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Synthesis of Tetrazolo[1,5-*a*]quinoxaline based Azetidinones & Thiazolidinones as Potent Antibacterial & Antifungal Agents

Shiv Kumar,* S. A. Khan, Ozair Alam, Rizwan Azim, Atul Khurana, M. Shaquiquzzaman, Nadeem Siddiqui, and Waquar Ahsan

Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Jamia Hamdard (Hamdard University), New Delhi-110062, India
**E-mail: shiv_hamdard@yahoo.co.in, shiv_hamdard@rediffmail.com*
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4-Chlorotetrazolo[1,5-*a*]quinoxaline **(III)** was synthesized by azide (2+3) cycloaddition of 2,3-dichloroquinoxaline **(II)**. Compound **(III)** on further refluxing with hydrazine hydrate furnished 4-hydrazinotetrazolo[1,5-*a*]quinoxaline **(IV)**. Further refluxing of (IV) with different aromatic aldehydes in methanol yielded corresponding Schiff's bases **V(a-j)**. Various 4-aminotetrazolo[1,5-*a*]quinoxaline based azetidinones **VII(a-j)** were synthesized by stirring the compounds **V(a-j)**, at low temperature, with equimolar mixture of chloroacetylchloride & triethylamine in dry benzene, while 4-aminotetrazolo[1,5-*a*]quinoxaline based thiazolidinones **VIII(a-j)** were synthesized by refluxing Schiff's bases **V(a-j)** with thioglycolic acid in oil-bath. The structures of all the compounds were confirmed on the basis of ^{1}H-NMR & FT-IR spectral data. All the newly synthesized compounds were screened for *in-vitro* antimicrobial activity against *E. coli*, *S. aureus*, *K. pneumoniae* & *P. aeruginosa* & antifungal activity against *C. albicans*. Few of them have exhibited the promising activity.

Key Words : Tetrazolo[1,5-*a*]quinoxaline, Thiazolidinones, Azetidinones, Antibacterial, Antifungal

Introduction

In the recent years, the incidences and severity of human bacterial and fungal infections have increased dramatically. The use of powerful immunosuppressive agents for cancer chemotherapy & for organ transplants, combined with AIDS epidemic, has led to this significant increase. In the healthy individuals, a normally functioning immune system tends to ward off fungal infections. However, in persons with impaired immune system, primarily AIDS patients, opportunistic fungi such as *Candida albicans* (deep-seated systemic infections), *Cryptococcus neoformans* (a yeast, CNS infection), *Aspergillus* spp. may be fatal.

Nitrogen-containing heterocyclic compounds are indispensable structural units for both the chemists and the biochemists. Among the various classes of heterocyclic compounds, quinoxaline derivatives form an important component of pharmacologically active compounds. Quinoxaline ring is a part of various antibiotics such as hinomycin, levomycin, and actinoleutin that are known to inhibit growth of gram positive bacteria and are active against various transplantable tumors.[1-7] In addition quinoxaline derivatives are also associated with a wide spectrum of biological activities ranging from antifungal,[8-10] antibacterial,[10-14] antitubercular,[8,9,15-18] anti-inflammatory[19,20] and analgesic.[12,20]

Experimental

General. Melting points were determined in open capillary tubes in a Hicon melting point apparatus and are uncorrected. All the Fourier-Transform Infra Red (FT-IR) spectra were recorded in KBr pellets on a Jasco FT-IR 410 spectrometer. The ^{1}H- NMR spectra were recorded on Bruker-Spectrospin DCX (300 MHz) NMR spectrometer. Chemical shifts (δ) are expressed in ppm relative to tetramethylsilane (TMS) as an internal standard. The purity of the compounds was checked by thin layer chromatography (TLC) on Merck Silica Gel 60F254 precoated sheets. Iodine chamber and UV lamp were used for the visualization of TLC spots.

General Procedure for the Synthesis of Titled Compounds.

(1*H*,4*H*)Quinoxaline-2,3-dione (I): *o*-Phenylenediamine (0.1 mol) & oxalic acid (0.15 mol) were added to 20% HCl (200 mL) & refluxed for about 3 hours. White crystalline solid was separated by filtration. TLC was monitored by Toluene:Ethylacetate:Formic acid (5:4:1, TEF). Product was washed with methanol & chloroform & finally recrystallized with dimethylformamide (DMF); White crystalline solid, yield 75%, $R_{f\,(TEF)}$ 0.80, mp > 320 °C; ^{1}H-NMR (DMSO-d_6, 300 MHz, ppm): δ 7.042-7.125 (m, 4H, quinoxaline ring protons, J = 1.8-5.7 Hz, *ortho* & *meta*-coupling), δ 11.902 (s, 2H, N**H**CO); FT-IR (KBr), in cm^{-1}: 854 (aromatic C=C, bend), 1387 (=C-N, str.), 1499 (aromatic C=C, str.), 1535 (-NH, bend), 1688 (>C=O, str.), 3304 (N-H, str.)

2,3-Dichloroquinoxaline (II): Compound **I** (0.12 mol) was added to cold $POCl_3$ (120 mL) in small portions to get a slurry. 5 mL (0.04 mol) of *N,N*-dimethylaniline (DMA) was added to this slurry. Reaction mixture was refluxed till the appearance of brownish color (it may take nearly 4 hours). Reaction mixture was cooled & poured into 1500 mL of ice chilled water. White creamy solid was filtered, air dried & recrystallized with DMF; White needle like crystals, yield 70%, $R_{f\,(TEF)}$ 0.85, mp 142 °C; ^{1}H-NMR ($CDCl_3$, 300 MHz, ppm): δ 7.782-7.807 (q, 2H, A_2B_2 pattern, quinoxaline ring

protons, J = 3.6 Hz, *meta*-coupling), δ 7.995-8.019 (q, 2H, A_2B_2 pattern, quinoxaline ring protons, J = 3.2 Hz, *meta*-coupling); FT-IR (KBr), in cm^{-1}: 769 (*ortho*-disubstituted ring, str.), 964 (aromatic =C-H, bend), 1121 (C-Cl, str.), 1171 (C-N, str.), 1393 (=C-N, str.), 1533 (aromatic C=C, str.), 1688 (C=N, str.)

4-Chlorotetrazolo[1,5-*a*]quinoxaline (III): A mixture of compound II (0.056 mol), sodium azide (0.067 mol) in 15 mL of water, acetic acid (10 mL) in DMSO (200 mL) was stirred at 40 °C for 5 hours. Mixture was cooled to room temperature & added to ice cold water. Product was filtered, air dried & recrystallized with ethanol-methanol mixture (1:1); Light-yellowish crystals, yield 62%, $R_{f\,(TEF)}$ 0.75, $R_{f\,(Benzene:Acetone\,=\,9:1)}$ 0.82, $R_{f\,(Ethylacetate:Hexane\,=\,1:1)}$ 0.85, mp 143 °C; ^{1}H-NMR (DMSO-d_6, 300 MHz, ppm): δ 8.659-8.697 (m, 2H, quinoxaline ring protons, J = 3.6 Hz), δ 7.957-7.994 (m, 2H, quinoxaline ring protons, J = 3.2 Hz); FT-IR (KBr), in cm^{-1}: 971, 1073 (aryl C-Cl), 1199 (C-N, str.), 1393 (=C-N, str.), 1510, 1648, 2345 (N-N, str.), 2368 (N=N, str.).

4-Hydrazinotetrazolo[1,5-*a*]quinoxaline (IV): A mixture of compound III (0.05 mol), hydrazine hydrate (0.06 mol) in ethanol (100 mL), was refluxed for 8 hours. Mixture was kept overnight in deep freezer. Product was filtered, air dried & recrystallized with DMF; Orange red solid, yield 80%, $R_{f\,(Benzene:Acetone\,=\,7:3)}$ 0.68, mp 238-240 °C; ^{1}H-NMR (DMSO-d_6, 300 MHz, ppm): δ 8.731-8.762 (q, 2H, A_2B_2 pattern, quinoxaline ring protons, J = 3.6 Hz), δ 8.028-8.059 (q, 2H, A_2B_2 pattern, quinoxaline ring protons, J = 2.4-3.6 Hz), δ 7.485-7.510 (br, d, 1H, $NHNH_2$); ^{1}H-NMR (DMSO-d_6, D_2O exchange, 300 MHz, ppm): δ 8.667-8.707 (q, 2H, quinoxaline ring protons, J = 2.4-3.6 Hz), δ 7.994-8.024 (q, 2H, quinoxaline ring protons, J = 2.4-3.3 Hz), δ 7.4 (br, s, 2H, N**H**N**H**D/N**D**N**H**$_2$); FT-IR (KBr), in cm^{-1}: 971, 1199, 1374, 1510, 1582 (-NH, bend), 1663, 2344, 2371, 2942 (-NH of -$NHNH_2$, str.), 3134 (-NH of -$NHNH_2$, str.)

4-{(2*E*)-2-[(Substitutedphenyl)methylidene]hydrazino}tetrazolo[1,5-*a*]quinoxalines V(a-j). Compound IV (0.005 mol) & aromatic aldehydes (0.005 mol) in methanol (30 mL) & glacial acetic acid (3 mL) were refluxed for 3-4 hours. Mixtures were kept overnight. Products were filtered & washed with methanol (15 mL), air dried & recrystallized with DMF.

4-[(2*E*)-Benzylidenehydrazinyl]tetrazolo[1,5-*a*]quinoxaline (Va): Light red solid, yield 62%, $R_{f\,(Benzene:Acetone\,=\,9:1)}$ 0.80, $R_{f\,(Ethylacetate:Hexane\,=\,1:1)}$ 0.80, mp 287 °C; ^{1}H-NMR (DMSO-d_6, 300 MHz, ppm): δ 8.733-8.763 (q, A_2B_2 pattern, 4H, quinoxaline ring protons, J = 3.0-3.3 Hz), δ 8.030-8.061 (m, 5H, Ar-H, J = 2.7-3.6 Hz), δ 7.934 (s, 1H, N**H**-N), δ 7.478-7.501 (d, 1H, C**H**=N, J = 6.9 Hz, strong allylic coupling); FT-IR (KBr), in cm^{-1}: 721 (*mono*-substituted aromatic ring, str.), 971, 1199, 1402, 1509, 1581, 1650 (aromatic CH=N, str.), 2346, 2373, 3381 (aromatic 2^0-NH, str.)

4-[(2*E*)-2-(2-Chlorobenzylidene)hydrazinyl]tetrazolo-[1,5-*a*]quinoxaline (Vb): Light orange solid, yield 61%, $R_{f\,(Ethylacetate:Hexane\,=\,1:1)}$ 0.71, mp 220 °C; ^{1}H-NMR (DMSO-d_6, 300 MHz, ppm): δ 7.552-7.581 (d, 1H, Ar-H, J = 8.7 Hz, *ortho*-coupling), δ 7.333-7.359 (d, 1H, Ar-H, J = 7.8 Hz, *ortho*-coupling), δ 7.451-7.476 (t, 2H, Ar-H, J = 3.3-4.2 Hz), δ 9.141 (s, 1H, -N**H**-N), δ 8.140 (s, 1H, C**H**=N), δ 8.731-8.762 (q, A_2B_2 pattern, 4H, quinoxaline ring protons, J = 3.0-3.3 Hz); FT-IR (KBr), in cm^{-1}: 780 (*ortho*-disubstituted aromatic ring, str.), 971, 1086 (aryl C-Cl, str.), 1198, 1384, 1537, 1592, 1648, 2348, 2378, 3388.

4-[(2*E*)-2-(2-Fluorobenzylidene)hydrazinyl]tetrazolo-[1,5-*a*]quinoxaline (Vc): Light brown solid, yield 50%, $R_{f\,(Ethylacetate:Hexane\,=\,1:1)}$ 0.76, mp 188-190 °C; ^{1}H-NMR (DMSO-d_6, 300 MHz, ppm): δ 7.555-7.585 (d, 1H, Ar-H, J = 9 Hz, *ortho*-coupling), δ 7.381-7.410 (d, 1H, Ar-H, J = 8.7 Hz, *ortho*-coupling), δ 7.452-7.48 (t, 2H, Ar-H, J = 3.3-4.2 Hz), δ 9.143 (s, 1H, -N**H**-N), δ 8.973 (s, 1H, C**H**=N), δ 8.732-8.763 (q, A_2B_2 pattern, 4H, quinoxaline ring protons, J = 3.0-3.3 Hz); FT-IR (KBr), in cm^{-1}: 780, 1198, 1287 (aryl C-F, str.), 1384, 1509, 1581, 1660, 2346, 2373, 3318.

4-[(2*E*)-2-(2-Nitrobenzylidene)hydrazinyl]tetrazolo[1,5-*a*]quinoxaline (Vd): Light brown solid, yield 70%, $R_{f\,(Ethylacetate:Hexane\,=\,1:1)}$ 0.75, mp 223 °C; FT-IR (KBr), in cm^{-1}: 738, 780, 1198, 1325 (N-O, sym. str), 1384, 1480 (N-O, asym. str.), 1509, 1581, 1660, 2346, 2373, 3410.

4-[(2*E*)-2-(4-Chlorobenzylidene)hydrazinyl]tetrazolo[1,5-*a*]quinoxaline (Ve): Red solid, yield 80%, $R_{f\,(Ethylacetate:Hexane\,=\,7:3)}$ 0.70, mp 230 °C; ^{1}H-NMR (DMSO-d_6, 300 MHz, ppm): δ 8.734-8.766 (q, A_2B_2 pattern, 4H, quinoxaline ring protons, J = 2.7-3.6 Hz, *meta*-coupling), δ 8.032-8.064 (q, A_2B_2 pattern, 4H, Ar-H, J = 3.3 Hz), δ 8.663 (s, 1H, N**H**-N), δ 7.546-7.573 (d, 1H, N=C**H**, J = 8.1 Hz, strong allylic coupling); FT-IR (KBr), in cm^{-1}: 823 (*para*-disubstituted aromatic ring, str.), 971, 1129 (aryl C-Cl), 1388, 1500, 1592, 1666, 2356, 2388, 3240.

4-[(2*E*)-2-(4-Fluorobenzylidene)hydrazinyl]tetrazolo[1,5-*a*]quinoxaline (Vf): Red solid, yield 77%, $R_{f\,(Ethylacetate:Hexane\,=\,7:3)}$ 0.76, mp 243 °C; ^{1}H-NMR (DMSO-d_6, 300 MHz, ppm): δ 8.743-8.775 (q, A_2B_2 pattern, 4H, quinoxaline ring protons, J = 2.7-3.6 Hz, *meta*-coupling), δ 8.040-8.072 (q, A_2B_2 pattern, 4H, Ar-H, J = 3.3 Hz), δ 8.631 (s, 1H, N**H**-N), δ 7.840-7.866 (d, 1H, N=C**H**, J = 7.8 Hz, strong allylic coupling); FT-IR (KBr), in cm^{-1}: 867, 1287 (aryl C-F, str.), 1199, 1384, 1509, 1581, 1660, 2346, 2373, 3321.

4-{(2*E*)-2-[4-(Trifluoromethyl)benzylidene]hydrazinyl}-tetrazolo[1,5-*a*]quinoxaline (Vg): Red solid, yield 67%, $R_{f\,(Ethylacetate:Hexane\,=\,7:3)}$ 0.66, mp 253 °C; ^{1}H-NMR (DMSO-d_6, 300 MHz, ppm): δ 8.740-8.772 (q, A_2B_2 pattern, 4H, quinoxaline ring protons, J = 2.7-3.6 Hz, *meta*-coupling), δ 8.028-8.060 (q, A_2B_2 pattern, 4H, Ar-H, J = 3.3 Hz), δ 8.628 (s, 1H, N**H**-N), δ 7.836-7.862 (d, 1H, N=C**H**, J = 7.8 Hz, strong allylic coupling); FT-IR (KBr), in cm^{-1}: 780, 869, 1288 (aryl C-F, str.), 1198, 1387, 1509, 1581, 1661, 2348, 2369, 3401.

4-[(2*E*)-2-(Tetrazolo[1,5-*a*]quinoxalin-4-yl)hydrazinylidene]methyl}phenol (Vh): Deep red solid, yield 73%, mp 276 °C; ^{1}H-NMR (DMSO-d_6, 300 MHz, ppm): δ 8.735-8.767 (q, A_2B_2 pattern, 4H, quinoxaline ring protons, J = 3.0-3.3 Hz, *meta*-coupling), δ 8.033-8.065 (q, A_2B_2 pattern, 4H, Ar-H, J = 3.3 Hz), δ 8.723 (s, 1H, N**H**-N), δ 7.931 (s, 1H, N=C**H**), δ 2.486 (s, 1H, O**H**); FT-IR (KBr), in cm^{-1}: 971, 1199, 1288 (C-O, str., coupled with H-C-H), 1326, 1510, 1582, 1666, 2345, 2371, 3682 (phenolic -OH, str.).

4-[(2*E*)-2-(4-Nitrobenzylidene)hydrazinyl]tetrazolo[1,5-*a*]quinoxaline (Vi): Brick red solid, yield 72%, $R_{f\,(\text{Ethylacetate:Hexane = 7:3})}$ 0.82, mp 243 °C; ^{1}H-NMR (DMSO-d_6, 300 MHz, ppm): δ 8.735-8.766 (q, A_2B_2 pattern, 4H, quinoxaline ring protons, J = 2.7-3.3 Hz), δ 8.033-8.064 (q, A_2B_2 pattern, 4H, Ar-H, J = 2.7-3.6 Hz), δ 7.212 (s, 1H, N=C**H**), δ 8.238 (s, 1H, N**H**-N); FT-IR (KBr), in cm^{-1}: 982, 1206, 1369 (aromatic -NO_2, sym. str.), 1517, 1551 (aromatic -NO_2, asym. str.), 1572, 1634, 2318, 2371, 3271.

4-[(2*E*)-2-(4-Methoxybenzylidene)hydrazinyl]tetrazolo-[1,5-*a*]quinoxaline (Vj): Orange red solid, yield 82%, $R_{f\,(\text{Ethylacetate:Hexane = 7:3})}$ 0.82, mp 222 °C; ^{1}H-NMR (DMSO-d_6, 300 MHz, ppm): δ 8.752 (s, 4H, quinoxaline ring protons), δ 8.05-8.061 (d, 4H, Ar-H, J = 3.3 Hz, allylic coupling), δ 3.369 (s, 3H, OCH_3), δ 8.6 (s, 1H, N**H**-N), δ 7.761-7.788 (d, 1H, C**H**=N, J = 8.1 Hz, strong allylic coupling); FT-IR (KBr), in cm^{-1}: 825 (*para*-disubstituted aromatic ring, str.), 1040 (C-O-C, sym. str.), 1129 (aromatic C-O, str.), 1240 (C-O-C, asym., str.), 1380, 1393, 1631, 2341, 2370, 3345.

3-Chloro-4-(substitutedphenyl)-1-(tetrazolo[1,5-*a*]quinoxalin-4-ylamino)azetidin-2-ones VII(a-j). To a solution of compound **(Va-j)** (0.0013 mol), in dry benzene (30 mL) was added to a well stirred mixture of triethylamine (0.0016 mol) & chloroacetylchloride (0.0016 mol), at low temperature (below 5 °C). The resulting solids were filtered & recrystallized with chloroform-methanol mixture (1:1).

3-Chloro-4-phenyl-1-(tetrazolo[1,5-*a*]quinoxalin-4-ylamino)azetidin-2-one (VIIa): Brick red crystals, yield 70%, $R_{f\,(\text{Ethylacetate:Hexane = 6:4})}$ 0.6, mp 182 °C; ^{1}H-NMR (DMSO-d_6, 300 MHz, ppm): δ 8.731-8.762 (q, 4H, A_2B_2 pattern, quinoxaline ring protons, J = 2.7-3.3 Hz), δ 8.028-8.059 (m, 5H, Ar-H, J = 3.3 Hz), δ 3.340 (s, 1H, NH), δ 3.165 (s, 1H, C**H**-Cl), δ 3.788 (s, 1H, C**H**-Ar); FT-IR (KBr), in cm^{-1}: 971, 1198, 1288 (CH-Cl, str.), 1380, 1407, 1581, 1666 (-NCO, str.), 2345, 2370.

3-Chloro-4-(2-chlorophenyl)-1-(tetrazolo[1,5-*a*]quinoxalin-4-ylamino)azetidin-2-one (VIIb): Red crystals, yield 50%, $R_{f\,(\text{Benzene:Acetone = 9:1})}$ 0.8, mp 210 °C; ^{1}H-NMR (DMSO-d_6, 300 MHz, ppm): δ 7.662-7.686 (d, 2H, quinoxaline ring protons, J = 7.2 Hz, *ortho*-coupling), δ 7.424-7.475 (t, 2H, quinoxaline ring protons, J = 7.2-8.1 Hz, *ortho*-coupling), δ 7.221-7.271 (t, 4H, Ar-H, J = 7.2-7.8 Hz), δ 3.318 (s, 1H, NH), δ 2.716 (s, 1H, C**H**-Cl), δ 4.118 (s, 1H, C**H**-Ar); FT-IR (KBr), in cm^{-1}: 971, 1037 (aryl C-Cl, str.), 1198, 1287, 1509, 1581, 1644, 2344, 2375, 3381.

3-Chloro-4-(2-fluorophenyl)-1-(tetrazolo[1,5-*a*]quinoxalin-4-ylamino)azetidin-2-one (VIIc): Light red solid, yield 50%, $R_{f\,(\text{Benzene:Acetone = 9:1})}$ 0.84, mp 237 °C; ^{1}H-NMR (DMSO-d_6, 300 MHz, ppm): δ 8.755-8.783 (q, 4H, A_2B_2 pattern, quinoxaline ring protons, J = 2.7-3.3 Hz), δ 8.126-8.159 (q, 4H, Ar-H, J = 3.3 Hz), δ 3.345 (s, 1H, NH), δ 2.729 (s, 1H, C**H**-Cl), δ 4.368 (s, 1H, C**H**-Ar); FT-IR (KBr), in cm^{-1}: 971, 1038 (aryl C-Cl, str.), 1197, 1286 (aryl C-F, str.), 1502, 1586, 1664, 2348, 2369, 3341.

3-Chloro-4-(2-nitrophenyl)-1-(tetrazolo[1,5-*a*]quinoxalin-4-ylamino)azetidin-2-one (VIId): Light red solid, yield 78%; $R_{f\,(\text{Benzene:Acetone = 9:1})}$ 0.76, mp 229 °C; FT-IR (KBr), in cm^{-1}: 972, 1191, 1327 (N-O, sym. str), 1483 (N-O, asym. str.), 1509, 1580, 1641, 2345, 2370, 3456.

3-Chloro-4-(4-chlorophenyl)-1-(tetrazolo[1,5-*a*]quinoxalin-4-ylamino)azetidin-2-one (VIIe): Brick red crystals, yield 60%, $R_{f\,(\text{Benzene})}$ 0.5, mp 267 °C; ^{1}H-NMR (DMSO-d_6, 300 MHz, ppm): δ 8.735-8.766 (q, 4H, A_2B_2 pattern, quinoxaline ring protons, J = 2.7-3.3 Hz), δ 8.032-8.063 (q, 4H, A_2B_2 pattern, Ar-H, J = 2.7-3.3 Hz), δ 3.357 ppm (s, 1H, NH), δ 3.151 (s, 1H, C**H**-Cl), δ 3.288 (s, 1H, C**H**-Ar); FT-IR (KBr), in cm^{-1}: 971, 1085 (aryl C-Cl, str.), 1198, 1287, 1405, 1589, 1642, 2333, 2367, 3382.

3-Chloro-4-(4-fluorophenyl)-1-(tetrazolo[1,5-*a*]quinoxalin-4-ylamino)azetidin-2-one (VIIf): Brown crystals, yield 65%, $R_{f\,(\text{Benzene:Acetone = 8:2})}$ 0.7, mp 213 °C; ^{1}H-NMR (DMSO-d_6, 300 MHz, ppm): δ 8.738-8.770 (q, 4H, A_2B_2 pattern, quinoxaline ring protons, J = 2.7-3.6 Hz), δ 8.047-8.078 (q, 4H, A_2B_2 pattern, Ar-H, J = 3.3 Hz), δ 3.364 (s, 1H, NH), δ 3.161 (s, 1H, C**H**-Cl), δ 3.365 (s, 1H, C**H**-Ar); FT-IR (KBr), in cm^{-1}: 830, 1198, 1286 (aryl C-F, str.), 1509, 1586, 1641, 1740, 2345, 2367, 3354.

3-Chloro-4-(4-trifluoromethylphenyl)-1-(tetrazolo[1,5-*a*]quinoxalin-4-ylamino)azetidin-2-one (VIIg): Black solid, yield 70%, $R_{f\,(\text{TEF})}$ 0.8, mp 238 °C; ^{1}H-NMR (DMSO-d_6, 300 MHz, ppm): δ 8.725-8.757 (q, 4H, A_2B_2 pattern, quinoxaline ring protons, J = 2.7-3.6 Hz), δ 8.027-8.058 (q, 4H, A_2B_2 pattern, Ar-H, J = 3.3 Hz), δ 3.342 (s, 1H, NH), δ 3.150 (s, 1H, C**H**-Cl), δ 3.688 (s, 1H, C**H**-Ar); FT-IR (KBr), in cm^{-1}: 830, 1198, 1287, 1510, 1587, 1648, 1740, 2344, 2369, 3341.

3-Chloro-4-(4-hydroxyphenyl)-1-(tetrazolo[1,5-*a*]quinoxalin-4-ylamino)azetidin-2-one (VIIh): Light red solid, yield 64%, $R_{f\,(\text{TEF})}$ 0.79, mp 246 °C; ^{1}H-NMR (DMSO-d_6, 300 MHz, ppm): δ 8.729-8.761 (q, 4H, A_2B_2 pattern, quinoxaline ring protons, J = 2.4-3.3 Hz), δ 8.030-8.061 (q, 4H, A_2B_2 pattern, Ar-H, J = 2.7-3.3 Hz), δ 3.352 (s, 1H, NH), δ 3.165 (s, 1H, -OH), δ 2.487 (s, 1H, C**H**-Cl), δ 2.987 (s, 1H, C**H**-Ar); FT-IR (KBr), in cm^{-1}: 830, 962, 1199, 1288 (C-O, str.), 1391, 1510, 1581, 1635, 2346, 2378, 3354, 3564.

3-Chloro-4-(4-nitrophenyl)-1-(tetrazolo[1,5-*a*]quinoxalin-4-ylamino)azetidin-2-one (VIIi): Light red solid, yield 58%, $R_{f\,(\text{TEF})}$ 0.49, mp 258 °C; ^{1}H-NMR (DMSO-d_6, 300 MHz, ppm): δ 8.719-8.763 (q, 4H, A_2B_2 pattern, quinoxaline ring protons, J = 2.7-3.9 Hz), δ 8.031-8.063 (q, 4H, A_2B_2 pattern, Ar-H, J = 2.7-3.6 Hz), δ 3.314 (s, 1H, NH), δ 2.487 (s, 1H, C**H**-Cl), δ 3.612 (s, 1H, C**H**-Ar); FT-IR (KBr), in cm^{-1}: 824, 963, 1199, 1287, 1327 (aromatic -NO_2, str.), 1509, 1564 (aromatic -NO_2, str.), 1640, 2325, 2380, 3355.

3-Chloro-4-(4-methoxyphenyl)-1-(tetrazolo[1,5-*a*]quinoxalin-4-ylamino)azetidin-2-one (VIIj): Light red solid, yield 64%, $R_{f\,(\text{TEF})}$ 0.72, mp 227 °C; ^{1}H-NMR (DMSO-d_6, 300 MHz, ppm): δ 8.731-8.763 (q, 4H, A_2B_2 pattern, quinoxaline ring protons, J = 3.0-3.3 Hz), δ 8.031-8.063 (q, 4H, A_2B_2 pattern, Ar-H, J = 3.3-3.6 Hz), δ 3.558 (s, 1H, NH), δ 2.487 (s, 1H, C**H**-Cl), δ 2.988 (s, 1H, C**H**-Ar), δ2.514 (s, 3H, OCH_3); FT-IR (KBr), in cm^{-1}: 828,963, 1096 (sym. C-O-C, str.), 1129 (aromatic C-O, str.), 1199, 1225 (asym. C-O-C, str.), 1288, 1510, 1580, 1644, 2340, 2376, 3383.

2-(Substitutedphenyl)-3-(tetrazolo[1,5-*a*]quinoxalin-4-

ylamino)-1,3-thiazolidin-4-one VIII(a-j). Compound **V(a-j)** (200 mg) was added to 8 mL of thioglycollic acid & refluxed at oil-bath for 20 hours. Then excess thioglycollic acid was removed by vacuum distillation. Then resulting mass was treated with 20 mL of 10% sodium bicarbonate & product was isolated. Products were recrystallized with chloroform-methanol (1:1) mixture.

2-Phenyl-3-(tetrazolo[1,5-*a*]quinoxalin-4-ylamino)-1,3-thiazolidin-4-one (VIIIa): Brown solid, yield 51%, $R_{f\,(TEF)}$ 0.86, mp 249 °C; ^{1}H-NMR (DMSO-d_6, 300 MHz, ppm): δ 7.206-7.260 (t, 5H, Ar-H, J = 7.2-8.4 Hz), δ 7.648-7.674 (d, 2H, quinoxaline ring protons, J = 7.8 Hz), δ 7.410-7.461 (t, 2H, quinoxaline ring protons, J = 7.8-8.1 Hz), δ 2.489 (s, 2H, CH_2), δ 3.326 (s, 1H, NH), δ 2.375-2.419 (d, 1H, CH, J = 13.2 Hz, strong allylic coupling); FT-IR (KBr), in cm^{-1}: 742 (*mono*-substituted aromatic ring, str.), 799 (C-S, str.), 964, 1202, 1392, 1517, 1582, 1659, 1759, 2320, 2365, 3293.

2-(2-Chlorophenyl)-3-(tetrazolo[1,5-*a*]quinoxalin-4-ylamino)-1,3-thiazolidin-4-one (VIIIb): Brown solid, yield 58%, $R_{f\,(TEF)}$ 0.79, mp 248 °C; ^{1}H-NMR (DMSO-d_6, 300 MHz, ppm): δ 7.245 (t, 4H, Ar-H, J = 7.8 Hz), δ 7.662-7.688 (d, 2H, quinoxaline ring protons, J = 7.8 Hz), δ 7.408-7.458 (t, 2H, quinoxaline ring protons, J = 7.8-8.1 Hz), δ 3.308 (s, 1H, NH), δ 2.385 (s, 2H, CH_2), δ 2.486-2.490 (d, 1H, CH); FT-IR (KBr), in cm^{-1}: 777, 799, 952, 1106 (aryl C-Cl, str.), 1166, 1513, 1574, 1711, 1727, 2341, 2365, 3394.

2-(2-Flurophenyl)-3-(tetrazolo[1,5-*a*]quinoxalin-4-ylamino)-1,3-thiazolidin-4-one (VIIIc): Brown solid, yield 54%, $R_{f\,(TEF)}$ 0.83, mp 248 °C; ^{1}H-NMR (DMSO-d_6, 300 MHz, ppm): δ 7.237 (t, 4H, Ar-H, J = 7.8 Hz), δ 7.660-7.685 (d, 2H, quinoxaline ring protons, J = 7.8 Hz), δ 7.407-7.458 (t, 2H, quinoxaline ring protons, J = 7.8-8.1 Hz), δ 3.318 (s, 1H, NH), δ 2.387 (s, 2H, CH_2), δ 2.492-2.497 (d, 1H, CH); FT-IR (KBr), in cm^{-1}: 778, 799, 964, 1166, 1286 (aryl C-F, str.), 1509, 1644, 1727, 2346, 2370, 3374.

2-(2-Nitrophenyl)-3-(tetrazolo[1,5-*a*]quinoxalin-4-ylamino)-1,3-thiazolidin-4-one (VIIId): Brown solid, yield 63%, $R_{f\,(TEF)}$ 0.87, mp 267 °C; ^{1}H-NMR (DMSO-d_6, 300 MHz, ppm) δ 7.239 (t, 4H, Ar-H, J = 7.8 Hz), δ 7.656-7.681 (d, 2H, quinoxaline ring protons, J = 7.8 Hz), δ 7.410-7.461 (t, 2H, quinoxaline ring protons, J = 7.8-8.1 Hz), δ 3.310 (s, 1H, NH), δ 2.384 (s, 2H, CH_2), δ 2.490-2.494 (d, 1H, CH); FT-IR (KBr), in cm^{-1}: 779, 796, 966, 1178, 1326, 1499, 1515, 1666, 1714, 2338, 2365, 2389, 3408.

2-(4-Chlorophenyl)-3-(tetrazolo[1,5-*a*]quinoxalin-4-ylamino)-1,3-thiazolidin-4-one (VIIIe): Brown solid, yield 53%, $R_{f\,(TEF)}$ 0.79, mp 237 °C; ^{1}H-NMR (DMSO-d_6, 300 MHz, ppm): δ 8.729-8.761 (q, 4H, A_2B_2 pattern, quinoxaline ring protons, J = 2.7-3.6 Hz), δ 8.030-8.061 (q, 4H, A_2B_2 pattern, Ar-H, J = 2.7-3.3 Hz), δ 3.352 (s, 1H, NH), δ 2.487 (s, 2H, CH_2), δ 2.510 (s, 1H, CH); FT-IR (KBr), in cm^{-1}: 795 (C-S, str.), 837, 963, 1041 (aryl C-Cl, str.), 1507, 1586, 1657, 1729, 2344, 2377, 3344.

2-(4-Flurophenyl)-3-(tetrazolo[1,5-*a*]quinoxalin-4-ylamino)-1,3-thiazolidin-4-one (VIIIf): Brown solid, yield 42%, $R_{f\,(TEF)}$ 0.75, mp 212 °C; ^{1}H-NMR (DMSO-d_6, 300 MHz, ppm): δ 8.725-8.757 (q, 4H, A_2B_2 pattern, quinoxaline ring protons, J = 2.7-3.6 Hz), δ 8.041-8.072 (q, 4H, A_2B_2 pattern, Ar-H, J = 2.7-3.3 Hz), δ 3.358 (s, 1H, NH), δ 2.484 (s, 2H, CH_2), δ 2.512 (s, 1H, CH); FT-IR (KBr), in cm^{-1}: 799 (C-S, str.), 839, 963, 1286 (aryl C-F, str.), 1510, 1588, 1666, 1729, 2345, 2367, 3354.

2-(4-trifluromethylphenyl)-3-(tetrazolo[1,5-*a*]quinoxalin-4-ylamino)-1,3-thiazolidin-4-one (VIIIg): Brown solid, yield 48%, $R_{f\,(TEF)}$ 0.89, mp 229 °C; ^{1}H-NMR (DMSO-d_6, 300 MHz, ppm): δ 8.715-8.737 (q, 4H, A_2B_2 pattern, quinoxaline ring protons, J = 2.7-3.6 Hz), δ 8.030-8.061 (q, 4H, A_2B_2 pattern, Ar-H, J = 2.7-3.3 Hz), δ 3.338 (s, 1H, NH), δ 2.464 (s, 2H, CH_2), δ 2.522 (s, 1H, CH); FT-IR (KBr), in cm^{-1}: 792 (C-S, str.), 836, 963, 1288 (aryl C-F, str.), 1509, 1587, 1666, 1739, 2344, 2367, 3324.

2-(4-Hydroxyphenyl)-3-(tetrazolo[1,5-*a*]quinoxalin-4-ylamino)-1,3-thiazolidin-4-one (VIIIh): Light brown solid, yield 62%, $R_{f\,(TEF)}$ 0.78, mp 222 °C; ^{1}H-NMR (DMSO-d_6, 300 MHz, ppm): δ 8.659-8.697 (m, 4H, quinoxaline ring protons), δ 7.957-7.994 (m, 4H, Ar-H), δ 3.290 (s, 1H, NH), δ 3.261 (s, 1H, OH), δ 2.048 (s, 2H, CH_2), δ 3.285 (s, 1H, CH); FT-IR (KBr), in cm^{-1}: 792, 819, 1178, 1257 (C-O, str.), 1515, 1572, 1684, 1714, 2338, 2365, 3339, 3362 (phenolic -OH, str.)

2-(4-Nitrophenyl)-3-(tetrazolo[1,5-*a*]quinoxalin-4-ylamino)-1,3-thiazolidin-4-one (VIIIi): Brown solid, yield 64%, $R_{f\,(TEF)}$ 0.85, mp 279 °C; ^{1}H-NMR (DMSO-d_6, 300 MHz, ppm): δ 8.657-8.697 (m, 4H, quinoxaline ring protons), δ 7.958-7.994 (m, 4H, Ar-H), δ 3.285 (s, 1H, NH), δ 3.261 (s, 1H, CH), δ 2.048 (s, 2H, CH_2); FT-IR (KBr), in cm^{-1}: 793, 846, 934, 1173, 1342 (sym. aromatic -NO_2, str.), 1512, 1528 (asym. aromatic -NO_2, str.), 1600, 1684, 1730, 2333, 2363, 3274.

2-(4-Methoxyphenyl)-3-(tetrazolo[1,5-*a*]quinoxalin-4-ylamino)-1,3-thiazolidin-4-one (VIIIj): Brown solid, yield 74%, $R_{f\,(TEF)}$ 0.68, mp 264 °C; ^{1}H-NMR (DMSO-d_6, 300 MHz, ppm): δ 7.658-7.683 (d, 2H, quinoxaline ring protons, J = 7.5 Hz), δ 7.444 (t, 2H, quinoxaline ring protons), δ 7.240-7.266 (d, 4H, Ar-H, J = 7.8 Hz), δ 3.220 (s, 1H, CH), δ 2.486 (s, 2H, CH_2), δ 2.380 (s, 3H, OCH_3); FT-IR (KBr), in cm^{-1}: 799, 841, 1096 (sym. C-O-C, str.), 1148 (aromatic C-O, str.), 1245 (asym. C-O-C, str.), 1502, 1584, 1681, 1729, 2355, 2379, 3359.

Antibacterial Activity & Antifungal Activity. All the synthesized have been screened for antibacterial activity against gram positive bacteria *S. aureus* (ATCC-2913), gram negative bacteria *K. pneumonia* (ATCC-700603), *P. aeruginosa* (ATCC-27853), *E. coli* (ATCC-25922) & antifungal activity against *C. albicans* (ATCC-2091) by using cup-plate method.

The growth media (Nutrient Agar media for bacterial growth & Sabouraud Dextrose Agar media for fungal growth) were prepared & sterilized in autoclave at 15 psig for 15 minutes. These media were poured into petri-plates under standard conditions & allowed to solidify. On the surface of media, test microorganisms were inoculated with sterilized nickel loop wire. Cups were made by boring on the surface of growth media with previously sterilized borer. Four cups were made on each petri-plate. These cups were

filled with different concentrations (50 μg/mL & 100 μg/mL in DMSO) of the test compounds, third with control (DMSO) & fourth one with standard drug. The plates were kept in cold for 1 hour to allow the diffusion of test compounds & then incubated at 35 °C for 48 hours (for antifungal activity) & at 37 °C for 24 hours (for antibacterial activity). The zones of inhibition formed around the cups after respective incubation were measured.

Result and Discussion

Chemistry. The mentioned compounds were synthesized by represented scheme in Figure 1. Initial compound quinoxaline-2,3-dione **I**, was synthesized in good yield by condensation of oxalic acid & *o*-phenylenediamine in 20% HCl. Reaction of compound **I** with $POCl_3$ under refluxing conditions lead to chlorination & formation of 2,3-dichloroquinoxaline **II.** Compound **II**, on (2+3) cycloaddition with sodium azide in DMSO at acidic pH, cyclized to 4-chlorotetrazolo[1,5-*a*]quinoxaline **III**. Compound **III**, on treatment with hydrazine hydrate gave 4-hydrazinotetrazolo[1,5-*a*]-quinoxaline **IV**, which on treatment with various aromatic aldehydes under refluxing condition, furnished corresponding schiff's bases **V(a-j)**. Cyclization of compounds **V(a-j)** to azetidinone derivatives **VII(a- j)** was achieved by stirring compounds **V(a-j)** at very low temperature (5 °C), with equimolar mixture of chloroacetylchloride & triethylamine in dry benzene. Compounds **V(a-j)** were also cyclized to thiazolidinone derivatives **VIII(a-j)** by refluxing these compounds with thioglycollic acid in oil-bath. The structure of all the newly synthesized 4-aminotetrazolo[1,5-*a*]quinoxaline based azetidinone & thiazolidinone derivatives were confirmed on the basis of their elemental analysis & spectral analysis.

