



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)azetid-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 ($35^\circ C$) 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 $100^\circ C$ to obtain ethyl 2-(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. Monochloroacetyl chloride (0.01) was added then drop wise to Schiff's 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) azetid-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 $0^\circ C$, when 2-(3-(4-chloro-3-oxo-1-((4-(4-(trifluoromethyl)phenyl)thiazol-2-yl) amino)azetid-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)azetid-2-yl)-1H-indol-1-yl)methyl) piperidine-1-carboxamide. The structures of these newly synthesized compounds were characterised by 1H NMR, ^{13}C NMR, Mass, IR, and elemental analysis. The antimicrobial 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

to possess 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 antibacterial¹⁻⁴, anticonvulsant⁵, analgesic, antitubercular⁶⁻⁸, antiinflammatory⁹, antifungal¹⁰⁻¹³, as synthetic precursors for amino acids, to mediate cholesterol absorption, for antiviral and CNS activity, etc. 2-Oxoazetidines also serve as synthons for many biologically active compounds. Many antibiotics like penicillin and cephalosporin contain 2-oxoazetidine ring.

Thiazolidinones moiety is associated with variety of biological activities including antifungal¹⁴, antiinflammatory¹⁵, anticonvulsant¹⁶, antitubercular¹⁷, antihistaminic¹⁸, etc.

Tetrazole and its derivatives have attracted much attention because of their unique structure and applications as antihypertensive, antiallergic, antibiotic and anticonvulsant agents¹⁹⁻²⁷. Development of tetrazole chemistry has been largely associated with wide scale of applications of these classes of compounds in medicine, biochemistry, agriculture²⁸⁻³¹, 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 Losartan³⁸. 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 F₂₅₄) 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. ¹H-NMR spectrum were recorded on Varian Gemini 300 MHz and 200 MHz spectrometers using TMS as internal standard (chemical shifts in ppm) ¹³C NMR spectra were recorded on a Bruker 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 purchased 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 K₂CO₃, 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 ethyl-2-(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 characterized by H-NMR and IR spectral data.

NMR spectrum: 5.42 (s, 2H, $-CH_2$ thioxazole 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 $4000-667\text{ cm}^{-1}$ 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)-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 recrystallised from hot MeOH to obtain pure **2(a)**.

The structures of this newly synthesized compounds **2(a-f)** were characterized 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, $-CH_2$ thioxazole 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)-1,3,4-oxadiazole-2 (3H)-thione **2(a)** was recorded in the range $4000-667\text{ cm}^{-1}$ 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)azetidione (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, (CH₂)₃ of piperidine ring, E), 2.60 (t, 4H, -CH₂-N-CH₂-), 4.50 (s, 2H, -N-CH₂-N-), 5.45 (s, 2H, -CH₂ thiazole attached to indole ring), 5.40 (d, 1H, -CH of azetidione attached to indole ring), 5.75 (d, 1H, -CH of azetidione 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 spectra; 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)azetidione **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 Schiff's 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 recrystallised from absolute alcohol. The formation of compound was confirmed by IR and NMR spectral data.

NMR spectrum: 1.55-1.65 (m, 6H, (CH₂)₃ of piperidine ring, E), 2.35 (s, 1H, -CH of thiazolidinone attached to indole ring), 2.60 (t, 4H, -CH₂-N-CH₂-), 3.92 (d, 1H, Ha of -CH₂ of thiazolidinone), 4.20 (d, 1H, Hb of -CH₂ of thiazolidinone), 4.40 (s, 2H, -N-CH₂-N-), 5.40 (s, 2H, -CH₂ thiazole 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-one **4(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)

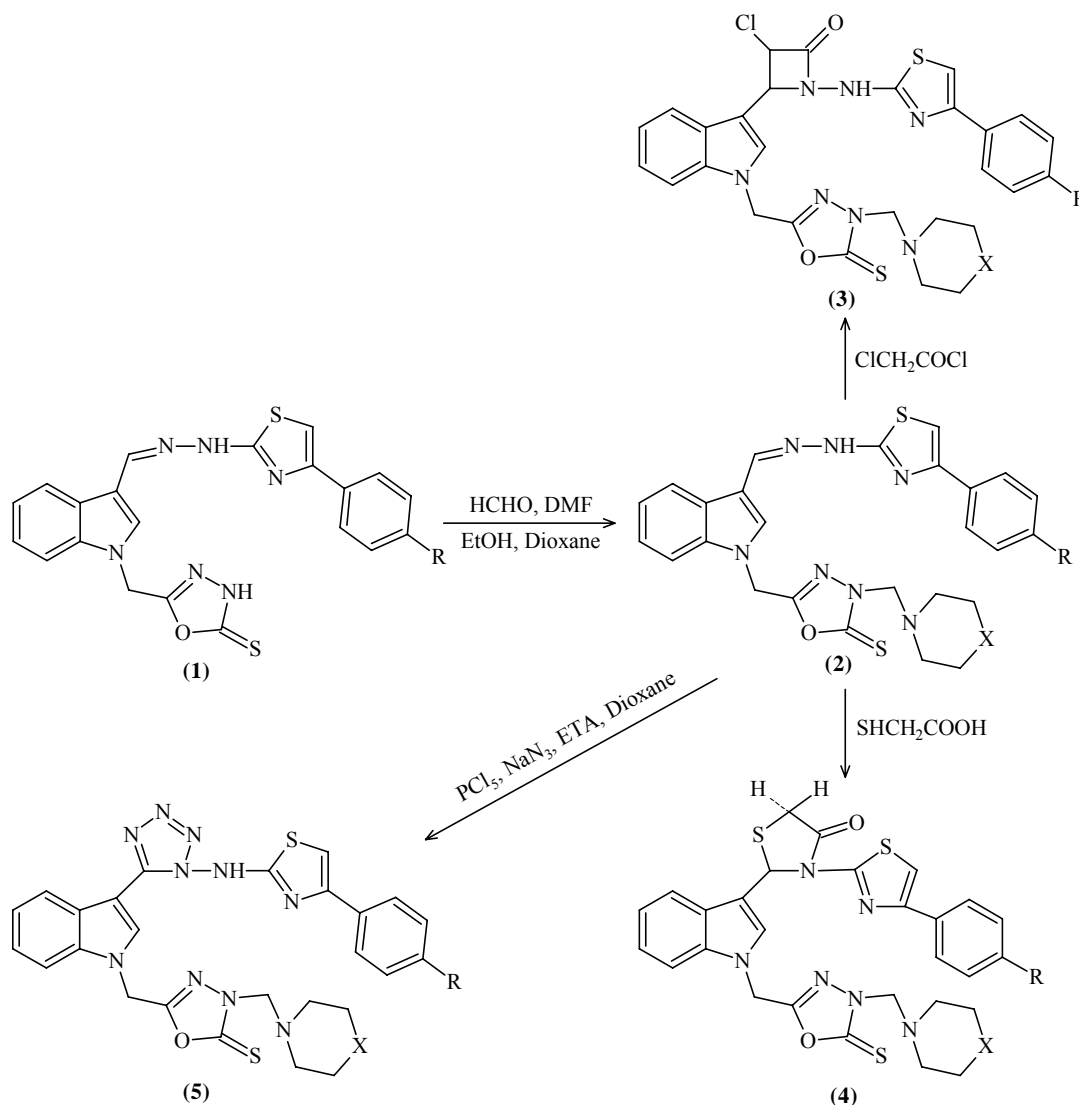
Schiff's base (0.004 mol) and PCl₅ (0.004 mol) were heated at 100°C for one hour till the evolution of fumes of HCl ceased. Excess of PCl₃ was removed under reduced pressure and the residual imidoyl chloride was treated with an ice cold solution of sodium azide (0.0075 mol) and excess of sodium acetate 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, (CH₂)₃ of piperidine ring, E), 2.56 (t, 4H, -CH₂-N-CH₂-), 4.45 (s, 2H, -N-CH₂-N-), 5.45 (s, 2H, -CH₂ thiazoxazole 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 **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 monitored 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 ₇ O ₃ S ₂	55.30 (55.35)	4.31 (4.28)	16.12 (16.14)
3(b)	CH ₃	S	185	60%	C ₂₉ H ₂₈ ClN ₇ O ₂ S 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 ₇ O ₃ S 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 ₈ O ₂ S 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 ₈ O ₄ S 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 ₃ N ₇ O ₂ S ₃	50.32 (50.36)	3.64 (3.61)	14.16 (14.18)
4(a)	H	O	182	58%	C ₂₈ H ₂₆ N ₆ O ₃ S ₃	56.93 (56.94)	4.44 (4.40)	14.23 (14.25)
4(b)	CH ₃	S	185	60%	C ₂₉ H ₂₈ N ₆ O ₂ S 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 ₆ O ₃ S 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 ₇ O ₂ S 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 ₇ O ₄ S 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 ₃ N ₆ O ₂ S 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 ₂ S ₂	54.53 (54.54)	4.22 (4.19)	24.46 (24.47)
5(b)	CH ₃	S	185	60%	C ₃₀ H ₂₄ ClF ₃ N ₆ O ₂ S	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 ₃ N ₆ O ₃ S	55.98 (56.00)	4.70 (4.66)	23.32 (23.33)
5(d)	Br	NCH ₃	195	59%	C ₂₉ H ₂₁ Cl ