (C = O, cyclized), 1508 (C-N), 1372 (N-C), 1227 (OCH_3), 1072 (C-O-C of oxazole), 748 (C-S-C of oxothiazole). ^1H NMR ($CDCl_3$ + DMSO-d_6) δ in ppm: 7.40-8.20 (m, 8H, Ar-H), 7.26 (s, 1H, NH exchangeable with D_2O), 6.99 (s, 1H, CH at C_5 of oxazole), 6.70 (s, 1H, N-CH of oxothiazole), 3.75 (s, 2H, CH_2 of oxothiazole), 3.39 (s, 3H, OCH_3), 2.17 (s, 3H, $NHCOCH_3$). Anal. Calcd. for $C_{21}H_{19}\ N_3O_4S$: C, 61.60; H, 4.68; N, 10.26; Found: C, 61.73; H, 4.80; N, 10.45.

N-2-[2-(4-hydroxyphenyl)-4-oxo-1-thiazoli- dinyl]-4-(3-acetanilido)oxazole (5b)

Yield (68%) (Acetone) m.p.: 247°C; IR (KBr)

νcm^{-1}: 3452 (OH), 3299 (NH), 1677 (C = O, amide), 1667 (N = C), 1628 (C = C of aromatic ring), 1597 (C = O, cyclized), 1506 (C-N), 1374 (N-C), 1071 (C-O-C of oxazole), 761 (C-Cl), 746 (C-S-C of oxothiazole). ^{1}H NMR ($CDCl_3$ + DMSO-d_6) δ in ppm: 11.00 (s, 1H, OH exchangeable with D_2O), 7.42-8.21 (m, 8H, Ar-H), 7.27 (s, 1H, NH exchangeable with D_2O), 6.98 (s, 1H, CH at C_5 of oxazole), 6.71 (s, 1H, N-CH of oxothiazole), 3.74 (s, 2H, CH_2 of oxothiazole) 2.16 (s, 3H, $NHCOCH_3$). Anal. Calcd. for $C_{20}H_{17}N_3O_4S$: C, 60.75; H, 4.33; N, 10.63; Found: C, 60.53; H, 4.64; N, 10.85.

N-2-[2-(4-chlorophenyl)-4-oxo-1-thiazolidinyl]-4-(3-acetanilido)oxazole (5c)

Yield (67%) (Methanol) m.p.: 250°C; IR (KBr) νcm^{-1}: 3296 (NH), 1679 (C = O, amide), 1667 (N = C), 1625 (C = C of aromatic ring), 1596 (C = O, cyclized), 1504 (C-N), 1375 (N-C), 1073 (C-O-C of oxazole), 760 (C-Cl), 748 (C-S-C of oxothiazole). ^{1}H NMR ($CDCl_3$ + DMSO-d_6) δ in ppm: 7.41-8.21 (m, 8H, Ar-H), 7.28 (s, 1H, NH exchangeable with D_2O), 6.97 (s, 1H, CH at C_5 of oxazole), 6.70 (s, 1H, N-CH of oxothiozole), 3.75 (s,2H, CH_2 of oxothiazole), 2.16 (s, 3H, $NHCOCH_3$). Anal. Calcd. for $C_{20}H_{16}ClN_3O_3S$: C, 58.04; H, 3.90; N, 10.15;Found: C, 58.06; H, 3.81; N, 10.47.

N-2-[2-(2-chlorophenyl)-4-oxo-1-thiazolidinyl]-4-(3-acetanilido)oxazole (5d)

Yield (65%) (DMF-water) m.p.: 253°C; IR (KBr) νcm^{-1}: 3299 (NH), 1677 (C = O, amide), 1665 (N = C), 1628 (C = C of aromatic ring), 1599 (C = O, cyclized), 1508 (C-N), 1372 (N-C), 1075 (C-O-C of oxazole), 749 (C-S-C of oxothiazole).^{1}H NMR ($CDCl_3$ + DMSO-d_6) δ in ppm: 7.43-8.23 (m, 8H, Ar-H), 7.27 (s, 1H, NH exchangeable with D_2O), 6.99 (s, 1H, CH at C_5 of oxazole), 6.71 (s, 1H, N-CH of oxothiazole), 3.78 (s, 2H, CH_2 of oxothiazole), 2.17 (s, 3H, $NHCOCH_3$). Anal. Calcd. for $C_{20}H_{16}ClN_3O_3S$: C, 58.04; H, 3.90; N, 10.15; Found: C, 58.06; H, 3.81; N, 10.43.

N-2-[2-(2-methoxyphenyl)-4-oxo-1-thiazolidinyl]-4-(3-acetanilido)oxazole (5e)

Yield (64%) (Petroleum ether) m.p.: 256°C; IR (KBr) νcm^{-1}: 3297 (NH), 1676 (C = O, amide), 1665 (N = C), 1629 (C = C of aromatic ring), 1596 (C = O, cyclized), 1507 (C-N), 1376 (N-C), 1229 (OCH_3), 1073 (C-O-C of oxazole), 746 (C-S-C of oxothiazole). ^{1}H NMR ($CDCl_3$ + DMSO-d_6) δ in ppm: 7.40-8.21 (m, 8H, Ar-H), 7.28 (s, 1H, NH exchangeable with D_2O), 6.98 (s, 1H, CH at C_5 of oxazole), 6.72 (s, 1H, N-CH of oxothiozole), 3.76 (s, 2H, CH_2 of oxothiazole), 3.37 (s, 3H, OCH_3), 2.18 (s, 3H, $NHCOCH_3$). Anal. Calcd. for $C_{21}H_{19}N_3O_4S$: C, 61.60; H, 4.68; N, 10.26; Found: C, 61.83; H, 4.70; N, 10.34.

N-2-[2-(4-dimethylamino)phenyl)-4-oxo-1-thiazolidinyl]-4-(3-acetanilido)oxazole (5f)

Yield (62%) (Acetone) m.p.: 258°C; IR (KBr) νcm^{-1}: 3293 (NH), 1677 (C = O, amide), 1667 (N = C), 1626 (C = C of aromatic ring), 1597 (C = O, cyclized), 1509 (C-N), 1374 (N-C), 1075 (C-O-C of oxazole), 747 (C-S-C of oxothiazole). ^{1}H NMR ($CDCl_3$ + DMSO-d_6) δ in ppm: 7.40-8.20 (m, 8H, Ar-H), 7.27 (s, 1H, NH exchangeable with D_2O), 6.97 (s, 1H, CH at C_5 of oxazole), 6.71 (s, 1H, N-CH of oxothiozole), 3.78 (s, 2H, CH_2 of oxothiazole), 2.97 (s, 6H, $N(CH_3)_2$), 2.16 (s, 3H, $NHCOCH_3$). Anal. Calcd. for $C_{22}H_{22}N_4O_3S$: C, 62.54; H, 5.25; N, 13.26; Found: C, 62.65; H, 5.37; N, 13.34.

N-2-[2-(4-hydroxy-3-methoxyphenyl)-4-oxo-1-thiazolidinyl]-4-(3-acetanilido)oxazole (5g)

Yield (63%) (Ethanol) m.p.: 260°C; IR (KBr) νcm^{-1}: 3452 (OH), 3294 (NH), 1675 (C = O, amide), 1664 (N = C), 1628 (C = C of aromatic ring), 1597 (C = O, cyclized), 1506 (C-N), 1374 (N-C), 1229 (OCH_3), 1071 (C-O-C of oxazole), 748 (C-S-C of oxothiazole). ^{1}H NMR ($CDCl_3$ + DMSO-d_6) δ in ppm: 11.01 (s, 1H, OH exchangeable with D_2O), 7.42-8.21 (m, 7H, Ar-H), 7.27 (s, 1H, NH exchangeable with D_2O), 6.98 (s, 1H, CH at C_5 of oxazole), 6.70 (s, 1H, N-CH of oxothiozole), 3.76 (s, 2H, CH_2 of oxothiazole), 3.35 (s, 3H, OCH_3), 2.16 (s, 3H, $NHCOCH_3$). Anal. Calcd. for $C_{21}H_{19}N_3O_5S$: C, 59.28; H, 4.50; N, 9.88; Found: C, 59.37; H, 4.62; N, 9.86.

