SYNTHESIS, CHARACTERIZATION AND ANTIMICROBIAL ACTIVITY OF SOME NEWLY 1, 2, 4-TRIAZOLE DERIVATIVES

I. Singh* and A. Kumar

Department of Chemistry, Janta Vadic College, Baraut (Baghpat), Uttar Pradesh, India
Department of Community Medicine, LLRM Medical College, Meerut, Uttar Pradesh, India

ABSTRACT: A series of 1-(2-(4H-1,2,4-triazol-4-yl)ethylamino)-3-chloro-4-(5-methoxy/ethoxy-2-substituted alkyl/aryl-1H-indol-3-yl)azetidinones (4a-4h) and 1-(2-(4H-1,2,4-triazol-4-yl)ethylamino)-3-chloro-4-(5-methoxy/ethoxy-2-substituted alkyl/aryl-1H-indol-3-yl)thiazolidinones (5a-5h) have been synthesized by the reaction of 3-(2-(2-(4H-1,2,4-triazol-4-yl)ethyl)hydrazono)methyl)-5-methoxy/ethoxy-2-substituted-1H-indoles (3a-3h) with chloroacetyl chloride and thioglycolic acid respectively. All the newly synthesized compounds were screened for their antibacterial activity against S. aureus, E. coli, P. vulgaris, K. pneumoniae and antifungal activity against A. fumigatus, C. albicans, C. albicans ATCC and C. Krusei G03. The antibacterial activity of newly synthesized compounds compared with standard drug gattifloxacin and ciprofloxacin against different bacteria and antifungal activity of newly compounds compared with standard drug fluconazole against different fungi. The compounds 5d, 5e, 5g and 5h exhibited good antibacterial activity while compounds 4g, 5g and 5h also showed notable antifungal activity. The purity of the newly synthesized compounds was checked by thin layer chromatography (TLC) on silica gel-G coated plates using different solvent systems. The structure of all the compounds were established by the elemental (C, H, N) and spectral (IR, 1H NMR and mass) analysis.

INTRODUCTION: The triazole ring is an important pharmacophore in modern drug discovery. The chemistry and pharmacology of triazoles have been of great interest to medicinal chemistry because its derivatives possessed various biological activities such as antimicrobial 1-3, anti-inflammatory 4, anticancer 5, anti-histaminic 6. Triazole derivatives having indole moiety are found to possess a wide spectrum of antimicrobial activity. A large number of indole derivatives 7-9 having substitution at 2 and 5 position increases the antimicrobial activity. Penicillins are the family of antimicrobial drugs which are derivatives of azetidinone 10.

Azetidinone derivatives have been reported to show a variety of antimicrobial 11-12, antituberculosis 13. Thiazolidinone moiety with triazole ring increases the antimicrobial activity 14-16. These all activities showed that the minor change in the substitution batter activities of azetidine and thiazolidine derivatives have enhanced dramatically so our

Keywords:
1,2,4-triazoles, indoles, azetidinones, thiazolidinones, antibacterial activity, antifungal activity

Correspondence to Author:
Dr. Indu Singh

Assistant Professor, Department of Chemistry, Janta Vadic College, Baraut (Baghpat), Uttar Pradesh, India

E-mail: draruunmrt@gmail.com

DOI: 10.13040/IJPSR.0975-8232.5(10).4386-94

Article can be accessed online on: www.ijpsr.com
research group decide to synthesized a new series azeti/thiazolidine derivatives with several substitutions.

**MATERIAL AND METHODS:**

**Antimicrobial activity:** All the newly synthesized compounds 3a-3h, 4a-4h and 5a-5h were tested for their antimicrobial activity. The effects of unknown compounds were compared with the standard drug; gatifloxacin and ciprofloxacin for bacteria and fluconazole for fungi. The antimicrobial activity was assayed by using cup plate method by using the inhibition zones in mm. Antibacterial activity was performed against Staphylococcus aureus, Escherichia coli, Proteus vulgaris, Klebsiella pneumoniae and antifungal activity against Aspergillus fumigatus, Candida albicans, Candida albicans ATCC and Candida krusei.

**Chemistry:** All reagents and solvents were of analytical grade and used directly. Reactions were routinely performed in oven-dried borosil glassware. The melting points of compounds were determined in open capillaries with the help of thermonic melting point apparatus and were uncorrected. The homogeneity of all newly synthesized compounds was routinely checked by thin layer chromatography (TLC) on silica gel G plates and spots were located by using iodine chamber. Elemental analysis (C, H, N) of all the synthesized compounds were determined by perkin-Elmer 2400 elemental analyzer, and results were found within the ± 0.4% of theoretical values.

The IR spectra were recorded on a Beckman Acculab-10 spectrometer (\( \nu \) max in cm\(^{-1} \)) and the \(^1\)H NMR spectra were recorded by Brucker DPX-300 MHz using CDCl\(_3\) as solvent. Mass spectra were determined on VG-70-S instrument.

**RESULTS AND DISCUSSION**

All the newly synthesized compounds 3a-3h, 4a-4h and 5a-5h were tested for their antimicrobial activity. The pharmacological data of all the compounds have been reported in table 1. The results revealed that the majority of the synthesized compounds showed varying degree of inhibition against the tested microorganism. The alkyl, phenyl and chlorophenyl substitution is beneficial for the antibacterial as well as antifungal activities. The methoxy and ethoxy substituent’s on indole nucleus increase the antimicrobial activity. Compounds having azetidinone and thiazolidinone moiety exhibited better antimicrobial activities. It can be seen in table 1, although all the compounds are not as active as standard drugs. Compounds 5g was found more potent antibacterial agents against different bacteria with standard drug gatifloxacin and ciprofloxacin. Compounds 4e, 4g, 5a, 5b, 5d, 5e, 5f and 5h showed moderate activity and rest compounds showed less activity against all the strains. Compounds 5g (against C. albicans), 5h (against C. albicans ATCC), 4g, 5g and 5h (against C. krusei GO3) showed good antifungal activity compared with fluconazole.

**TABLE 1: ANTIBACTERIAL AND ANTIFUNGAL ACTIVITY OF THE COMPOUNDS 3a-3h, 4a-4h AND 5a-5h**

![Chemical Structures](image-url)
CONCLUSION: From this study, we may conclude that:

1. Compounds (5a-5h) containing thiazolidinone ring exhibited better antibacterial activity than compounds (4a-4h) having azetidinone ring.

2. Para chlorophenyl substituted indole derivatives showed more efficiency due to presence of more electronegative atom.

EXPERIMENTAL PROCEDURE: The synthetic route of the title compounds is outlined in Scheme 1 which are mentioned below as follows.

Synthesis of 4-(2-hydrazinylethyl)-4H-1,2,4-triazole (2): A mixture of compound 1 (1.0 mol) and hydrazine hydrate (1.0 mol) in methanol was refluxed on a steam bath for 4 h the excess solvent was removed under reduced pressure and the product crystallized from methanol to obtain compound 2.

Yield 86%; mp 147°C; IR (KBr): 1261 (N-CH2), 1298 (C=N), 1507 (N-N), 1682 (C=O) cm⁻¹; 1H-NMR (DMSO-d6 δ ppm): 3.32 (q, 2H, NCH2CH2), 4.54 (t, 2H, N-CH2), 5.69 (d, 2H, NH2), 7.60 (m, 1H, NH) 8.61 (s, 2H, -N=CH). MS: [M]+ at m/z 127.15. Elemental analysis found (calculated) for C4H9N5: C, 37.76 (37.79); H, 7.12 (7.13); N, 55.06 (55.08)%.

General procedure for the synthesis of 3-((2-(4H-1,2,4-triazol-4-yl)ethyl)hydrazono)methyl)-5-methoxy/ethoxy-2-substituted-1H-indoles (3a-3h): In the ethanolic solution of compound 2 (0.8 mol) several substituted aryl/alkyl-5-methoxy/ethoxy indol-3- aldehydes (1.0 mol) was added in the presence of glacial acetic acid. The reaction mixture was refluxed for 8-10 h. The completion of the reaction was checked by TLC. The excess of ethanol was distilled off. Reaction mixture was poured into ice water, filtered, washed with water, dried and recrystallized from ethanol to give title compounds.
Scheme 1: Synthetic route of triazole derivatives

R = OCH₃, OC₂H₅
R = H, CH₃, C₆H₅, 4-ClC₆H₄

3-((2-(2-(4H-1,2,4-triazol-4-yl)ethyl)hydrazono)methyl)-5-methoxy-1H-indole (3a): Yield 85%; (Acetone); mp 147° C; IR (KBr): 1261 (N-CH2), 1298 (C-N), 1507 (N-N), 1576 (-N=CH), 1682 (C=N), 3323 (-C-NH) cm⁻¹; ¹H-NMR (DMSO-d6 δ ppm): 3.45 (s, 3H, OCH3), 3.32 (q, 2H, NCH2CH3), 4.56 (t, 2H, -N-CH2), 7.50 (d, 1H, C-CH of pyrole ring of indole), 7.60 (m, 1H, CH2NH), 7.69 (d, 1H, NH of indole), 7.71-8.31 (m, 3H, ArH), 8.61 (s, 2H, -N=CH of triazole), 8.85 (s, 1H, N=CH-indole); MS: [M]+ at m/z 284.32. Elemental analysis found (calculated) for C14H16N6O: C, 59.16 (59.14); H, 5.69 (5.67); N, 29.57 (29.56)%.

3-((2-(2-(4H-1,2,4-triazol-4-yl)ethyl)hydrazono)methyl)-5-ethoxy-1H-indole (3b): Yield 83%; (Methanol); mp 155° C; IR (KBr): 1263 (N-CH2), 1297 (C-N), 1509 (N-N), 1577 (-N=CH), 1685 (C=N), 3324 (-C-NH) cm⁻¹; ¹H-NMR (DMSO-d6 δ ppm): 3.25 (s, 5H, OC2H5), 3.31 (q, 2H, NCH2CH3), 4.58 (t, 2H, -N-CH2), 7.52 (d, 1H, C-CH of pyrole ring of indole), 7.63 (m, 1H, CH2NH), 7.66 (d, 1H, NH of indole), 7.71-8.30 (m, 3H, ArH), 8.63 (s, 2H, -N=CH of triazole), 8.83 (s, 1H, N=CH-indole); MS: [M]+ at m/z 298.34. Elemental analysis found (calculated) for C15H18N6O: C, 60.37 (60.39); H, 6.07 (6.08); N, 28.15 (28.17)%.

3-((2-(2-(4H-1,2,4-triazol-4-yl)ethyl)hydrazono)methyl)-5-methoxy-2-methyl 1H-indole (3c): Yield 82%; (Acetone); mp 157° C; IR (KBr): 1261 (N-CH2), 1298 (C-N), 1507 (N-N), 1576 (-N=CH), 1682 (C=N), 2850 (CH3 of indole), 3323 (-C-NH) cm⁻¹; ¹H-NMR (DMSO-d6 δ ppm): 2.23 (s, 3H, CH3 of indole), 3.45 (s, 3H, OCH3), 3.30 (q, 2H, NCH2CH3), 4.49 (t, 2H, -N-CH2), 7.60 (m, 1H, CH2NH), 7.68 (d, 1H, NH of indole), 7.70-8.31 (m, 3H, ArH), 8.65 (s, 2H, -N=CH of triazole), 8.84 (s, 1H, N=CH-indole); MS: [M]+ at m/z 298.34. Elemental analysis found (calculated) for C15H18N6O: C, 60.36 (60.39); H, 6.05 (6.08); N, 28.14 (28.17)%.

3-((2-(2-(4H-1,2,4-triazol-4-yl)ethyl)hydrazono)methyl)-5-ethoxy-2-methyl 1H-indole (3d): Yield 83%; (Ethanol); mp 165° C; IR (KBr): 1261 (N-CH2), 1298 (C-N), 1507 (N-N), 1576 (-N=CH), 1682 (C=N), 2850 (CH3 of indole), 3323 (-C-NH) cm⁻¹; ¹H-NMR (DMSO-d6 δ ppm): 2.23 (s, 3H, CH3 of indol), 3.45 (s, 5H, OC2H5), 3.31 (q, 2H, NCH2CH3), 4.50 (t, 2H, -N-CH2), 7.62 (m, 1H, CH2NH), 7.67 (d, 1H, NH of indole), 7.70-8.31 (m, 3H, ArH), 8.63 (s, 2H, -N=CH of triazole), 8.85 (s, 1H, N=CH-indole); MS: [M]+ at m/z 312.37. Elemental analysis found (calculated) for C15H18N6O: C, 61.50 (61.52); H, 6.43 (6.45); N, 26.91 (26.90)%.

3-((2-(2-(4H-1,2,4-triazol-4-yl)ethyl)hydrazono)methyl)-5-methoxy-2-phenyl 1H-indole (3e): Yield 82%; (Methanol); mp 172° C; IR (KBr): 1261 (N-CH2), 1298 (C-N), 1507 (N-N), 1576 (-N=CH), 1610 (C=C of aromatic ring), 1682 (C=N), 3150 (CH aromatic), 3323 (-C-NH) cm⁻¹; ¹H-NMR (DMSO-d6 δ ppm): 3.45 (s, 3H, OCH3), 3.31 (q, 2H, NCH2CH3), 4.51 (t, 2H, -N-CH2), 7.60 (m, 1H, CH2NH), 7.69 (d, 1H, NH of indole), 7.71-8.32 (m, 8H, ArH), 8.62 (s, 2H, -N=CH of triazole), 8.86 (s, 1H, N=CH-indole); MS: [M]+ at m/z 360.41. Elemental analysis found (calculated) for C20H20N6O: C, 66.67 (66.65); H, 5.57 (5.59); N, 23.30 (23.32)%.

3-((2-(2-(4H-1,2,4-triazol-4-yl)ethyl)hydrazono)methyl)-5-ethoxy-2-phenyl 1H-indole (3f): Yield 80%; (Acetone); mp 180° C; IR (KBr): 1261 (N-CH2), 1298 (C-N), 1507 (N-N), 1576 (-N=CH), 1610 (C=C of aromatic ring), 1682 (C=N), 3150 (CH aromatic), 3323 (-C-NH) cm⁻¹; ¹H-NMR (DMSO-d6 δ ppm): 3.45 (s, 5H, OC2H5), 3.31 (q, 2H, NCH2CH3), 4.51 (t, 2H, -N-CH2), 7.68 (d, 1H, NH of indole), 7.59 (m, 1H, CH2NH) 7.70-8.31 (m, 8H, ArH), 8.63 (s, 2H, -N=CH of triazole), 8.84 (s, 1H, N=CH-indole); MS: [M]+ at m/z 374.44. Elemental analysis found (calculated) for C21H22N6O: C, 67.38 (67.36); H, 5.90 (5.92); N, 22.43 (22.44)%.

3-((2-(2-(4H-1,2,4-triazol-4-yl)ethyl)hydrazono)methyl)-5-methoxy-2-(4-chlorophenyl)1H-indole (3g): Yield 80%; (Ethanol); mp 195° C; IR (KBr): 770 (C=Cl), 1261 (N-CH2), 1298 (C-N), 1507 (N-N), 1576 (-N=CH), 1610 (C=C of aromatic ring), 1682 (C=N), 3150 (CH aromatic), 3323 (-C-NH) cm⁻¹; ¹H-NMR (DMSO-d6 δ ppm): 3.45 (s, 3H, OCH3), 3.34 (q, 2H, NCH2CH3), 4.57 (t, 2H, -N-CH2), 7.60 (m, 1H, CH2NH), 7.68 (d, 1H, NH of indole), 7.72-8.30 (m, 7H, ArH), 8.63 (s, 2H, -
N=CH of triazole), 8.83 (s, 1H, N=CH-indole); MS: [M]+ at m/z 394.86. Elemental analysis found (calculated) for C_{20}H_{19}ClN_{6}O_{2}: C, 60.82 (60.84); H, 4.83 (4.85); N, 21.26 (21.28)%.

3-((2-(2-(4H-1,2,4-triazol-4-yl)ethyl)hydrazono)methyl)-5-ethoxy-2-(4-chlorophenyl) 1H-indole (3h): Yield 78%; (Methanol); mp 178°C; IR (KBr): 770 (C-Cl), 1261 (N-Ch2), 1298 (C-N), 1507 (N-N), 1576 (-N=CH), 1610 (C=C of aromatic ring), 1682 (C=C), 3150 (CH aromatic), 3323 (-C-NH) cm^{-1}; ^{1}H-NMR (DMSO-d6 δ ppm): 3.45 (s, 5H, OCH_{2}H), 3.31 (q, 2H, NCH_{2}CH_{3}), 4.55 (t, 2H, -N-CH_{2}), 7.60 (m, 1H, CH_{2}NH), 7.68 (d, 1H, NH of indole), 8.63 (s, 2H, -N=CH of triazole), 7.70-8.31 (m, 7H, ArH), 8.84 (s, 1H, N=CH-indole); MS: [M]^+ at m/z 408.88 Elemental analysis found (calculated) for C_{21}H_{21}ClN_{6}O_{2}: C, 61.67 (61.69); H, 5.16 (5.18); N, 20.57 (20.55)%.

General procedure for the synthesis of 1-(2-(4H-1,2,4-triazol-4-yl)ethylamino)-3-chloro-4-(5-methoxy/ethoxy-2-substituted alkyl/aryl-1H-indol-3-yl)azetidin-2-ones (4a-4h): A mixture of compounds 3a-3h (0.6 mol), dry dioxane (100 ml) and triethylamine (0.8 mol) were taking in round bottom flask. The reaction was stirred on an ice bath and when temperature dropped below 0-5°C, then chloroacetylchloride (0.10 mol) was added dropwise with stirring. After completion of addition, the stirring was further continued for 6 h. at room temperature. The reaction mixture was then kept a side for 48h. Finally, the reaction mixture was added to ice cold water to obtain the desired product. The products were dried and purified by recrystallization from methanol to yield title compounds.

1-(2-(4H-1,2,4-triazol-4-yl)ethylamino)-3-chloro-4-(5-methoxy-1H-indol-3-yl)azetidin-2-one (4a): Yield 76%; (Acetone); mp 197°C; IR (KBr): 772 (C-Cl), 1261 (N-Ch2), 1298 (C-N), 1507 (N-N), 1576 (-N=CH), 1682 (C=C), 1755 (C=O), 3323 (-C-NH) cm^{-1}; ^{1}H-NMR (DMSO-d6 δ ppm): 2.28 (s, 3H, CH_{3} of indole), 3.32 (q, 2H, NCH_{2}CH_{3}), 3.45 (s, 3H, OCH_{3}), 4.56 (t, 2H, -N-CH_{2}), 4.60 (s, 1H, CH-Cl), 7.60 (m, 1H, CH_{2}NH), 7.66 (d, 1H, NH of indole), 7.70-8.31 (m, 7H, ArH), 8.63 (s, 2H, -N=CH of triazole), 8.87 (s, 1H, N-CH-azetidinone); MS: [M]^+ at m/z 384.72 Elemental analysis found (calculated) for C_{18}H_{17}ClN_{6}O_{2}: C, 53.28 (53.26); H, 4.74 (4.75); N, 23.25 (23.29)%.

1-(2-(4H-1,2,4-triazol-4-yl)ethylamino)-3-chloro-4-(5-ethoxy-1H-indol-3-yl)azetidin-2-one (4b): Yield 73%; (Ethanol); mp 189°C; IR (KBr): 772 (C-Cl), 1261 (N-Ch2), 1298 (C-N), 1507 (N-N), 1576 (-N=CH), 1682 (C=C), 1755 (C=O), 3323 (-C-NH) cm^{-1}; ^{1}H-NMR (DMSO-d6 δ ppm): 3.32 (q, 2H, NCH_{2}CH_{3}), 3.45 (s, 5H, OCH_{2}H), 4.56 (t, 2H, -N-CH_{2}), 4.60 (s, 1H, CH-Cl), 7.60 (m, 1H, CH_{2}NH) 7.65 (d, 1H, NH of indole), 7.50 (d, 1H, C=CH of pyrole ring of indole), 7.71-8.31 (m, 3H, ArH), 8.61 (s, 2H, -N=CH of triazole), 8.85 (s, 1H, N-CH-azetidinone); MS: [M]^+ at m/z 374.82 Elemental analysis found (calculated) for C_{17}H_{19}ClN_{6}O_{2}: C, 54.49 (54.47); H, 5.10 (5.11); N, 22.43 (22.42)%.

1-(2-(4H-1,2,4-triazol-4-yl)ethylamino)-3-chloro-4-(5-methoxy-2-methyl-1H-indol-3-yl)azetidin-2-one (4c): Yield 71%; (Methanol); mp 187°C; IR (KBr): 772 (C-Cl), 1261 (N-Ch2), 1298 (C-N), 1507 (N-N), 1576 (-N=CH), 1682 (C=C), 1755 (C=O), 2854 (CH_{3}), 3323 (-C-NH) cm^{-1}; ^{1}H-NMR (DMSO-d6 δ ppm): 2.28 (s, 3H, CH_{3} of indole), 3.32 (q, 2H, NCH_{2}CH_{3}), 3.45 (s, 3H, OCH_{3}), 4.50 (t, 2H, -N-CH_{2}), 4.60 (s, 1H, CH-Cl), 7.60 (m, 1H, CH_{2}NH), 7.66 (d, 1H, NH of indole), 7.70-8.31 (m, 3H, ArH), 8.63 (s, 2H, -N=CH of triazole), 8.87 (s, 1H, N-CH-azetidinone); MS: [M]^+ at m/z 374.82 Elemental analysis found (calculated) for C_{17}H_{19}ClN_{6}O_{2}: C, 54.48 (54.47); H, 5.12 (5.11); N, 22.41 (22.42)%.

