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# SYNTHESIS, CHARACTERIZATION AND BIOLOGICAL EVALUATION OF CERTAIN NOVEL MANNICH BASES CONTAINING INDOLE MOIETY LINKED WITH THIONE POSSESSING AZETIDINE-4-ONE, THIAZOLIDINE-2-ONE AND TETRAZOLES

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## ABSTRACT

The article is aimed to synthesize, characterize and screening the biological activity of a series of N-((3-(4-chloro-3-oxo-1-((4-(4-(trifluoromethyl)phenyl)thiazol-2-yl)amino)azetidin-2-yl)-1H-indol-1-yl) methyl) piperidine-1-carboxamide. Indole-3-carbaldehyde and chloroethyl acetate were dissolved in DMF. To this reaction mixture, anhydrous $K_2CO_3$ was added and the reaction mixture was stirred at room temperature ($35^0$C) for 8 hrs to afford 2-(3-formyl-1H-indol-1-yl)acetate. To this reaction mixture, equimolar quantity of hydrazinecarbothioamide were dissolved in absolute alcohol, three drops of acetic acid was added and it was then heated on a steam bath for 5-6 hrs at $100^o$C to obtain ethyl2-(3-((2-carbamoylhydrazono)methyl)-1H-indol-1-yl)acetate. α-Halo ketones (chloro acetophenone, chloro acetone) 10 mM was added and the mixture was stirred at room temperature for 30 min compound to obtain ethyl 2-(3-((2-(4-(4-(trifluoromethyl) phenyl)thiazol-2-yl) hydrazono)methyl)-1H-indol-1-yl)acetate. Monocholoroacetyl chloride (0.01) was added then drop wise to Schiffs base (0.01 mol) and triethylamine (0.02 mol) in dioxane (25 mL) at room temperature to get ethyl 2-(3-(4-chloro-3-oxo-1-((4-(4-(trifluoromethyl)phenyl)thiazol-2-yl)amino) azetidin-2-yl)-1H-indol-1-yl)acetate. After hydrolysis of this reaction mixture isobutyl, chloroformate (1:1 eq) was added and stirred for 30 min, and then aq. $NaN_3$ (3 eq) was added and stirred for 20 min at $0^o$C, when 2-(3-(4-chloro-3-oxo-1-((4-(4-(trifluoromethyl)phenyl)thiazol-2-yl) amino)azetidin-2-yl)-1H-indol-1-yl)acetyl azide was obtained. The reaction mixture is treated with Mannich bases to obtain N-((3-(4-chloro-3-oxo-1-((4-(4-(trifluoromethyl)phenyl)thiazol-2-yl)amino)azetidin-2-yl)-1H-indol-1-yl)methyl) piperidine-1-carboxamide. The structures of these newly synthesized compounds were characterised by $^1$H NMR, $^{13}$C NMR, Mass, IR, and elemental analysis. The antimicriobial activity of the novel compounds was screened by agar discdiffusion method.

**Key words**: Antibacterial activity, Antifungal activity, Indole, Mannich base, Azetidine-4-one, Thiazolidine-2-one, Tetrazole.

## INTRODUCTION

Heterocyclic compounds represents an important class of biological molecules. The heterocyclic molecules, which posses indole, pyrazole and azetidine moieties exhibit wide range of biological activities. Indoles are one of the most important alkaloids molecules found extensively in biological systems, which play vital role in many of the biochemical process. Indole ring constitutes an important basic skeleton and development of the drug. The classical indole drugs are indomethacin and indoxole. Indole derivatives found

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to posses high activity like, antibacterial, analgesic, antipyretic, antifungal, anti-inflammatory, anthelmintic, cardiovascular, anticonvulsant, etc.