N-2-[2-(2,6-dichlorophenyl)-4-oxo-1-thiazolidinyl]-4-(3-acetanilido)oxazole (5h)

Yield (61%) (Methanol) m.p.: 263°C; IR (KBr) νcm^{-1}: 3295 (NH), 1673 (C = O, amide), 1668 (N =

C), 1629 (C = C of aromatic ring), 1593 (C = O, cyclized), 1508 (C-N), 1378 (N-C), 1075 (C-O-C of oxazole), 760 (C-Cl), 746 (C-S-C of oxothiazole). ^{1}H NMR ($CDCl_3$ + DMSO-d_6) δ in ppm: 7.41-8.21 (m, 7H, Ar-H), 7.28 (s, 1H, NH exchangeable with D_2O), 6.97 (s, 1H, CH at C_5 of oxazole), 6.72 (s, 1H, N-CH of oxothiozole), 3.75 (s, 2H, CH_2 of oxothiazole), 2.17 (s, 3H, $NHCOCH_3$). Anal. Calcd. for $C_{20}H_{15}Cl_2N_3O_3S$: C, 53.58; H, 3.37; N, 9.37; Found: C, 53.60; H, 3.66; N, 9.38.

N-2-[2-(2,6-dibromophenyl)-4-oxo-1-thiazolidinyl]-4-(3-acetanilido)oxazole (5i)

Yield (59%) (Acetone) m.p.: 265°C; IR (KBr) νcm^{-1}: 3299 (NH), 1676 (C = O, amide), 1667 (N = C), 1628 (C = C of aromatic ring), 1597 (C = O, cyclized), 1507 (C-N), 1374 (N-C), 1071 (C-O-C of oxazole), 748 (C-S-C of oxothiazole), 610 (C-Br). ^{1}H NMR ($CDCl_3$ + DMSO-d_6) δ in ppm: 7.40-8.21 (m, 7H, Ar-H), 7.27 (s, 1H, NH exchangeable with D_2O), 6.97 (s, 1H, CH at C_5 of oxazole), 6.71 (s, 1H, N-CH of oxothiozole), 3.76 (s, 2H, CH_2 of oxothiazole), 2.18 (s, 3H, $NHCOCH_3$). Anal. Calcd. for $C_{20}H_{15}Br_2N_3O_3S$: C, 44.71; H, 2.81; N, 7.82; Found: C, 44.92; H, 2.75; N, 7.66.

N-2-[2-(2-hydroxyphenyl)-4-oxo-1-thiazolidinyl]-4-(3-acetanilido)oxazole (5j)

Yield (58%) (DMF-water) m.p.: 284°C; IR (KBr) νcm^{-1}: 3452 (OH), 3295 (NH), 1677 (C = O, amide), 1669 (N = C), 1625 (C = C of aromatic ring), 1598 (C = O, cyclized), 1506 (C-N), 1379 (N-C), 1075 (C-O-C of oxazole), 746 (C-S-C of oxothiazole). ^{1}H NMR ($CDCl_3$ + DMSO-d_6) δ in ppm: 11.01 (s, 1H,OH exchangeable with D_2O), 7.42-8.22 (m, 8H, Ar-H), 7.26 (s, 1H, NH exchangeable with D_2O), 6.99 (s, 1H, CH at C_5 of oxazole), 6.70 (s, 1H, N-CH of oxothiozole), 3.78 (s, 2H, CH_2 of oxothiazole), 2.17 (s, 3H, $NHCOCH_3$). Anal. Calcd. for $C_{20}H_{17}N_3O_4S$: C, 60.75; H, 4.33; N, 10.63; Found: C, 60.78; H, 4.32; N, 10.64.

2-Amino-4-(3-acetanilido)thiazole (6a)

A mixture of iodine (0.02 mole) and thiourea (0.04 mole) was triturated and the mixture poured into a conical flask containing m-Acetamidoacetophenone compound **(1)** (0.02 mole). The reaction mixture was heated for 8 hr. The solid obtained was washed with diethyl ether, after and then it was washed with sodium thiosulphate. Finally, the reaction mixture was poured in ice water. The solid thus obtained was filtered, washed with water , dried and recrytallized from acetone/hexane to yield compound **(6a)** (57%) m.p.: 224°C; IR (KBr) νcm^{-1}: 3342 (NH_2), 3290 (NH), 1673 (C = O, amide), 1621 (C = C of aromatic ring), 745 (C-S-C of thiazole). ^{1}H NMR ($CDCl_3$ + DMSO-d_6) δ in ppm: 8.48 (s, 2H, NH_2 exchangeable with D_2O), 7.43-8.21 (m, 4H, Ar-H), 7.28 (s, 1H, NH exchangeable with D_2O), 6.97 (s, 1H, CH at C_5 of thiozole), 2.14 (s, 3H, $NHCOCH_3$). Anal. Calcd. for $C_{11}H_{11}N_3OS$: C, 56.63; H, 4.75; N, 18.01; Found: C, 56.85; H, 4.54; N, 18.36.

2-[(substitutedbenzylidene)amino]-4-(3-acetanilido)thiazoles (7a-7j)

A mixture of 2-Amino-4-(3-acetanilido)thiazole **(6a)** (0.01 mole) and 4-methoxy benzaldehyde (0.01 mole) in 40mL of ethanol along with glacial acetic acid (2-3 drops) were refluxed for 12 h. The reaction mixtures were cooled. The solids obtained were filtered, washed with water, dried and recrystallized from appropriate solvents to yield compounds **(7a-7j)**.

2-[(4-methoxybenzylidene)amino]-4-(3-acetanilido)thiazole (7a)

Yield (56%) (Acetone) m.p.: 223°C; IR (KBr) νcm^{-1}: 3294 (NH), 1675 (C = O, amide), 1665 (N = C), 1622 (C = C of aromatic ring), 1508 (C-N), 1227 (OCH_3), 746 (C-S-C of thiazole). ^{1}H NMR ($CDCl_3$ + DMSO-d_6) δ in ppm : 8.89 (s, 1H, N = CH), 7.40-8.20 (m, 8H, Ar-H), 7.26 (s, 1H, NH exchangeable with D_2O), 6.98 (s, 1H, CH at C_5 of thiazole), 3.37 (s, 3H, OCH_3), 2.17 (s, 3H, $NHCOCH_3$). Anal. Calcd. for $C_{19}H_{17}N_3O_2S$: C, 64.94; H, 4.88; N, 11.96; Found: C, 64.87; H, 4.69; N, 11.88.

2-[(4-hydroxybenzylidene)amino]-4-(3-acetanilido)thiazole (7b)

Yield (92%) (Ethanol) m.p.: 224°C; IR (KBr) νcm^{-1}: 3428 (OH), 3295 (NH), 1672 (C = O, amide), 1662 (N = C), 1624 (C = C of aromatic ring), 1506 (C-N), 745 (C-S-C of thiazole). ^{1}H NMR ($CDCl_3$ + DMSO-d_6) δ in ppm: 11.00 (s, 1H, OH exchangeable with D_2O), 8.97 (s, 1H, N = CH), 7.41-8.21 (m, 8H, Ar-H), 7.28 (s, 1H, NH exchangeable with D_2O), 6.99 (s, 1H, CH at C_5 of thiazole), 2.18 (s, 3H,

$NHCOCH_3$). Anal. Calcd. for $C_{18}H_{15}N_3O_2S$: C, 64.08; H, 4.48; N, 12.45; Found: C, 64.32; H, 4.58; N, 12.64.