1-(2-(4H-1,2,4-triazol-4-yl)ethylamino)-3-chloro-4-(5-ethoxy-2-methyl-1H-indol-3-yl)azetidin-2-one (4d): Yield 69%; (Acetone); mp 201°C; IR (KBr): 772 (C-Cl), 1261 (N-Ch2), 1298 (C-N), 1507 (N-N), 1576 (-N=CH), 1682 (C=C), 1755 (C=O), 3323 (-C-NH) cm^{-1}; ^{1}H-NMR (DMSO-d6 δ ppm): 2.28 (s, 3H, CH_{3} of indole), 3.32 (q, 2H, NCH_{2}CH_{3}), 3.35 (s, 5H, OCH_{2}H), 4.56 (t, 2H, -N-CH_{2}), 4.60 (s, 1H, CH-Cl), 7.60 (m, 1H, CH_{2}NH), 7.69 (d, 1H, NH of indole), 7.71-8.30 (m, 3H, ArH), 8.61 (s, 2H, -N=CH of triazole), 8.84 (s, 1H, N-CH-azetidinone); MS: [M]^+ at m/z 388.85 Elemental analysis found (calculated) for C_{18}H_{21}ClN_{6}O_{2}: C, 55.62 (55.60); H, 5.46 (5.44); N, 21.62 (21.61)%.
1-(2-(4H-1,2,4-triazol-4-yl)ethylamino)-3-chloro-4-(5-methoxy-2-phenyl-1H-indol-3-yl)azetidin-2-one (4c): Yield 67%; (Ethanol); mp 195°C; IR (KBr): 772 (C-Cl), 1261 (N-CH₂), 1298 (C-N), 1507 (N-N), 1576 (~N=CH), 1610 (C=O of aromatic ring), 1682 (C=N), 1755 (C=O), 3153 (CH Aromatic), 3323 (~C=NH) cm⁻¹; ¹H-NMR (DMSO-d₆ δ ppm): 3.35 (q, 2H, NCH₂CH₃), 3.45 (s, 3H, OCH₃), 4.56 (t, 2H, -NCH₂), 4.60 (s, 1H, CH-Cl), 7.50 (m, 1H, CH₂NH), 7.64 (d, 1H, NH of indole), 7.73-8.31 (m, 8H, ArH), 8.61 (s, 2H, -N=CH of triazole), 8.83 (s, 1H, N-CH-azetidinone); MS: [M⁺] at m/z 436.89. Elemental analysis found (calculated) for C₂₂H₂₂ClN₆O₂: C, 60.49 (60.48); H, 4.83 (4.84); N, 19.26 (19.24)%.

1-(2-(4H-1,2,4-triazol-4-yl)ethylamino)-3-chloro-4-(5-ethoxy-2-phenyl-1H-indol-3-yl)azetidin-2-one (4d): Yield 65%; (Acetone); mp 225°C; IR (KBr): 775 (C-Cl), 1262 (N-CH₂), 1297 (C-N), 1507 (N-N), 1576 (~N=CH), 1610 (C=O of aromatic ring), 1682 (C=N), 1755 (C=O), 3153 (CH Aromatic), 3323 (~C=NH) cm⁻¹; ¹H-NMR (DMSO-d₆ δ ppm): 3.25 (s, 5H, OC₂H₅), 3.52 (q, 2H, NCH₂CH₃), 4.76 (t, 2H, -NCH₂), 4.60 (s, 1H, CH-Cl), 7.60 (m, 1H, CH₂NH), 7.69 (d, 1H, NH of indole), 7.71-8.31 (m, 8H, ArH), 8.61 (s, 2H, -N=CH of triazole), 8.86 (s, 1H, N-CH-azetidinone); MS: [M⁺] at m/z 450.92. Elemental analysis found (calculated) for C₂₅H₂₆ClN₆O₂: C, 61.24 (61.26); H, 5.16 (5.14); N, 18.62 (18.64)%.

1-(2-(4H-1,2,4-triazol-4-yl)ethylamino)-3-chloro-4-(5-methoxy-2-chlorophenyl-1H-indol-3-yl) azetidin-2-one (4g): Yield 65%; (Methanol); mp 211°C; IR (KBr): 770 (C-Cl), 1265 (N-CH₂), 1293 (C-N), 1502 (N-N), 1575 (~N=CH), 1615 (C=O of aromatic ring), 1684 (C=N), 1753 (C=O), 3152 (CH Aromatic), 3321 (~C=NH) cm⁻¹; ¹H-NMR (DMSO-d₆ δ ppm): 3.31 (q, 2H, NCH₂CH₃), 3.47 (s, 3H, OCH₃), 4.57 (t, 2H, -NCH₂), 4.72 (s, 1H, CH-Cl), 7.60 (m, 1H, CH₂NH), 7.67 (d, 1H, NH of indole), 7.70-8.30 (m, 7H, ArH), 8.62 (s, 2H, -N=CH of triazole), 8.83 (s, 1H, N-CH-azetidinone); MS: [M⁺] at m/z 471.34. Elemental analysis found (calculated) for C₂₁H₁₈N₆O₂S: C, 53.64 (53.62); H, 5.07 (5.06); N, 23.48 (23.45)%.