Heterocyclic compounds have also captured our attention for many reasons, mainly due to their biological activities. A wide variety of 2-oxoazetidine derivatives have been described for their chemotherapeutic importance. 2-Oxoazetidine and its derivatives possess various types of biological activities, such as antibacterial[1-4], anticonvulsant[5], analgesic, antitubercular[6-8], antiinflammatory[9], antifungal[10-13], as synthetic precursors for amino acids, to mediate cholesterol absorption, for antiviral and CNS activity, etc. 2-Oxozetidines also serve as synthons for many biologically active compounds. Many antibiotics like penicillin and cep-halosporin contain 2-oxoazetidine ring.

Thiazolidinones moiety is associated with variety of biological activities including antifungal[14], antiinflammatory[15], anticonvulsant[16], antitubercular[17], antihistaminic[18], etc.

Tetrazole and its derivatives have attracted much attention because of their unique structure and applications as antihypertensive, antialergic, antibiotic and anticonvulsant agents[19-27]. Development of tetrazole chemistry has been largely associated with wide scale of applications of these classes of compounds in medicine, biochemistry, agriculture[28-31], and also a large number of medicinally important tetrazole heterocyclic incorporated drugs approved by the FDA[32,33]. The medicinal activity of tetrazole functionality is due to its ability to serve as bioequivalent (bioisostere) of the carboxylic acid group. 1, 5-Disubstituted tetrazoles can be used as isosteres of the *cis*-amide bond of peptides[34,35]. Biphenyl tetrazole compounds play important role in the medicinal chemistry. Losartan was described as the first non-peptide AT1 receptor antagonist and the coined group was named as sartans[36,37]. Most of these compounds share the biphenyl tetrazole unit or replacements thereof with the original advanced lead Losartan[38]. All these sartan drugs contain some common structural features represented by a biphenyl fragment bearing an acidic moiety (i.e. tetrazole, carboxylic- or sulphonamidocarboxyl- group), linked to tetrazole.

## EXPERIMENTAL

### Materials and methods

Melting points were determined on open capillaries using a cintex melting point apparatus. T.L.C. analyses were performed on precoated silica gel (E-Merck Kieselgel 60 $F_{254}$) plates and visualisation was done by exposing to iodine vapour. Solvents were purified by standard procedures before use. Column chromatography was conducted by using silica gel with different solvent systems as elutes. IR Spectra were recorded in KBr on Perkin-Elmer spectrum BX series FTIR spectrometer. $^1$H-NMR spectrum were recorded on Varian Zemini 300 MHz and 200 MHz spectrometers using TMS as internal standard (chemical shifts in ppm) $^{13}$C NMR spectra were recorded on a Brucker 75 MHz spectrometer. Mass spectra were scanned on a Varian MATCH-7 and jeol JMSD-300 mass spectrometer at 70 eV. Elemental analysis were carried out on Carlo Erba 106 and Perkin-analyser. All the chemicals used in the present investigation were perchased from Aldrich chemicals; U.S.A. Indole-3-carbaldehyde was prepared by a reported method.

### 5-((3-((2-(4-Phenylthiazole-2-yl)hydrazono)methyl)-1H-indol-1-yl)methyl)-1,3,4-oxadiazole-2(3H)-thione (1)

Indole-3-carbaldehyde can be prepared by using Vilsmier-Huck reaction and it is commercially available also. An equimolar mixture of indole-3-carbaldehyde and anhydrous $K_2CO_3$, and chloroethyl acetate in DMF was stirred at room temperature for 8 hrs to afford ethyl-2-(3-formyl-1H-indol-1-yl) acetate **(A)**. To a solution of **(A)**, thiosemicarbazide (0.19 g, mol) in methanol (20 mL) and few drops of acetic acid were added and the mixture refluxed for 5 hrs to afford ethyl2-(3-((2-carbamoylhydrazono)methyl)-1H-indol-1-yl)