2-[(4-chlorobenzylidene)amino]-4-(3-acetanilido)thiazole (7c)

Yield (54%) (Methanol) m.p.: 206°C; IR (KBr) νcm^{-1}: 3297 (NH), 1676 (C = O, amide), 1663 (N = C), 1626 (C = C of aromatic ring), 1507 (C-N), 762 (C-Cl), 749 (C-S-C of thiazole). ^1H NMR ($CDCl_3$ + DMSO-d_6) δ in ppm: 8.98 (s, 1H, N = CH), 7.42-8.22 (m, 8H, Ar-H), 7.28 (s, 1H, NH exchangeable with D_2O), 7.00 (s, 1H, CH at C_5 of thiazole), 2.17 (s, 3H, $NHCOCH_3$). Anal. Calcd. for $C_{18}H_{14}ClN_3OS$: C, 60.76; H, 3.97; N, 11.81; Found: C, 60.95; H, 3.36; N,11.57.

2-[(2-chlorobenzylidene)amino]-4-(3-acetanilido)thiazole (7d)

Yield (53%) (DMF-water) m.p.: 210°C; IR (KBr) νcm^{-1}: 3293 (NH), 1678 (C = O, amide), 1665 (N = C), 1627 (C = C of aromatic ring), 1509 (C-N), 761 (C-Cl), 748 (C-S-C of thiazole). ^1H NMR ($CDCl_3$ + DMSO-d_6) δ in ppm: 9.89 (s, 1H, N = CH), 7.40-8.21 (m, 8H, Ar-H), 7.27 (s, 1H, NH exchangeable with D_2O), 7.01 (s, 1H, CH at C_5 of thiazole), 2.16 (s, 3H, $NHCOCH_3$). Anal. Calcd. for $C_{18}H_{14}ClN_3OS$: C, 60.76; H, 3.97; N, 11.81; Found: C, 60.95; H, 3.36; N, 11.57.

2-[(2-methoxybenzylidene)amino]-4-(3-acetanilido)thiazole (7e)

Yield (52%) (Ethanol) m.p.: 212°C; IR (KBr) νcm^{-1}: 3295 (NH), 1679 (C = O, amide), 1667 (N = C), 1629 (C = C of aromatic ring), 1507 (C-N), 1229 (OCH_3), 747 (C-S-C of thiazole).^1H NMR ($CDCl_3$ + DMSO-d_6) δ in ppm: 8.88 (s, 1H, N = CH), 7.42-8.21 (m, 8H, Ar-H), 7.26 (s, 1H, NH exchangeable with D_2O), 7.02 (s, 1H, CH at C_5 of thiazole), 3.39 (s, 3H, OCH_3), 2.17 (s, 3H, $NHCOCH_3$). Anal. Calcd. for $C_{19}H_{17}N_3O_2S$: C, 64.94; H, 4.88;N, 11.96; Found: C, 64.85; H, 4.59; N, 11.68.

2-[(4-(dimethylamino)benzylidene)amino]-4-(3-acetanilido)thiazole (7f)

Yield (51%) (Acetone) m.p.: 215°C; IR (KBr) νcm^{-1}: 3293 (NH), 1674 (C = O, amide), 1669 (N = C), 1625 (C = C of aromatic ring), 1509 (C-N), 745 (C-S-C of thiazole).^1H NMR ($CDCl_3$ + DMSO-d_6) δ in ppm: 8.89 (s, 1H, N = CH), 7.41-8.21 (m, 8H, Ar-H), 7.28 (s, 1H, NH exchangeable with D_2O), 7.00 (s, 1H, CH at C_5 of thiazole), 3.00 (s, 6H, $N(CH_3)_2$), 2.18 (s, 3H, $NHCOCH_3$). Anal. Calcd. for $C_{20}H_{20}N_4OS$: C, 65.91; H, 5.53 ;N, 15.37; Found: C, 65.92; H, 5.54; N, 15.36.

2-[(4-hydroxy-3-methoxybenzylidene)amino]-4-(3-acetanilido)thiazole (7g)

Yield (50%) (Petroleum ether) m.p.: 218°C; IR (KBr) νcm^{-1}: 3448 (OH), 3295 (NH), 1673 (C = O, amide), 1666 (N = C), 1623 (C = C of aromatic ring), 1506 (C-N), 1227 (OCH_3), 746 (C-S-C of thiazole).^1H NMR ($CDCl_3$ + DMSO-d_6) δ in ppm: 11.01 (s, 1H, OH exchangeable with D_2O), 8.89 (s, 1H, N = CH), 7.42-8.23 (m, 7H, Ar-H), 7.26 (s, 1H, NH exchangeable with D_2O), 7.01 (s, 1H, CH at C_5 of thiazole), 3.39 (s, 3H, OCH_3), 2.16 (s, 3H, $NHCOCH_3$). Anal. Calcd. for $C_{19}H_{17}N_3O_3S$: C, 62.11; H, 4.66; N, 11.44; Found: C, 62.34; H, 4.97; N, 11.58.

2-[(2,6-dichlorobenzylidene)amino]-4-(3-acetanilido)thiazole (7h)

Yield (49%) (Methanol) m.p.: 221°C; IR (KBr) νcm^{-1}: 3293 (NH), 1674 (C = O, amide), 1669 (N = C), 1625 (C = C of aromatic ring), 1509 (C-N), 747 (C-S-C of thiazole).^1H NMR ($CDCl_3$ + DMSO-d_6) δ in ppm: 8.78 (s, 1H, N = CH), 7.43-8.23 (m, 7H, Ar-H), 7.27 (s, 1H, NH exchangeable with D_2O), 7.03 (s, 1H, CH at C_5 of thiazole), 2.18 (s, 3H, $NHCOCH_3$). Anal. Calcd. for $C_{18}H_{13}Cl_2N_3OS$: C, 55.39; H, 3.36; N, 10.77; Found: C, 55.68; H, 3.25; N, 10.98.

2-[(2,6-dibromobenzylidene)amino]-4-(3-acetanilido)thiazole (7i)

Yield (48%) (Ethanol) m.p.: 224°C; IR (KBr) νcm^{-1}: 3295 (NH), 1672 (C = O, amide), 1664 (N = C), 1624 (C = C of aromatic ring), 1504 (C-N), 745 (C-S-C of thiazole), 610 (C-Br).^1H NMR ($CDCl_3$ + DMSO-d_6) δ in ppm: 8.88 (s, 1H, N = CH), 7.40-8.20 (m, 7H, Ar-H), 7.27 (s, 1H, NH exchangeable with D_2O), 7.00 (s, 1H, CH at C_5 of thiazole), 2.15 (s, 3H, $NHCOCH_3$). Anal. Calcd. for $C_{18}H_{13}Br_2N_3OS$: C, 45.12; H, 2.73; N, 8.77; Found: C, 45.35; H, 2.58; N, 8.98.

2-[(2-hydroxybenzylidene)amino]-4-(3-acetanilido)thiazole (7j)

Yield (47%) (DMF-water) m.p.: 227°C; IR (KBr) νcm^{-1}: 3451 (OH), 3296 (NH), 1675 (C = O, amide), 1665 (N = C), 1626 (C = C of aromatic ring), 1512 (C-N), 746 (C-S-C of thiazole). ^1H NMR ($CDCl_3$ + DMSO-d_6) δ in ppm: 11.01 (s, 1H, OH exchangeable with D_2O), 8.89 (s, 1H, N = CH), 7.42-8.21 (m, 8H, Ar-H), 7.26 (s, 1H, NH exchangeable with D_2O), 7.02 (s, 1H, CH at C_5 of oxazole), 2.17 (s, 3H, $NHCOCH_3$). Anal. Calcd. for $C_{18}H_{15}N_3O_2S$: C, 64.08; H, 4.48; N, 12.45; Found: C, 64.29; H, 4.78; N, 12.67.

N-2-[3-chloro-4-(substitutedphenyl)-2-oxoazetidin-1-yl]-4-(3-acetanilido)thiazoles (8a-8j)

A mixture of 2-[(substitutedbenzylidene)amino]-4-(3-acetanilido)thiazoles **(7a-7j)** (0.01 mole), dry dioxane (10mL) and triethylamine (0.03 mole) were taking in a conical flask. The reactions were stirred on an ice bath and when the temperature dropped bellow 5°C, then choroacetylchloride (0.015 mole) was added drop wise with stirring. After completion of addition the stirring was continued for 10 h at room temperature. The reaction mixtures were then kept a side for 52 h. Finally, the reaction masses were added to ice cold water to obtain the final product. It was filtered, washed with water, dried and recrystallized from ethanol to yield compounds **(8a-8j)**.

N-2-[3-chloro-4-(4-methoxyphenyl)-2-oxoazetidin-1-yl3]-4-(3-acetanilido)thiazole (8a)

Yield (46%) (Acetone) m.p.: 240°C; IR (KBr) νcm^{-1}: 3293 (NH), 1674 (C = O, amide), 1668 (N = C), 1625 (C = C of aromatic ring), 1595 (C = O, cyclized), 1509 (C-N), 1371 (N-C), 1229 (OCH_3), 762 (C-Cl), 745 (C-S-C of thiazole). ^1H NMR ($CDCl_3$ + DMSO-d_6) δ in ppm: 7.44-8.24 (m, 8H, Ar-H), 7.27 (s, 1H, NH exchangeable with D_2O), 7.00 (s, 1H, CH at C_5 of thiazole), 6.76 (d, 1H, N-CH of oxoazetidine), 3.76 (d, 1H, CH-Cl), 3.39 (s, 3H, OCH_3), 2.18 (s, 3H, $NHCOCH_3$). Anal. Calcd. for $C_{21}H_{18}Cl\ N_3O_3S$: C, 58.94; H, 4.24; N, 9.82; Found: C, 58.75; H, 4.46; N, 9.65.

N-2-[3-chloro-4-(4-hydroxyphenyl)-2-oxoazetidin-1-yl]-4-(3-acetanilido)thiazole (8b)

Yield (45%) (DMF-water), m.p.: 243°C; IR (KBr) νcm^{-1}: 3450 (OH), 3294 (NH), 1672 (C = O, amide), 1669 (N = C), 1627 (C = C of aromatic ring), 1597 (C = O, cyclized), 1506 (C-N), 1372 (N-C), 760 (C-Cl), 743 (C-S-C of thiazole). ^1H NMR ($CDCl_3$ + DMSO-d_6) δ in ppm: 11.00 (s, 1H, OH exchangeable with D_2O), 7.42-8.22 (m, 8H, Ar-H), 7.28 (s, 1H, NH exchangeable with D_2O), 7.03 (s, 1H, CH at C_5 of thiazole), 6.78 (d, 1H, N-CH of oxoazetidine), 3.75 (d, 1H, CH-Cl), 2.17 (s, 3H, $NHCOCH_3$). Anal. Calcd. for $C_{20}H_{16}Cl\ N_3O_3S$: C, 58.04; H, 3.90; N, 10.15; Found: C, 58.25; H, 3.76; N, 10.45.

N-2-[3-chloro-4-(4-chlorophenyl)-2-oxoazetidin-1-yl]-4-(3-acetanilido)thiazole (8c)

Yield (44%) (Ethanol) m.p.: 247°C; IR (KBr) νcm^{-1}: 3293 (NH), 1674 (C = O, amide), 1664 (N = C), 1625 (C = C of aromatic ring), 1595 (C = O, cyclized), 1509 (C-N), 1371 (N-C), 763 (C-Cl), 745 (C-S-C of thiazole). ^1H NMR ($CDCl_3$ + DMSO-d_6) δ in ppm: 7.40-8.20 (m, 8H, Ar-H), 7.26 (s, 1H, NH exchangeable with D_2O), 7.00 (s, 1H, CH at C_5 of thiazole), 6.77 (d, 1H, N-CH of oxoazetidine), 3.76 (d, 1H, CH-Cl), 2.16 (s, 3H, $NHCOCH_3$). Anal. Calcd. for $C_{20}H_{15}Cl_2\ N_3O_2S$: C, 55.56; H, 3.50; N, 9.72; Found: C, 55.87; H, 3.89; N, 9.56.

N-2-[3-chloro-4-(2-chlorophenyl)-2-oxoazetidin-1-yl]-4-(3-acetanilido)thiazole (8d)

Yield (43%) (Methanol) m.p.: 251°C; IR (KBr) νcm^{-1}: 3295 (NH), 1678 (C = O, amide), 1667 (N = C), 1624 (C = C of aromatic ring), 1593 (C = O, cyclized), 1507 (C-N), 1375 (N-C), 762 (C-Cl), 746 (C-S-C of thiazole). ^1H NMR ($CDCl_3$ + DMSO-d_6) δ in ppm: 7.41-8.21 (m, 8H, Ar-H), 7.28 (s, 1H, NH exchangeable with D_2O), 7.01 (s, 1H, CH at C_5 of thiazole), 6.76 (d, 1H, N-CH of oxoazetidine), 3.77 (d, 1H, CH-Cl), 2.17 (s, 3H, $NHCOCH_3$). Anal. Calcd. for $C_{20}H_{15}Cl_2\ N_3O_2S$: C, 55.56; H, 3.50; N, 9.72; Found: C, 55.87; H, 3.89; N, 9.56.

N-2-[3-chloro-4-(2-methoxyphenyl)-2-oxoazetidin-1-yl]-4-(3-acetanilido)thiazole (8e)

Yield (42%) (DMF-water) m.p.: 254°C; IR (KBr) νcm^{-1}: 3293 (NH), 1674 (C = O, amide), 1669 (N = C), 1625 (C = C of aromatic ring), 1595 (C = O, cyclized), 1505 (C-N), 1371 (N-C), 1228 (OCH_3), 765 (C-Cl),

745 (C-S-C of thiazole). ^{1}H NMR ($CDCl_3$ + DMSO-d_6) δ in ppm: 7.40-8.21 (m, 8H, Ar-H), 7.26 (s, 1H, NH exchangeable with D_2O), 7.02 (s, 1H, CH at C_5 of thiazole), 6.78 (d, 1H, N-CH of oxoazetidine), 3.78 (d, 1H, CH-Cl), 3.38 (s, 3H, OCH_3), 2.18 (s, 3H, $NHCOCH_3$). Anal. Calcd. for $C_{21}H_{18}Cl\ N_3O_3S$: C, 58.94; H, 4.24; N, 9.82; Found: C, 58.75; H, 4.46; N, 9.65.

N-2-[3-chloro-4-(4-(dimethylamino)phenyl)-2-oxoazetidin-1-yl]-4-(3-acetanilido)thiazole (8f)

Yield (41%) (Petroleum ether) m.p.: 258°C; IR (KBr) νcm^{-1}: 3292 (NH), 1672 (C = O, amide), 1667 (N = C), 1626 (C = C of aromatic ring), 1594 (C = O, cyclized), 1509 (C-N), 1373 (N-C), 760 (C-Cl), 746 (C-S-C of thiazole). ^{1}H NMR ($CDCl_3$ + DMSO-d_6) δ in ppm: 7.40-8.22 (m, 8H, Ar-H), 7.28 (s, 1H, NH exchangeable with D_2O), 7.01 (s, 1H,CH at C_5 of thiazole), 6.77 (d, 1H, N-CH of oxoazetidine), 3.75 (d, 1H, CH-Cl), 3.00 (s, 6H, $N(CH_3)_2$), 2.17 (s, 3H, $NHCOCH_3$). Anal. Calcd. for $C_{22}H_{21}Cl\ N_4O_2S$: C, 59.92; H, 4.80; N, 12.71; Found: C, 59.85; H, 4.74; N, 12.5.

N-2-[3-chloro-4-(4-hydroxy-3-methoxyphenyl)-2-oxoazetidin-1-yl]-4-(3-acetanilido)thiazole (8g)

Yield (40%) (Ethanol) m.p.: 262°C; IR (KBr) νcm^{-1}: 3451 (OH), 3296 (NH), 1674 (C = O, amide), 1669 (N = C), 1625 (C = C of aromatic ring), 1595 (C = O, cyclized), 1506 (C-N), 1371 (N-C), 1227 (OCH_3) 762 (C-Cl), 745 (C-S-C of thiazole). ^{1}H NMR ($CDCl_3$ + DMSO-d_6) δ in ppm: 11.01 (s, 1H, OH exchangeable with D_2O), 7.42-8.22 (m, 7H, Ar-H), 7.27 (s, 1H, NH exchangeable with D_2O), 7.01 (s, 1H, CH at C_5 of thiazole), 6.76 (d, 1H, N-CH of oxoazetidine), 3.78 (d, 1H, CH-Cl), 3.37 (s, 3H, OCH_3), 2.17 (s, 3H, $NHCOCH_3$). Anal. Calcd. for $C_{21}H_{18}Cl\ N_3O_4S$: C, 56.82; H, 4.09; N, 9.47; Found: C, 56.74; H, 4.36; N, 9.65.