Formation of quinoxaline-2,3-dione **I** was confirmed by ^{1}H-NMR & FT-IR spectra interpretation. FT-IR of compound I showed bands at 3304 cm^{-1}, 1688 cm^{-1}, 1535 cm^{-1} & 1387 cm^{-1} corresponding to -NH, >C=O, -NHCO & =C-N groups respectively, while its ^{1}H-NMR spectra showed a multiplet peak at δ 7.042-7.125 ppm corresponding to quinoxaline ring protons & broad singlet peak at δ 11.902 ppm confirming the two protons of -NHCO group. FT-IR spectra of compound **II** showed bands at 1121 cm^{-1}, 1171 cm^{-1}, & 1688 cm^{-1} confirming C-Cl, C-N, C=N respectively & H^1-NMR of this compound showed two multiplet peaks. One multiplet peak with A_2B_2 pattern at δ 7.995-8.019 ppm for two quinoxaline ring protons close to nitrogen vicinity & another multiplet peak with A_2B_2 pattern were present at δ 7.782-7.807 ppm corresponding to other two protons of quinoxaline ring. FT-IR spectrum of compound **III** have the extra bands in the region 2345 cm^{-1} & 2368 cm^{-1} corresponding to N-N & N=N, which are part of tetrazole ring. This confirmed the cyclization of compound **II** to compound **III**. ^{1}H-NMR spectra of compound **III** showed the two multiplet peaks, one in the region of δ 8.659-8.697 ppm (for two protons of quinoxaline ring close to nitrogen vicinity) & another in the region δ 7.957-7.994 ppm (for remaining two protons of quinoxaline ring).

In the FT-IR spectrum of compound **IV** band at 1073 cm^{-1} (in compound **III**) had been replaced by band at 2942 cm^{-1} & 3134 cm^{-1} confirming -NH of -$NHNH_2$. Compound **IV** has also been confirmed by ^{1}H-NMR. ^{1}H-NMR spectrum of compound **IV** showed two multiplet peaks with A_2B_2 pattern at δ 8.731-8.762 ppm (for two protons of quinoxaline ring close to nitrogen vicinity) & at δ 8.028-8.059 ppm (for remaining two protons of quinoxaline ring) & a broad doublet peak at δ 7.485-7.510 ppm corresponding to -NH of -$NHNH_2$. Protons in -$NHNH_2$ showed characters of exchangeable protons, since after D_2O exchange, peak at δ 7.485 ppm have been shifted.

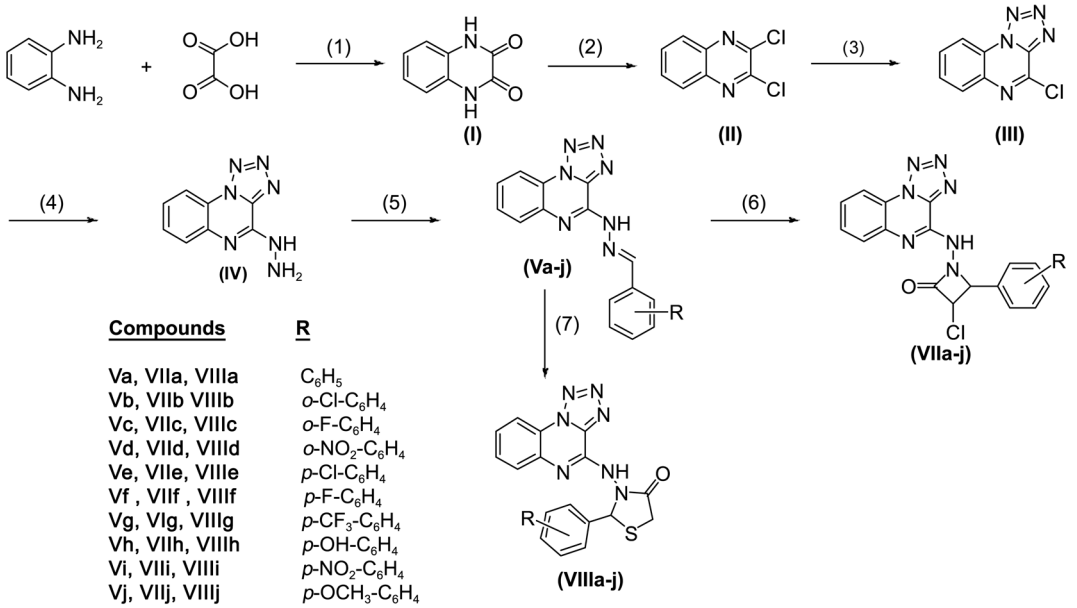


Figure 1. Reaction Scheme. Reagents and Conditions: (1) aq. HCl (20%), reflux; (2) $POCl_3$, DMA, reflux; (3) NaN_3/AcOH, DMSO; (4) $NH_2{\cdot}NH_2{\cdot}H_2O$, EtOH; (5) RCHO, MeOH; (6) $ClCH_2COCl$, Et_3N, dry benzene; (7) $HSCH_2COOH$.

Formation of various schiff's bases **V(a-j)** from the compound **IV** have also been confirmed by their FT-IR & ^{1}H-NMR spectra. FT-IR spectrum of compound **Va** has shown the bands at 1402 cm^{-1}, 1581 cm^{-1}, 1650 cm^{-1} & 3381 cm^{-1} corresponding to =C-N, -NH (def.), CH=N & -NH (str.) groups respectively, while ^{1}H-NMR spectrum of compound showed a quartlet peak with A_2B_2 pattern at δ 8.733-8.763 ppm with A_2B_2 pattern, corresponding to four quinoxaline ring protons (J = 3.0-3.3 Hz), another multiplet at δ 8.030-8.061 ppm (for other five aromatic protons), one singlet at δ 7.934 ppm (for proton of NH-N) & a doublet at δ 7.478-7.501 ppm, corresponding to one proton of CH=N with J value of 6.9 Hz, showing strong allylic coupling with one phenyl proton. Similarly, another synthesized schiff's bases have been confirmed.

Now, above schiff's bases have been cyclized to potent antibacterial & antifungal agents *viz.* azetidinone derivatives **VII(a-j)** & thiazolidinone derivatives **VIII(a-j)**. Formation of 4-aminotetrazolo[1,5-*a*]quinoxaline based azetidinones have been confirmed by their FT-IR & ^{1}H-NMR spectra. FT-IR spectrum of compound **VIIa** showed the bands at 1288 cm^{-1} & 1666 cm^{-1} confirming the CH-Cl & -NCO. ^{1}H-NMR spectrum of this compound showed a quartlet peak at δ 8.731-8.762 ppm with A_2B_2 pattern, corresponding to four quinoxaline ring protons (J = 3.3 Hz), another multiplet at δ 8.028-8.059 ppm (5H, Ar-H, J = 3.3 Hz) & a singlet at δ 3.34 ppm (1H, NH) & δ 3.778 ppm corresponding to CH-Ar of azetidonone ring. Similarly, other synthesized azetidinone derivatives have been confirmed.

Cyclization of different schiff's bases **V(a-j)** to 4-aminotetrazolo[1,5-*a*]quinoxaline based thiazolidinone derivatives **VIII(a-j)** also have been confirmed by FT-IR & ^{1}H-NMR spectra. FT-IR spectrum of compound **VIIIa** consists of a band at 799 cm^{-1} confirming C-S bond. ^{1}H-NMR spectra of this compound showed a doublet at δ 7.648-7.674 ppm, corresponding to two quinoxaline ring protons, a triplet at δ 7.410-7.461 ppm for two quinoxaline protons with J value ranging in 7.8-8.1 Hz confirming *ortho*-coupling, a triplet at δ 7.206-7.260 ppm corresponding to five aromatic protons with J value ranging in 7.8-8.1 Hz confirming *ortho*-coupling, a singlet at δ 2.489 ppm for two cyclic protons of thiazolidinone ring & a singlet at δ 3.326 ppm for single proton of -NH group & one doublet peak at δ 2.375-2.419 ppm corresponding to one proton of CH of thiazolidinone ring. Similarly, other 4-aminotetrazolo[1,5-*a*]quinoxaline based thiazolidinone derivatives have been confirmed.

Biological Activity. All the newly synthesized compounds have also been submitted for evaluation of antibacterial activity against gram positive bacteria *S. aureus*, gram negative bacteria *K. pneumoniae*, *P. aeruginosa*, *E. coli* & antifungal activity against *C. albicans* using cup-plate method. Ciprofloxacin (30 μg/mL) & voriconazole (30 μg/mL) were used as standard drugs for antibacterial & antifungal activity, while, Nutrient Agar Medium & Sabouraud Dextrose Agar Medium were selected as growth media for bacterial & fungal growth respectively. Observations are shown in Table 1.

Structures of synthesized compounds can be divided into three parts *viz.* tetrazolo[1,5-*a*]quinoxaline ring, amino group

Table 1. Zone of inhibition (mm) of different compounds

Compounds	*E. coli*		*S. aureus*		*P. aeruginosa*		*K. pneumoniae*		*C. albicans*	
	50 μg/mL	100 μg/mL	50 μg/mL	100 μg/mL	50 μg/mL	100 μg/mL	50 μg/mL	100 μg/mL	50 μg/mL	100 μg/mL
VIIa	10	16	11	15	6	8	6	9	7	9
VIIb	11	14	12	16	7	8	7	10	9	11
VIIc	10	14	9	13	6	8	6	10	8	10
VIId	11	15	10	12	5	7	6	9	8	11
VIIe	14	18	13	18	7	9	8	12	8	10
VIIf	10	15	10	14	5	7	7	10	7	10
VIIg	10	13	9	12	5	8	6	9	7	9
VIIh	12	15	11	15	6	7	7	10	9	12
VIIi	13	16	12	16	7	8	9	13	10	13
VIIj	8	11	9	12	5	6	6	8	8	11
VIIIa	11	14	10	14	5	7	6	9	7	9
VIIIb	12	15	12	16	7	8	7	9	10	13
VIIIc	10	14	9	12	5	7	6	8	7	10
VIIId	10	16	9	13	5	7	6	9	7	9
VIIIe	11	14	12	15	7	9	9	12	9	12
VIIIf	10	14	10	13	5	7	6	8	8	11
VIIIg	10	16	9	13	5	7	6	9	8	10
VIIIh	13	17	13	16	6	7	7	10	11	13
VIIIi	11	15	12	17	7	9	10	13	10	13
VIIIj	8	10	9	12	5	6	6	8	7	10
standard		23		22		13		16		18
control		3		3		1		2		4

Standard Drugs: For antibacterial activity: Ciprofloxacin 30 μg/mL. For antifungal activity: Voriconazole 30 μg/mL. Control: DMSO

attached to C-4 of tetrazolo[1,5-*a*]quinoxaline ring and five membered (thiazolidinone) or four membered (azetidinone) ring attached to amino group. We have concentrated on "the effect of different substitutions at phenyl ring attached to adjacent carbon of N-atom of azetidinone and thiazolidinone heterocyclic ring on antibacterial and antifungal activity. *p*-Methoxyphenyl substitution on fourth position of azetidinone ring **(VIIj)** and on second position of thiazolidinone ring **(VIIIj)** exhibited minimal activity against all bacterial and fungal strains under investigation, while *p*-chlorophenyl moiety at above mentioned positions in azetidinone ring **(VIIe)** enhanced antibacterial action against all the bacterial strains under investigation. Against *E. coli*, *p*-chlorophenyl **(VIIe)**, *p*-hydroxyphenyl **(VIIh)** and *p*-nitrophenyl **(VIIi)** substitutions at fourth position of azetidinone ring and *o*-chlorophenyl **(VIIIb)** and *p*-hydroxyphenyl **(VIIIh)** substitutions at second position of thiazolidinone ring exhibited promising activity, but presence of electron-donating methoxy group at *para* position in phenyl ring attached to azetidinone ring **(VIIj)** and thiazolidinone ring **(VIIIj)** exhibited minimal activity. Against *S. aureus*, pattern of antibacterial activity was found to be almost same as in case of *E. coli*, but here, *p*-nitrophenyl attached to thiazolizidinone **(VIIIi)** also showed better activity than other compounds. Against *P. aeruginosa* and *K. pneumonia*, all the synthesized compounds exhibited mild to moderate activity. Against *P. aeruginosa*, compound with *o*-chloro **(VIIb**, **VIIIb)**, *o*-nitro **(VIId**, **VIIId)** and *p*-nitro **(VIIi**, **VIIIi)** substituted phenyl ring attached to azetidinone and thiazolidinone nucleus exhibited some better activity as compared to other compounds. All the compounds, mentioned above in case of *P. aeruginosa*, except **VIIb** and **VIIIb** are more active against *K. pneumonia* as compared to other compounds. This discussion led to conclusion that presence of electron-withdrawing group such as -Cl, -NO_2 *etc.* at *ortho* and *para* positions of phenyl ring attached to fourth position of azetidinone and second position of thiazolidinone nucleus enhance the antibacterial against *E. coli*, *S. aureus*, *P. aeruginosa* and *K. pneumonia*. Against fungus *C. albicans*, 4-aminotetrazolo[1,5-*a*]quinoxaline based thiazolidinone derivatives were found to be more active than their azetidinone counterparts. Among 4-aminotetrazolo[1,5-*a*]quinoxaline based azetidinone derivatives, compound with *p*-nitro phenyl ring **(VIIi)** attached to azetidinone ring exhibited promising activity, but in case of their thiazolidinone counterparts, compounds with *o*-chlorophenyl **(VIIIb)**, *p*-hydroxyphenyl **(VIIIh)** and *p*-nitro **(VIIIi)** attached to thiazolidinone nucleus showed fantastic activity.

Conclusion

All the synthesized compounds were evaluated for antibacterial activity against *E. coli*, *S. aureus*, *P. aeruginosa* & *K. pneumoniae* & antifungal activity against *C. albicans* using cup-plate method. 4-Aminotetrazolo[1,5-*a*]quinoxaline based thiazolidinone & azetidinone derivatives having the aromatic ring substituted with electron-withdrawing groups *viz.* Cl, NO_2, CF_3 & F at *para*-position have exhibited better antibacterial & antifungal activity against bacteria & fungi under investigation. These compounds may act as leads for further investigations.

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