acetate compound **(B)**. To this compound hydrazine hydrate (0.015 mol) in ethanol (20 mL) was added and refluxed for 5 hrs to obtain 2-((1-(2-hydrazinyl-2-oxoethyl)-1H-indol-3-yl)methylene) hydrazine carboxamide compound **(C)**. Mixture of compound **(C)** (19.9 g, 0.1 mol) KOH (5.5 g, 0.1 mol) ethanol (100 mL) and carbon disulphide (6.02 mL, 0.1 mol) was refluxed on a water bath till the evaluation of hydrogen disulphide ceased. The excess of alcohol was removed by distillation to obtain 2-((1-((5-thioxo-4,5-dihydro-1,3,4-oxadiazole-2-yl) methyl)-1H-indol-3-yl)methylene) hydrazine carboxamide compound **(D)**. Mixture of compound **(D)** (2.18 g) and $K_2CO_3$ (0.69 g) in methanol (20 mL), and α-halo ketones (chloroacetophenone) 10mM and the mixture was stirred at room temperature for 30 min to obtain 5-((3-((2-(4-phenylthiazole-2-yl)hydrazono)methyl)-1H-indol-1-yl)methyl)-1,3,4-oxadiazole-2(3H)-thione compound **(1)**.

The structures of this newly synthesized compounds **1(a-f)** were charecterised by H-NMR and IR spectral data.

NMR spectrum: 5.42 (s, 2H, -$CH_2$ thiaoxazole attached to indole ring), 7.05-8.30 (complex, m, 6H, four aryl protons of the indole ring, one α-proton of the indolyl ring, one aldehydimine proton), 7.18-8.26 (complex, m, 6H, one proton of the thiazolyl ring, five phenyl protons), 11.189 (s, 1H, -NH), 14.7 (s, 1H, thiol-thione tautomeric proton SH).

IR spectrum: The IR (KBr) spectrum of 5-((3-((2-(4-phenylthiazole-2-yl)hydrazono)methyl)-1H-indol-1-yl)methyl)-1,3,4-oxadiazole-2(3H)-thione **1(a)** was recorded in the range 4000-667 $cm^{-1}$ and the absorption signals were found at 1626 (C=N), 1180 (-C-O-C-), 1156 (C=S), 670 (C-S-C) and 3185 $cm^{-1}$ (-NH).

**3-((4-Methylpiperazine-1-yl)methyl)-5-((3-((2-(4-phenylthiazol-2-yl)hydrazono)methyl)-1H-indol-1-yl)methyl)-1H-indol-1-yl)methyl)-1,3,4-oxadiazole-2(3H)-thione (2)**

A solution of **7(a)** (0.01 mol) in absolute ethanol and dioxane mixture (20 mL) was treated with formaldehyde (40%, 1.5 mL). Later, the p-toulidine (0.01 mol) in ethanol (10 mL) was added with stirring and the reaction mixture was stirred over night. The precipitated Mannich base was collected by filtration and dried, recrystallization was done from ethanol-DMF mixture to give compound the product **2(a)**.

To a mixture of **1(a)** and **2(a)**, (2.18 g) and $K_2CO_3$ (0.69 g) in methanol (20 mL), α-halo ketones (chloro aceto phenone, chloro acetone) 10 mM and the mixture stirred at room temperature for 30 min. At the end of this period, the solution was poured into ice cold water and neutralized with dil AcOH. The separated solid was filtered and dried to obtain crude **(2)**. The crude compound obtained was recrystalised from hot MeOH to obtain pure **2(a)**.

The structures of this newly synthesized compounds **2(a-f)** were charecterised by H-NMR and IR spectral data.

NMR spectrum: 1.53-1.59 (m, 6H, $(CH_2)_3$ of piperidine ring, E), 2.56 (t, 4H, -$CH_2$ –N-$CH_2$-), 4.45 (s, 2H, -N-$CH_2$-N-), 5.45 (s, 2H, -$CH_2$ thiaoxazole attached to indole ring), 7.06-8.35 (complex, m, 6H, four aryl protons of the indole ring, one α-proton of the indolyl ring, one aldehydimine proton), 7.28-8.30 (complex, m, 6H, one proton of the thiazolyl ring, five phenyl protons), 11.289 (s, 1H, -NH), 14.9 (s, 1H, thiol-thione tautomeric proton SH).

IR spectrum: The IR (KBr) spectrum of 3-((4-methylpiperazine-1-yl)methyl)-5-((3-((2-(4-phenylthiazol-2-yl)hydrazono)methyl)-1H-indol-1-yl)methyl)-1H-indol-1-yl)methyl)-1,3,4-oxadiazole-2 (3H)-thione **2(a)** was recorded in the range 4000-667 $cm^{-1}$ and the absorption signals were found at 1616 (C=N), 1185 (-C-O-C-), 1160 (C=S), 675 (C-S-C) and 3200 $cm^{-1}$ (-NH).

**1-(4-Phenylthiazol-2-ylamino)-3-chloro-4-(1-((4,5-dihydro-4-(morpholinomethyl)-5-thioxo-1,3,4-oxdiazol-2-yl)methyl)-1H-indol-3-yl)azetidine-2-one (3)**

A mixture of **4** (19.9 g, 0.1 mol), KOH (5.5 g, 0.1 mol) ethanol (100 mL), and carbon disulphide (6.02 mL, 0.1 mol) was taken in a round bottomed flask fitted with a water cooled condenser. It was refluxed on a water bath till the evolution of hydrogen sulphide ceased. The excess of alcohol was removed by distillation. The reaction mixture was cooled to room temperature and the contents were poured to ice cold water and neutralized with dil. HCl. The solid precipitated was filtered, washed thoroughly with water and dried. The product was further purified by recrystallization from ethanol-dioxane mixture to give **5(a)** yield 59%, m.p. 229-230.

NMR spectrum: 1.50-1.57 (m, 6H, $(CH_2)_3$ of piperidine ring, E), 2.60 (t, 4H, $-CH_2-N-CH_2-$), 4.50 (s, 2H, $-N-CH_2-N-$), 5.45 (s, 2H, $-CH_2$ thiaoxazole attached to indole ring), 5.40 (d, 1H, -CH of azetidine attached to indole ring), 5.75 (d, 1H, -CH of azetidine attached to-Cl), 7.06-8.40 (complex, m, 6H, four aryl protons of the indole ring, one α-proton of the indolyl ring, one aldehydimine proton), 7.30-8.35 (complex, m, 6H, one proton of the thiazolyl ring, five phenyl protons), 11.53 (s, 1H, -NH), 14.95 (s, 1H, thiol-thione tautomeric proton SH).

IR spedtra; The IR (KBr) spectrum of 1-(4-phenyl thiazol-2-ylamino)-3-chloro-4-(1-((4,5-dihydro-4-(morpholinomethyl)-5-thioxo-1,3,4-oxdiazol-2-yl)methyl)-1H-indol-3-yl)azetidine-2-one **3(a)** was recorded in the range 4000-667 $cm^{-1}$ and the absorption signals were found at 1610 (C=N), 1190 (-C-O-C-), 1165 (C=S), 670 (C-S-C) and 3158 $cm^{-1}$ (-NH).

**2-(1-((4,5-Dihydro-4-(morpholinomethyl)-5-thioxo-1,3,4-oxdiazol-2-yl)methyl)-1H-indol-3-yl)-3-(4- phenyl thiazol-2-yl)thiazolidin-4-one (4)**

A mixture of Schiffs base (0.01 mol) and mercaptoacetic acid (0.01 mol) dissolved in dioxane (20 mL) and anhydrous zinc chloride (0.5 mg) was taken and refluxed for 8 hrs. The reaction was cooled and the resulting solid was washed with sodium bicarbonate solution and recrystalised from absolute alcohol. The formation of compound was confirmed by IR and NMR spectral data.

NMR spectrum: 1.55-1.65 (m, 6H, $(CH_2)_3$ of piperidine ring, E), 2.35 (s, 1H, -CH of thiazolidinone attached to indole ring), 2.60 (t, 4H, $-CH_2-N-CH_2-$), 3.92 (d, 1H, Ha of $-CH_2$ of thiazolidinone), 4.20 (d, 1H, Hb of $-CH_2$ of thiazolidinone), 4.40 (s, 2H, $-N-CH_2-N-$), 5.40 (s, 2H, $-CH_2$ thiaoxazole attached to indole ring), 7.10-8.40 (complex, m, 6H, four aryl protons of the indole ring, one α-proton of the indolyl ring, one aldehydimine proton), 7.30-8.45 (complex, m, 6H, one proton of the thiazolyl ring, five phenyl protons), 11.35 (s, 1H, -NH), 14.85 (s, 1H, thiol-thione tautomeric proton SH).

IR spectrum: The IR (KBr) spectrum of 2-(1-((4,5-dihydro-4-(morpholinomethyl)-5-thioxo-1,3,4-oxdiazol-2-yl)methyl)-1H-indol-3-yl)-3-(4-phenyl thiazol-2-yl)thiazolidin-4-one4(a) was recorded in the range 4000-667 $cm^{-1}$ and the absorption signals were found at 1620 (C=N), 1165 (-C-O-C-), 1170 (C=S), 670 (C-S-C), 3250 (-NH).

**5-((3-(1-(4-Phenyl thiazol-2-ylamino)-1H-tetrazol-5-yl)-1H-indol-1-yl)methyl)-3-(morpholinomethyl) -1, 3, 4-oxdiazol-2(3H)-thione (5)**

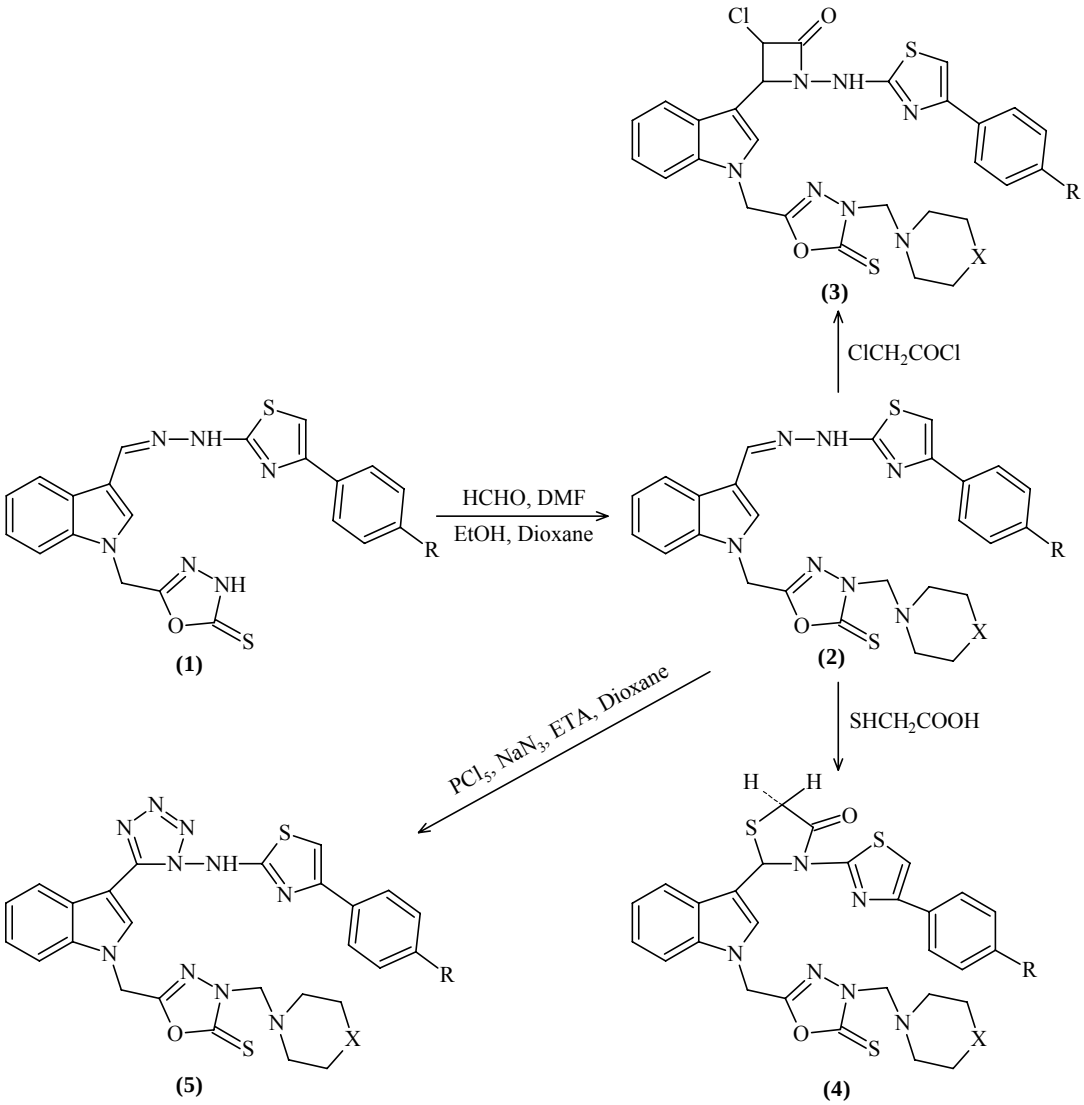
Schiffs base (0.004 mol) and $PCl_5$ (0.004 mol) were heated at 100°C for one hour till the evolution of fumes of HCl ceased. Excess of $PCl_3$ was removed under reduced pressure and the residual imidoyl chloride was treated with an ice cold solution of sodium azide (0.0075 mol) and excess of sodium acetate in water (25 mL) and acetone (30 mL) with stirring. Stirring was continued overnight; thereafter, acetone was removed under reduced pressure. The remaining aqueous portion was extracted with chloroform and dried. The newly synthesised compound was confirmed by IR and NMR, Mass spectral data.

NMR spectrum: 1.53-1.59 (m, 6H, $(CH_2)_3$ of piperidine ring, E), 2.56 (t, 4H, $-CH_2-N-CH_2-$), 4.45 (s, 2H, $-N-CH_2-N-$), 5.45 (s, 2H, $-CH_2$ thiaoxazole attached to indole ring), 7.06-8.35 (complex, m, 6H, four aryl protons of the indole ring, one α-proton of the indolyl ring, one aldehydimine proton), 7.28-8.30 (complex, m, 6H, one proton of the thiazolyl ring, five phenyl protons), 11.289 (s, 1H, -NH), 14.9 (s, 1H, thiol-thione tautomeric proton SH).

IR spedtrum: The IR (KBr) spectrum of 1 (a) 5-((3-(1-(4-phenyl thiazol-2-ylamino)-1H-tetrazol-5-yl)-1H-indol-1-yl)methyl)-3-(morpholinomethyl)-1,3,4-oxdiazol-2(3H)-thione **5(a)** was recorded in the range 4000-667 $cm^{-1}$ and the absorption signals were found at 1616 (C=N), 1185 (-C-O-C-), 1160 (C=S), 675 (C-S-C) and 3200 $cm^{-1}$ (-NH).

## RESULTS AND DISCUSSION

The target compounds were synthesized via the route shown in Scheme. The synthon required for the synthesis of the target molecules indole-3-carbaldehyde was prepared by a reported method. It was filtered and recrystallized from ethanol. These reactions are summarised in the **Schemes 1**. Yields were moderate to fair (55-70%). The purity of the compounds was monitered by TLC.




**Scheme 1**

**Table 1**

| Compound | (a) | (b) | (c) | (d) | (e) | (f) |
|---|---|---|---|---|---|---|
| R | H | $CH_3$ | $OCH_3$ | Br | $NO_2$ | $CF_3$ |
| X | O | S | $-CH_2$ | $N-CH_3$ | $-CH_2$ | S |

**Elemental analysis:** Elemental analysis of 1-((3-(4-chloro-3-oxo-1-((4-(4-(trifluoromethyl) phenyl) thiazol-2-yl)amino)azetidin-2-yl)-1H-indol-1-yl)methyl)-3-phenyl urea **3(a-f)**, **4(a-f)** and **5(a-f)** are shown in Table 2.

**Table 2: Physico-chemical analysis**

| Compd. | R | X | M.P. (°C) | Yield % | Mol. Formula | Found (%) Caluclated (%) | | |
|---|---|---|---|---|---|---|---|---|
| | | | | | | C | H | N |
| **3(a)** | H | O | 182 | 58% | $C_{28}H_{26}ClN_7O_3S_2$ | 55.30 (55.35) | 4.31 (4.28) | 16.12 (16.14) |
| **3(b)** | CH3 | S | 185 | 60% | $C_{29}H_{28}ClN_7O_2S_3$ | 54.57 (54.80) | 4.42 (4.40) | 15.43 (13.46) |
| **3(c)** | $OCH_3$ | $CH_2$ | 190 | 62% | $C_{30}H_{30}ClN_7O_3S_2$ | 56.64 (56.69) | 4.75 (4.72) | 15.41 (15.43) |
| **3(d)** | Br | $NCH_3$ | 195 | 59% | $C_{29}H_{28}BrClN_8O_2S_2$ | 49.75 (49.78) | 4.03 (4.00) | 16.01 (16.02) |
| **3(e)** | $NO_2$ | $CH_2$ | 205 | 56% | $C_{29}H_{27}ClN_8O_4S_2$ | 53.49 (53.53) | 4.18 (4.15) | 17.21 (17.23) |
| **3(f)** | $CF_3$ | S | 210 | 57% | $C_{29}H_{25}ClF_3N_7O_2S_3$ | 50.32 (50.36) | 3.64 (3.61) | 14.16 (14.18) |
| **4(a)** | H | O | 182 | 58% | $C_{28}H_{26}N_6O_3S_3$ | 56.93 (56.94) | 4.44 (4.40) | 14.23 (14.25) |
| **4b)** | $CH_3$ | S | 185 | 60% | $C_{29}H_{288}N_6O_2S_4$ | 56.10 (56.12) | 4.55 (4.51) | 13.54 (13.55) |
| **4(c)** | $OCH_3$ | $CH_2$ | 190 | 62% | $C_{30}H_{30}N_6O_3S_3$ | 58.23 (58.25) | 4.89 (4.85) | 13.58 (13.59) |
| **4(d)** | Br | $NCH_3$ | 195 | 59% | $C_{29}H_{28}BrN_7O_2S_3$ | 51.02 (51.05) | 4.13 (4.10) | 14.36 (14.38) |
| **4(e)** | $NO_2$ | $CH_2$ | 205 | 56% | $C_{29}H_{27}N_7O_4S_3$ | 54.96 (54.97) | 4.29 (4.26) | 15.47 (15.48) |
| **4(f)** | $CF_3$ | S | 210 | 57% | $C_{29}H_{25}F_3N_6O_2S_4$ | 51.62 (51.63) | 3.73 (3.70) | 12.45 (12.46) |
| **5(a)** | H | O | 182 | 58% | $C_{26}H_{24}N_{10}O_2S_2$ | 54.53 (54.54) | 4.22 (4.19) | 24.46 (24.47) |
| **5b)** | $CH_3$ | S | 185 | 60% | $C_{30}H_{24}ClF_3N_6O_2S$ | 53.80 (53.82) | 4.35 (4.31) | 23.24 (23.25) |

Cont…

| Compd. | R | X | M.P. (°C) | Yield % | Mol. Formula | Found (%) Caluclated (%) | | |
|---|---|---|---|---|---|---|---|---|
| | | | | | | C | H | N |
| **5(c)** | $OCH_3$ | $CH_2$ | 190 | 62% | $C_{30}H_{24}ClF_3N_6O_3S$ | 55.98 (56.00) | 4.70 (4.66) | 23.32 (23.33) |
| **5(d)** | Br | $NCH_3$ | 195 | 59% | $C_{29}H_{21}Cl_2F_3N_6O_2S$ | 48.79 (48.80) | 3.94 (3.91) | 23.18 (23.19) |
| **5(e)** | $NO_2$ | $CH_2$ | 205 | 56% | $C_{29}H_{21}ClF_3N_7O_4S$ | 52.67 (52.68) | 4.09 (4.06) | 25.02 (25.04) |
| **5(f)** | $CF_3$ | S | 210 | 57% | $C_{28}H_{22}ClN_7O_4S$ | 49.38 (49.39) | 3.53 (3.50) | 21.33 (21.34) |

## Antibacterial activity

The antibacterial activity of synthesized compounds was studied by the disc diffusion method against the following pathogenic organisms. The gram +ve bacteria screened were *Staphylococcus aureus* NCCS 2079 and *Bacillus cereus* NCCS 2106. The gram –ve bacteria screened were *Escherichia coli* NCCS 265 and *Pseudomonas aeruginosa* NCCS 2200.

The synthesized compounds were used at the concentration of 250 µg/mL and 500 µg/mL using DMSO as a solvent. The amoxicillin 10 µg/disc and cefaclor 30 µg/disc were used as a standard (Himedia Laboratories Limited. Mumbai).

## Antifungal activity

The antifungal activity of synthesized compounds were studied by disc diffusion method against the organisms of *Aspergillus Niger* NCCS 1196 and *Candida albicans* NCCS 3471

Compounds were treated at the concentrations of 100 µg/mL, 250 µg/mL, 500 µg/mL and 1000 µg/mL using DMSO as a solvent. The standard used was ketaconazole 50 µg/mL against both the organisms.

Antibacterial activity by disc diffusion method for azetidine **3(a-f)**

**Table 3: Antibacterial activity**

| Compd. | R | X | Zone of inhibition (mm) | | | |
|---|---|---|---|---|---|---|
| | | | ***staphylococcus aureus*** **NCCS 2079** | ***Bacillus cereus*** **NCCS 2106** | ***Escherichia coli*** **NCCS 2065** | ***Pseudo-manas aeruginosa.*** **NCCS 2200** |
| **3(a)** | H | O | 15 | 17 | 12 | 12 |
| **3(b)** | $CH_3$ | S | 12 | 11 | 14 | 14 |
| **3(c)** | $OCH_3$ | $CH_2$ | 11 | 12 | 12 | 10 |
| **3(d)** | Br | $NCH_3$ | 14 | 16 | 12 | 09 |
| **3(e)** | $NO_2$ | $CH_2$ | 17 | 15 | 13 | 11 |
| **3(f)** | $CF_3$ | S | 12 | 13 | 12 | 17 |
| **Cefaclor** | | | 19 | 22 | 19 | 20 |

Antifungal activity by disc diffusion method for indole linked thizole having azetidinone **3(a-f)**

**Table 4: Antifungal activity**

| Compound | Zone of inhibition (mm) | |
|---|---|---|
| | ***Aspergillus niger* NCCS 1196** | ***Candida albicans* NCCS 2106** |
| **3(a)** | 14 | 16 |
| **3(b)** | 15 | 13 |
| **3(c)** | 17 | 15 |
| **3(d)** | 18 | 17 |
| **3(e)** | 23 | 21 |
| **3(f)** | 15 | 13 |
| **Clotrimazole** | 25-30 | 25-30 |

## CONCLUSIONS

(i) The substitution with phenyl group having a chloro group at p-position showed better activities.

(ii) The urides showed better antibactirial and antifungal activities.

(iii) Thiazoles and its derivatives play an important role in medicinal chemistry as herbicidal, fungicidal, bacterial and anti-inflammatory.

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