N-2-[3-chloro-4-(2,6-dichlorophenyl)-2-oxoazetidin-1-yl]-4-(3-acetanilido)thiazole (8h)

Yield (39%) (Acetone) m.p.: 2265°C; IR (KBr) νcm^{-1}: 3295 (NH), 1675 (C = O, amide), 1668 (N = C), 1623 (C = C of aromatic ring), 1596 (C = O, cyclized), 1508 (C-N), 1372 (N-C), 761 (C-Cl), 746 (C-S-C of thiazole).^{1}H NMR ($CDCl_3$ + DMSO-d_6) δ in ppm: 7.40-8.21 (m, 7H, Ar-H), 7.27 (s, 1H, NH exchangeable with D_2O), 7.02 (s, 1H, CH at C_5 of thiazole), 6.78 (d, 1H, N-CH of oxoazetidine), 3.76 (d, 1H, CH-Cl), 2.17 (s, 3H, $NHCOCH_3$). Anal. Calcd. for $C_{20}H_{14}Cl_3N_3O_2S$: C, 51.46; H, 3.02; N, 9.00; Found: C, 51.68; H, 3.45; N, 9.08.

N-2-[3-chloro-4-(2,6-dibromophenyl)-2-oxoazetidin-1-yl]-4-(3-acetanilido)thiazole (8i)

Yield (38%) (Methanol) m.p.: 269°C; IR (KBr) νcm^{-1}: 3296 (NH), 1674 (C = O, amide), 1669 (N = C), 1625 (C = C of aromatic ring), 1595 (C = O, cyclized), 1509 (C-N), 1371 (N-C), 760 (C-Cl), 745 (C-S-C of thiazole), 610 (C-Br).^{1}H NMR ($CDCl_3$ + DMSO-d_6) δ in ppm: 7.40-8.22 (m, 7H, Ar-H), 7.28 (s, 1H, NH exchangeable with D_2O), 7.02 (s, 1H, CH at C_5 of thiazole), 6.78 (d, 1H, N-CH of oxoazetidine), 3.76 (d, 1H, CH-Cl), 2.17 (s, 3H, $NHCOCH_3$). Anal. Calcd. for $C_{20}H_{14}Br_2Cl\ N_3O_2\ S$: C, 43.23; H, 2.54; N, 7.56; Found: C, 43.47; H, 2.79; N, 7.50.

N-2-[3-chloro-4-(2-hydroxyphenyl)-2-oxoazetidin-1-yl]-4-(3-acetanilido)thiazole (8j)

Yield (37%) (Acetone) m.p.: 273°C; IR (KBr) νcm^{-1}: 3451 (OH), 3294 (NH), 1674 (C = O,amide), 1669 (N = C), 1625 (C = C of aromatic ring), 1593 (C = O, cyclized), 1509 (C-N), 1374 (N-C), 762 (C-Cl), 745 (C-S-C of thiazole). ^{1}H NMR ($CDCl_3$ + DMSO-d_6) δ in ppm: 11.02 (s, 1H, OH exchangeable with D_2O), 7.41-8.23 (m, 8H, Ar-H), 7.25 (s, 1H, NH exchangeable with D_2O), 7.02 (s,1H, CH at C_5 of thiazole), 6.77 (d, 1H, N-CH of oxoazetidine), 3.77 (d, 1H, CH-Cl), 2.17 (s, 3H, $NHCOCH_3$). Anal. Calcd. for $C_{20}H_{16}Cl\ N_3O_3S$: C, 58.04; H, 3.90; N, 10.15; Found: C, 58.27; H, 3.72; N, 10.30.

N-2-[2-(substitutedphenyl)-4-oxo-1-thiazolidinyl]-4-(3-acetanilido)thiazoles (9a-9j)

To ethanolic solution (60ml) of compounds **(8a-8j)** (0.01 mole) thioglycolic acid (0.02 mole) was added in the presence of anhydrous zinc chloride. The reaction mixtures were refluxed for 10 h. The excess of solvents were distilled off and separated masses were poured in to ice water, filtered, washed with water and recrystallized from appropriate solvents to furnish compound **(9a)**.

N-2-[2-(4-methoxyphenyl)-4-oxo-1-thiazolidinyl]-4-(3-acetanilido)thiazole (9a)

Yield (37%) (Ethanol) m.p.: 230°C; IR (KBr) νcm^{-1}:

3296 (NH), 1675 (C = O, amide), 1669 (N = C), 1629 (C = C of aromatic ring), 1598 (C = O, cyclized), 1506 (C-N), 1375 (N-C), 1224 (OCH_3), 748 (C-S-C of thiazole). ^{1}H NMR ($CDCl_3$ + DMSO-d_6) δ in ppm: 7.42-8.22 (m, 8H, Ar-H), 7.27 (s, 1H, NH exchangeable with D_2O), 7.03 (s, 1H, CH at C_5 of thiazole), 6.78 (s, 1H, N-CH of oxothiazole), 3.77 (s, 2H, CH_2 of oxothiazole), 3.39 (s, 3H, OCH_3), 2.14 (s, 3H, $NHCOCH_3$). Anal. Calcd. for $C_{21}H_{19}N_3O_3S_2$: C, 59.27; H, 4.50; N, 9.87; Found: C, 59.43; H, 4.70; N, 9.65.

N-2-[2-(4-hydroxyphenyl)-4-oxo-1-thiazolidinyl]-4-(3-acetanilido)thiazole (9b)

Yield (36%) (DMF-water) m.p.: 233°C; IR (KBr) νcm^{-1}: 3450 (OH), 3290 (NH), 1673 (C = O, amide), 1665 (N = C), 1627 (C = C of aromatic ring), 1596 (C = O, cyclized), 1504 (C-N), 1373 (N-C), 744 (C-S-C of thiazole). ^{1}H NMR ($CDCl_3$ + DMSO-d_6) δ in ppm: 11.00 (s, 1H OH exchangeable with D_2O), 7.40-8.21 (m, 8H, Ar-H), 7.28 (s, 1H, NH exchangeable with D_2O), 7.01 (s, 1H, CH at C_5 of thiazole), 6.72 (s, 1H, N-CH of oxothiozole), 3.75 (s, 2H, CH_2 of oxothiazole), 2.18 (s, 3H, $NHCOCH_3$). Anal. Calcd. for $C_{20}H_{17}N_3O_3S_2$: C, 58.38; H, 4.16; N, 10.21; Found: C, 58.40; H, 4.18; N, 10.20.

N-2-[2-(4-chlorophenyl)-4-oxo-1-thiazolidinyl]-4-(3-acetanilido)thiazole (9c)

Yield (38%) (Methanol) m.p.: 238°C; IR (KBr) νcm^{-1}: 3296 (NH), 1674 (C = O, amide), 1663 (N = C), 1629 (C = C of aromatic ring), 1598 (C = O, cyclized), 1506 (C-N), 1375 (N-C), 762 (C-Cl), 748 (C-S-C of thiazole).^{1}H NMR ($CDCl_3$ + DMSO-d_6) δ in ppm: 7.40-8.22 (m, 8H, Ar-H), 7.26 (s, 1H, NH exchangeable with D_2O), 7.00 (s, 1H, CH at C_5 of thiazole), 6.75 (s, 1H, N-CH of oxothiozole), 3.78 (s, 2H, CH_2 of oxothiazole), 2.18 (s, 3H, $NHCOCH_3$). Anal. Calcd. for $C_{20}H_{16}ClN_3O_2S_2$: C, 55.87; H, 3.75; N, 9.77; Found: C, 55.85; H, 3.86; N, 9.36.

N-2-[2-(2-chlorophenyl)-4-oxo-1-thiazolidinyl]-4-(3-acetanilido)thiazole (9d)

Yield (34%) (Petroleum ether) m.p.: 240°C; IR (KBr) νcm^{-1}: 3298 (NH), 1675 (C = O, amide), 1668 (N = C), 1625 (C = C of aromatic ring), 1597 (C = O, cyclized), 1506 (C-N), 1376 (N-C), 764 (C-Cl), 749 (C-S-C of thiazole). ^{1}H NMR ($CDCl_3$ + DMSO-d_6) δ in ppm: 7.43-8.23 (m, 8H, Ar-H), 7.27 (s, 1H, NH exchangeable with D_2O), 7.00 (s, 1H, CH at C_5 of thiazole), 6.70 (s, 1H, N-CH of oxothiozole), 3.75 (s, 2H, CH_2 of oxothiazole), 2.17 (s, 3H, $NHCOCH_3$). Anal. Calcd. for $C_{20}H_{16}ClN_3O_2S_2$: C, 55.87; H, 3.75; N, 9.77; Found: C, 55.69; H, 3.87; N, 9.89.

N-2-[2-(2-methoxyphenyl)-4-oxo-1-thiazolidinyl]-4-(3-acetanilido)thiazole (9e)

Yield (33%) (Ethanol) m.p.: 244°C; IR (KBr) νcm^{-1}: 3294 (NH), 1673 (C = O, amide), 1667 (N = C), 1627 (C = C of aromatic ring), 1598 (C = O, cyclized), 1503 (C-N), 1375 (N-C), 1225 (OCH_3), 748 (C-S-C of thiazole). ^{1}H NMR ($CDCl_3$ + DMSO-d_6) δ in ppm: 7.41-8.22 (m, 8H, Ar-H), 7.28 (s, 1H, NH exchangeable with D_2O), 7.02 (s, 1H, CH at C_5 of thiazole), 6.72 (s, 1H, N-CH of oxothiozole), 3.77 (s, 2H, CH_2 of oxothiazole), 3.39 (s, 3H, OCH_3), 2.18 (s, 3H, $NHCOCH_3$). Anal. Calcd. for $C_{21}H_{19}N_3O_3S_2$: C, 59.27; H, 4.50; N, 9.87; Found: C, 59.30; H, 4.56; N, 9.95.

N-2-[2-(4-(dimethylamino)phenyl)-4-oxo-1-thiazolidinyl]-4-(3-acetanilido)thiazole (9f)

Yield (32%) (Acetone) m.p.: 248°C; IR (KBr) νcm^{-1}: 3299 (NH), 1676 (C = O, amide), 1664 (N = C), 1625 (C = C of aromatic ring), 1594 (C = O, cyclized), 1509 (C-N), 1378 (N-C), 744 (C-S-C of thiazole).^{1}H NMR ($CDCl_3$ + DMSO-d_6) δ in ppm: 7.40-8.21 (m, 8H, Ar-H), 7.26 (s, 1H, NH exchangeable with D_2O), 7.04 (s, 1H, CH at C_5 of thiazole), 6.72 (s, 1H, N-CH of oxothiozole), 3.77 (s, 2H, CH_2 of oxothiazole), 3.00 (s, 6H, $(NH_3)_2$), 2.48 (s, 3H, $NHCOCH_3$). Anal. Calcd. for $C_{22}H_{22}N_4O_2S_2$: C, 60.25; H, 5.06; N, 12.78; Found: C, 60.34; H, 5.08; N, 12.96.

N-2-[2-(4-hydroxy-3-methoxyphenyl)-4-oxo-1-thiazolidinyl]-4-(3-acetanilido)thiazole (9g)

Yield (31%) (Dmf-water) m.p.: 251°C; IR (KBr) νcm^{-1}: 3450 (OH), 3296 (NH), 1679 (C = O, amide), 1667 (N = C), 1627 (C = C of aromatic ring), 1596 (C = O, cyclized), 1508 (C-N), 1375 (N-C), 1224 (OCH_3), 749 (C-S-C of thiazole). ^{1}H NMR ($CDCl_3$ + DMSO-d_6) δ in ppm: 11.01 (s, 1H, OH exchangeable

with D_2O), 7.41-8.21 (m, 7H, Ar-H), 7.24 (s, 1H, NH exchangeable with D_2O), 7.01 (s, 1H, CH at C_5 of thiazole), 6.73 (s, 1H, N-CH of oxothiozole), 3.75 (s, 2H, CH_2 of oxothiazole), 3.36 (s, 3H, OCH_3), 2.15 (s, 3H, $NHCOCH_3$). Anal. Calcd. for $C_{21}H_{19}N_3O_4S_2$: C, 57.13; H, 4.34; N, 9.52; Found: C, 57.45; H, 4.32; N, 9.60.

N-2-[2-(2,6-dichlorophenyl)-4-oxo-1-thiazolidinyl]-4-(3-acetanilido)thiazole (9h)

Yield (30%) (Ethanol) m.p.: 253°C; IR (KBr) νcm^{-1}: 3295 (NH), 1676 (C = O, amide), 1665(N = C), 1626 (C = C of aromatic ring), 1595(C = O, cyclized), 1503(C-N), 1379(N-C), 763 (C-Cl), 748 (C-S-C of thiazole). ^1H NMR ($CDCl_3$ + DMSO-d_6) δ in ppm: 7.42-8.22 (m, 7H, Ar-H), 7.27 (s, 1H, NH exchangeable with D_2O), 7.04 (s, 1H, CH at C_5 of thiazole), 6.73 (s, 1H, N-CH of oxothiozole), 3.78 (s, 2H, CH_2 of oxothiazole), 2.19 (s, 3H, $NHCOCH_3$). Anal. Calcd. for $C_{20}H_{15}Cl_2N_3O_2S_2$: C, 51.73; H, 3.26; N, 9.05; Found: C, 51.85; H, 3.38; N, 9.04.

N-2-[2-(2,6-dibromophenyl)-4-oxo-1-thiazolidinyl]-4-(3-acetanilido)thiazole (9i)

Yield (29%) (Methanol) m.p.: 254°C; IR (KBr) νcm^{-1}: 3296 (NH), 1675 (C = O, amide), 1669 (N = C), 1629 (C = C of aromatic ring), 1598 (C = O, cyclized), 1506 (C-N), 1375 (N-C), 748 (C-S-C of thiazole), 612 (C-Br). ^1H NMR ($CDCl_3$ + DMSO-d_6) δ in ppm: 7.41-8.23 (m, 7H, Ar-H), 7.27 (s, 1H, NH), 7.01 (s, 1H, CH at C_5 of thiazole), 6.73 (s, 1H, N-CH of oxothiozole), 3.76 (s, 2H, CH_2 of oxothiazole), 2.16 (s, 3H, $NHCOCH_3$). Anal. Calcd. for $C_{20}H_{15}Br_2N_3O_2S_2$: C, 43.42; H, 2.73; N, 7.59; Found: C, 43.65; H, 2.96; N, 7.85; MS.

N-2-[2-(2-hydroxyphenyl)-4-oxo-1-thiazolidinyl]-4-(3-acetanilido)thiazole (9j)

Yield (27%) (Acetone) m.p.: 256°C; IR (KBr) νcm^{-1}: 3450 (OH), 3295 (NH), 1678 (C = O, amide), 1664 (N = C), 1625 (C = C of aromatic ring), 1594 (C = O, cyclized), 1509 (C-N), 1378(N-C), 745 (C-S-C of thiazole). ^1H NMR ($CDCl_3$ + DMSO-d_6) δ in ppm: 11.00 (s, 1H, OH exchangeable with D_2O), 7.42-8.21 (m, 8H, Ar-H), 7.27 (s, 1H, NH exchangeable with D_2O), 7.02 (s, 1H, CH at C_5 of thiazole), 6.72 (s, 1H, N-CH of oxothiozole), 3.75 (s, 2H, CH_2 of oxothiazole), 2.19 (s, 3H, $NHCOCH_3$). Anal. Calcd. for $C_{20}H_{17}N_3O_3S_2$: C, 58.38; H, 4.16; N, 10.21; Found: C, 58.39; H, 4.20; N, 10.20.

RESULTS AND DISCUSSION

Various substituted derivatives of oxazole and thiazole were synthesized and screened for their anti bacterial activity. The pharmacological results of the compounds have been reported in TABLE 1(a-f).

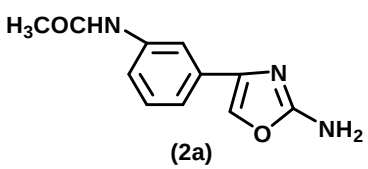
Coumpound **(2a)** has shown mild antibacterial activity against *S.aureus* and *E.coli*. In corporation of different aromatic aldehydes via NH_2 linkage of substituted oxazoles yielded compounds **(3a-3j)**. Among the compounds **(3a-3j)**, compound **(3a)** was devoid of antibacterial activity. Compounds **(3b)**, **(3c)**, **(3d)**, **(3e)**, **(3f)**, **(3g)** and **(3j)** had shown mild antibacterial activity and compounds **(3h)** and **(3i)** exhibited moderate zone of inhibition against various used pathogens.

Cyclization of compounds **(3a-3j)** with chloroacetyl chloride in presence of triethylamine yielded corresponding azetidinones **(4a-4j)**. Among the compounds **(4a-4j)**, compounds **(4a)**, **(4b)**, **(4e)**, **(4f)** and **(4g)** exhibited moderate antibacterial activity. These compounds exhibited 15-19 mm antibacterial activity against *S.aureus*, *E.coli*, *P.vulgaris* and *K.pneumoniae*. Compound **(4c)** have shown good antibacterial activity (i.e. zone of inhibition 20mm) against *E.coli*. Compounds **(4d)**, **(4i)** and **(4j)** were found to exhibited equipotent antibacterial activity than reference drug. Compound **(4h)** exhibited good antibacterial activity. This compound showed zone of inhibition 23mm against *S.aureus*, 22mm against *P.vulgaris*.

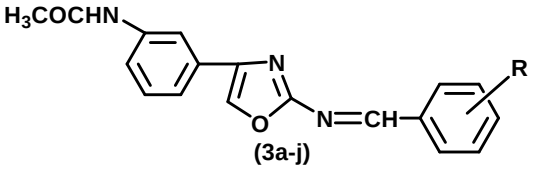
Cyclocandensation of compounds **(3a-3j)** with thioglycolic acid to give compounds **(5a-5j)**. Among the compounds **(5a-5j)**, compounds **(5a)**, **(5e)**, **(5f)** and **(5g)** exhibited moderate antibacterial activity. On the other hand compounds **(5b)**, **(5c)**, **(5d)**, **(5i)** and **(5j)** had shown better antibacterial activity. These compounds exhibited 19mm-23mm zone of inhibition against *S.aureus*, *E.coli*, *P.vulgaris* and *K.pneumoniae*. Compound **(5h)** showed antibacterial activity better than standard drug.

Compound **(6a)** exhibited zone of inhibition 5mm against *S.aureus*. The addition of different aromatic aldehydes on amino group of thiazole nucleus to give compounds **(7a-7j)**. Compounds **(7a-7j)** have shown

TABLE 1a : Antibacterial activity of the compounds: 2- Amino-4-(3-acetanilido) oxazole (2a), 2-[(substituted benzylidene) amino]-4-(3-acetanilido) oxazoles (3a-j)



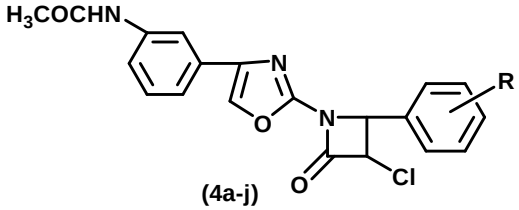
(2a)



(3a-j)

Compound No.	R	Bacterial growth inhibition (diameter)				ALD 50 Mg/kg i.p
		S.aureus	*E.coli*	*P.vulgaris*	*K.pneumonieae*	
2a	-	6mm	5mm	-	-	>1000
3a	4-OCH_3	-	-	-	-	>1000
3b	4-OH	8mm	-	7mm	-	>1000
3c	4-Cl	10mm	9mm	-	-	>1000
3d	2-Cl	-	10mm	9mm	10mm	>1000
3e	2-OCH_3	7mm	6mm	-	-	>1000
3f	4-$N(CH_3)_2$	-	-	7mm	-	>1000
3g	4-OH & 3-OCH_3	-	5mm	-	-	>1000
3h	2,6-Cl	12mm	10mm	-	-	>1000
3i	2,6-Br	-	-	11mm	10mm	>1000
3j		9mm	-	10mm	-	>1000
Ampicillin	2-OH	20mm	18mm	18mm	15mm	>1000
Ciprofloxacin		20mm	22mm	20mm	21mm	>1000

TABLE 1b : Antibacterial activity of the compounds: N-2-3-chloro-4-(substituted phenyl)-2-oxoazetidin-1-yl)-4-(3-acetanilido) oxazoles (4a-j)



(4a-j)

Compound No.	R	Bacterial growth inhibition (diameter)				ALD 50 Mg/kg i.p
		S.aureus	*E.coli*	*P.vulgaris*	*K.pneumoniae*	
4a	4-OCH_3	16mm	17mm	-	-	>1000
4b	4-OH	17mm	-	-	16mm	>1000
4c	4-Cl	-	20mm	-	-	>1000
4d	2-Cl	19mm	-	-	-	>1000
4e	2-OCH_3	-	19mm	18mm	-	>1000
4f	4-$N(CH_3)_2$	-	15mm	-	17mm	>1000
4g	4-OH & 3-OCH_3	18mm	-	19mm	-	>1000
4h	2,6-Cl	23mm	-	22mm	-	>1000
4i	2,6-Br	-	-	-	21mm	>1000
4j		19mm	21mm	-	-	>1000
Ampicillin	2-OH	20mm	18mm	18mm	15mm	>1000
Ciprofloxacin		20mm	22mm	20mm	21mm	>1000

better antibacterial activity than compounds **(3a-3j)**.

Substituted azetidinone **(8a-8j)**, resulted from **(7a-7j)**. Among the compounds **(8a-8j)**, compound **(8h)** exhibited zone of inhibition 21mm against *E.coli*, 23mm against *K.pneumoniae*. The later compound showed better antibacterial activity than standard drug. Compound **(8i)** was found to exhibited equipotent antibacterial activity than reference drugs. The compounds **(8a)**,

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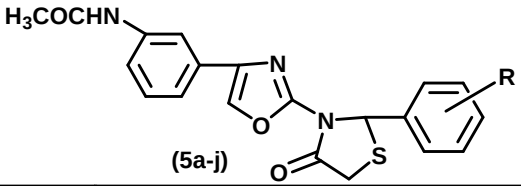
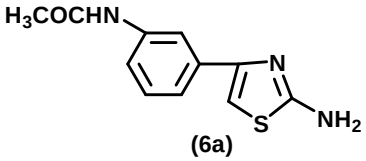
TABLE 1c : Antibacterial activity of the compounds: N-2-[(2R)-2-(substituted phenyl)-4-oxo-1-thiazolidinyl)-4-(3-acetanilido)oxazoles (5a-j)



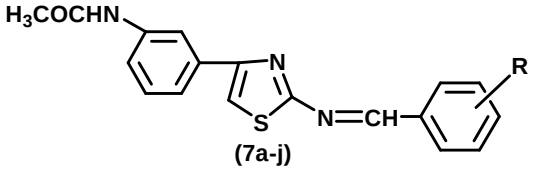
(5a-j)

Compound No.	R	Bacterial growth inhibition (diameter)				ALD 50 Mg/kg i.p
		S.aureus	*E.coli*	*P.vulgaris*	*K.pneumoniae*	
5a	4-OCH_3	18mm	-	-	20mm	>1000
5b	4-OH	20mm	-	-	-	>1000
5c	4-Cl	-	-	20mm	19mm	>1000
5d	2-Cl	-	20mm	-	21mm	>1000
5e	2-OCH_3	20mm	-	19mm	-	>1000
5f	4-$N(CH_3)_2$	-	17mm	-	-	>1000
5g	4-OH & 3-OCH_3	-	-	20mm	-	>1000
5h	2,6-Cl	25mm	-	-	23mm	>1000
5i	2,6-Br	-	-	22mm	-	>1000
5j		20mm	-	-	21mm	>1000
Ampicillin	2-OH	20mm	18mm	18mm	15mm	>1000
Ciprofloxacin		20mm	22mm	20mm	21mm	>1000

TABLE 1d : Antibacterial activity of the compounds: 2- Amino-4-(3-acetanilido) thiazole (6a), 2-[(substituted benzylidene) amino]-4-(3-acetanilido) thiazoles (7a-j)



(6a)



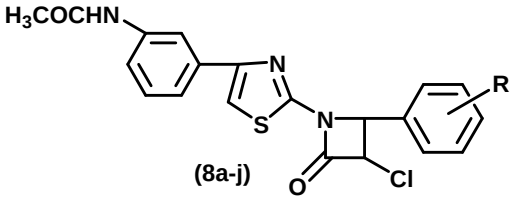
(7a-j)

Compound No.	R	Bacterial growth inhibition (diameter)				ALD 50 Mg/kg i.p
		S.aureus	*E.coli*	*P.vulgaris*	*K.pneumoniae*	
6a		5mm	-	-	-	>1000
7a	4-OCH_3	8mm	-	-	7mm	>1000
7b	4-OH	-	9mm	-	-	>1000
7c	4-Cl	10mm	-	-	9mm	>1000
7d	2-Cl	9mm	-	11mm	11mm	>1000
7e	2-OCH_3	-	7mm	-	-	>1000
7f	4-$N(CH_3)_2$	8mm	9mm	-	7mm	>1000
7g	4-OH & 3-OCH_3	-	-	7mm	-	>1000
7h	2,6-Cl	14mm	12mm	-	-	>1000
7i	2,6-Br	13mm	-	12mm	-	>1000
7j		-	11mm	-	10mm	>1000
Ampicillin	2-OH	20mm	18mm	18mm	15mm	>1000
Ciprofloxacin		20mm	22mm	20mm	21mm	>1000

(8b), **(8c)**, **(8d)**, **(8e)**, **(8f)**, **(8g)** and **(8j)** showed moderate antibacterial activity and better than the compounds **(4a-4j)** having oxazoles moiety.

Cyclization of compounds **(7a-7j)** by thioglycolic acid in presence of anhydrous zinc chloride yielded compounds thiazolidinones **(9a-9j)**. The compounds **(9h)**

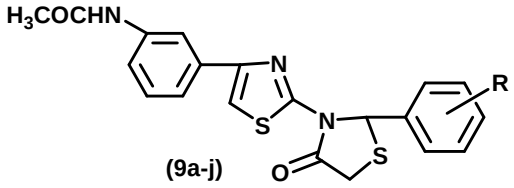
TABLE 1e : Antibacterial activity of the compounds: N-2-[(2R)-3-chloro-4-(substituted phenyl)-2-oxoazetidin-1yl)-4-(3-acetanilido) thiazoles (8a-j)



(8a-j)

Compound No.	R	Bacterial growth inhibition (diameter)				ALD 50 Mg/kg i.p
		S.aureus	*E.coli*	*P.vulgaris*	*K.pneumoniae*	
8a	4-OCH_3	18mm	-	-	16mm	>1000
8b	4-OH	-	19mm	-	-	>1000
8c	4-Cl	-	21mm	18mm	-	>1000
8d	2-Cl	-	-	-	20mm	>1000
8e	2-OCH_3	20mm	-	-	21mm	>1000
8f	4-$N(CH_3)_2$	-	16mm	17mm	-	>1000
8g	4-OH & 3-OCH_3	19mm	-	-	-	>1000
8h	2,6-Cl	-	21mm	-	23mm	>1000
8i	2,6-Br	20mm	-	20mm	-	>1000
8j		19mm	18mm	-	21mm	>1000
Ampicillin	2-OH	20mm	18mm	18mm	15mm	>1000
Ciprofloxacin		20mm	22mm	20mm	21mm	>1000

TABLE 1f : Antibacterial activity of the compounds: N-2-[(2R)-2-(substituted phenyl)-4-oxo-1-thiazolidinyl)-4-(3-acetanilido)thiazoles (9a-j)



(9a-j)

Compound No.	R	Bacterial growth inhibition (diameter)				ALD 50 Mg/kg i.p
		S.aureus	*E.coli*	*P.vulgaris*	*K.pneumoniae*	
9a	4-OCH_3	19mm	20mm	-	-	>1000
9b	4-OH	21mm	-	22mm	20mm	>1000
9c	4-Cl	-	20mm	-	21mm	>1000
9d	2-Cl	23mm	-	21mm	-	>1000
9e	2-OCH_3	21mm	20mm	-	-	>1000
9f	4-$N(CH_3)_2$	-	-	18mm	19mm	>1000
9g	4-OH & 3-OCH_3	-	-	-	21mm	>1000
9h	2,6-Cl	24mm	25mm	22mm	-	>2000
9i	2,6-Br	22mm	-	21mm	19mm	>1000
9j		-	22mm	-	21mm	>1000
Ampicillin	2-OH	20mm	18mm	18mm	15mm	>1000
Ciprofloxacin		20mm	22mm	20mm	21mm	>1000

and **(9i)** compounds exhibited better antibacterial activity than standard drug against *S.aureus*, *E.coli*, *P.vulgaris*. The compounds **(9a)**, **(9b)**, **(9c)**, **(9d)**, **(9e)**, **(9f)**, **(9g)** and **(9j)** exhibited better antibacterial activity than the compounds **(5a-5j)** having oxazoles moiety. The synthesized compounds were also tested for ap-

proximate lethal dose ALD_{50} and were found to exhibit a higher value of ALD_{50} i.e. more than 1000mg/kg i.p. except compound 9h which exhibited ALD_{50} of more than 2000mg/kg i.p. (maximum dose tested). As these compounds have shown high value of ALD_{50} thus indicating good safety margin.

While considering all the newly synthesized compounds of this series we may concluded that:

1. Presence of thiazoles moiety has shown better antibacterial and antifungal activities than the compounds having oxazoles moiety.
2. 2,6-dichlorophenyl substitution in thiazoles ring showed more potent activity than oxazoles ring.
3. Presence of electronegative atoms at 2 and 6 position in general beneficial for antibacterial and antifungal activities.

Pharmacological evaluation (Antibacterial activity)

All the synthesized compounds were tested for their antibacterial activity. The effect of unknown compounds were compared with the standard drug Ciprofloxacin and Gattifloxacin and propylene glycol treated group served as control. All the newly synthesized compounds were also screened for their approximate lethal dose (ALD_{50}).

Cup-Plate Method (CUPS): This activity was performed by following the method of Chuinckshank et. al[9]. in albino rats. Nutrient agar was poured onto the sterilized petri dishes (20-25mL each pertri dish). The poured material was allowed to set (1-1.5 h) and thereafter the "CUPS" (10 mm diameter) were made by punching into the agar surface with a sterile cork borer and scooping out the punched part of the agar. Into these cups the test compound solution was added with the help of sterile syringe. The plates were incubated at 37°C for 48 hr and the results were noted. A solvent control (10% DMSO in methanol) was also run to not the activity of the blank (solvent). The above said standard drugs were also screened under similar conditions for comparison.

Approximate lethal dose (ALD_{50}): The LD_{50} was determined in albino rats weighing 100-120gm of either sex by the method of Smith[10]. The test compounds were administered by i.p. route in one group and the same volume of propylene glycol in another group of animals consisting six rats in graded doses. The animals were allowed to take food and water adlibidum. After 24 h of drug administration percent mortality in each group was observed. From the data obtained ALD_{50} was calculated.

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