1-(2-(4H-1,2,4-triazol-4-yl)ethylamino)-3-chloro-4-(5-ethoxy-2-chlorophenyl-1H-indol-3-yl) azetidin-2-one (4h): Yield 63%; (Ethanol); mp 227°C; IR (KBr): 772 (C-Cl), 1261 (N-CH₂), 1298 (C-N), 1507 (N-N), 1576 (~N=CH), 1610 (C=O of aromatic ring), 1682 (C=N), 1755 (C=O), 3153 (CH Aromatic), 3323 (~C=NH) cm⁻¹; ¹H-NMR (DMSO-d₆ δ ppm): 3.32 (q, 2H, NCH₂CH₃), 3.40 (s, 5H, OC₂H₅), 4.53 (t, 2H, -NCH₂), 4.67 (s, 1H, CH-Cl), 7.55 (m, 1H, CH₂NH), 7.69 (d, 1H, NH of indole), 7.71-8.31 (m, 7H, ArH), 8.61 (s, 2H, -N=CH of triazole), 8.85 (s, 1H, N-CH-azetidinone); MS: [M⁺] at m/z 485.37. Elemental analysis found (calculated) for C₂₃H₂₂Cl₂N₆O₂: C, 56.90 (56.92); H, 4.59 (4.57); N, 17.30 (17.31)%.

General procedure for the synthesis of 3-(2-(4H-1,2,4-triazol-4-yl)ethylamino)-2-(5-methoxy/ ethoxy-2-substituted alkyl/aryl-1H-indol-3-yl) thiazolidin-4-ones (5a-5h): In a ethanolic solution of compounds (4a-4h) (0.4 mol), thioglycolic acid (0.8 mol) was added in the presence of anhydrous zinc chloride. The reaction mixture was refluxed for 15 h. The excess of solvent was distilled off and separated solid was poured into ice water, filtered, washed with water and recrystallized from ethanol to yield title compounds.

3-(2-(4H-1,2,4-triazol-4-yl)ethylamino)-2-(5-methoxy-1H-indol-3-yl)thiazolidin-4-one (5a): Yield 61%; (Methanol); mp 239°C; IR (KBr): 684 (C-S-C), 1260 (N-CH₂), 1296 (C-N), 1509 (N-N), 1575 (~N=CH), 1685 (C=N), 1758 (C=O), 3155 (CH Aromatic), 3321 (~C=NH) cm⁻¹; ¹H-NMR (DMSO-d₆ δ ppm): 3.45 (s, 3H, OCH₃), 3.60 (q, 2H, NCH₂CH₃), 3.75 (s, 2H, CH₂ of thiazolidinone), 4.75 (t, 2H, -N-CH₂), 6.64 (s, 1H, N-CH of thiazolidinone), 7.62 (m, 1H, CH₂NH), 7.68 (d, 1H, NH of indole), 7.70-8.30 (m, 3H, ArH), 8.61 (s, 2H, -N=CH of triazole), 8.84 (s, 1H, N-CH-iodide); MS: [M⁺] at m/z 358.42. Elemental analysis found (calculated) for C₁₆H₁₈N₆O₂S: C, 53.64 (53.62); H, 5.07 (5.06); N, 23.48 (23.45)%.

3-(2-(4H-1,2,4-triazol-4-yl)ethylamino)-2-(5-ethoxy-1H-indol-3-yl)thiazolidin-4-one (5b): Yield 60%; (Ethanol); mp 253°C; IR (KBr): 686 (C-S-C), 1263 (N-CH₂), 1296 (C-N), 1503 (N-N), 1576 (~N=CH), 1685 (C=N), 1751 (C=O), 3152 (CH Aromatic), 3321 (~C=NH) cm⁻¹; ¹H-NMR (DMSO-d₆ δ ppm): 3.35 (s, 5H, OC₂H₅), 3.42 (q, 2H, NCH₂CH₃), 3.73 (s, 2H, CH₂ of thiazolidinone),
3-(2-(4H-1,2,4-triazol-4-yl)ethylenylamino)-2-(5-methoxy-2-methyl-1H-indol-3-yl)thiazolidin-4-one (5c): Yield 58%; (Acetone); mp 247°C; IR (KBr): 683 (C-S-C), 1265 (N-CH2), 1298 (C-N), 1507 (N=N), 1576 (-N=CH), 1682 (C=N), 1755 (C=O), 2857 (CH2), 3158 (CH Aromatic), 3323 (-C-NH) cm⁻¹; 1H-NMR (DMSO-d6 δ ppm): 2.26 (s, 3H, CH3), 3.32 (q, 2H, NCH2CH2), 3.42 (s, 2H, CH2 of thiazolidinone), 3.67 (s, 3H, OCH3), 3.79 (t, 2H, -N(CH2)3), 6.65 (s, 1H, N-CH of thiazolidinone), 7.50 (m, 1H, CH=N), 7.66 (d, 1H, NH of indole), 7.73-8.31 (m, 3H, Ar), 8.61 (s, 2H, -N=CH of triazole); MS: [M]+ at m/z 372.44. Elemental analysis found (calculated) for C17H20N6O2S: C, 54.81 (54.82); H, 5.43 (5.41); N, 22.55 (22.56)%.

3-(2-(4H-1,2,4-triazol-4-yl)ethylenylamino)-2-(5-methoxy-2-phenyl-1H-indol-3-yl)thiazolidin-4-one (5d): Yield 57%; (Methanol); mp 252°C; IR (KBr): 685 (C-S-C), 1261 (N-CH2), 1294 (C-N), 1505 (N=N), 1573 (-N=CH), 1686 (C=N), 1758 (C=O), 2856 (CH3), 3154 (CH Aromatic), 3320 (-C-NH) cm⁻¹; 1H-NMR (DMSO-d6 δ ppm): 2.27 (s, 3H, CH3), 3.35 (s, 5H, OC2H5), 3.45 (q, 2H, NCH2CH2), 3.55 (s, 2H, CH2 of thiazolidinone), 4.68 (t, 2H, -NCH2), 6.65 (s, 1H, N-CH of thiazolidinone), 7.61 (m, 1H, CH2NH), 7.67 (d, 1H, NH of indole), 7.72-8.30 (m, 3H, Ar), 8.64 (s, 2H, -N=CH of triazole); MS: [M]+ at m/z 386.47. Elemental analysis found (calculated) for C18H22N6O2S: C, 55.93 (55.94); H, 5.75 (5.74); N, 21.73 (21.75)%.

3-(2-(4H-1,2,4-triazol-4-yl)ethylenylamino)-2-(5-methoxy-2-chlorophenyl-1H-indol-3-yl)thiazolidin-4-one (5f): Yield 50%; (Methanol); mp 169°C; IR (KBr): 681 (C-S-C), 772 (C-Cl), 1261 (N-CH2), 1298 (C-N), 1507 (N=N), 1576 (-N=CH), 1610 (C=C of aromatic ring), 1682 (C=N),1755 (C=O), 3153 (CH Aromatic), 3323 (-C-NH) cm⁻¹; 1H-NMR (DMSO-d6 δ ppm): 3.20 (s, 5H, OC2H5), 3.39 (q, 2H, NCH2CH2) 3.70 (s, 2H, CH2 of thiazolidinone), 4.75 (t, 2H, -NCH2), 6.65 (s, 1H, N-CH of thiazolidinone), 7.53 (m, 1H, CH2NH), 7.65 (d, 1H, NH of indole), 7.70-8.31 (m, 8H, Ar), 8.63 (s, 2H, -N=CH of triazole); MS: [M]+ at m/z 448.54. Elemental analysis found (calculated) for C22H22N6O2S: C, 61.57 (61.59); H, 5.37 (5.39); N, 18.76 (18.74)%.

3-(2-(4H-1,2,4-triazol-4-yl)ethylenylamino)-2-(5-methoxy-2-chlorophenyl-1H-indol-3-yl)thiazolidin-4-one (5g): Yield 47%; (Ethanol); mp 178°C; IR (KBr): 682 (C-S-C), 770 (C-Cl), 1260 (N-CH2), 1295 (C-N), 1504 (N=N), 1572 (-N=CH), 1612 (C=C of aromatic ring), 1680 (C=N),1753 (C=O), 3151 (CH Aromatic), 3321 (-C-NH) cm⁻¹; 1H-NMR (DMSO-d6 δ ppm): 3.26 (s, 5H, OC2H5), 3.36 (q, 2H, NCH2CH2), 3.71 (s, 2H,
CH$_2$ of thiazolidinone), 3.74 (t, 2H, -N-CH$_2$), 6.67 (s, 1H, N-CH of thiazolidinone), 7.56 (m, 1H, CH$_2$NH), 7.68 (d, 1H, NH of indole), 7.72-8.30 (m, 7H, ArH), 8.60 (s, 2H, -N=CH of triazole); MS: [M]$^+$ at m/z 482.99. Elemental analysis found (calculated) for C$_{23}$H$_{23}$ClN$_8$O$_2$: C, 57.22 (57.20); H, 4.81 (4.80); N, 17.42 (17.40) %.

ACKNOWLEDGEMENT: I am thankful to SAIF Punjab University, Chandigarh India for spectral and analytical analysis of newly synthesized compounds. I am also thankful to Department of microbiology LLRM Medical College for microbial activity.

REFERENCES: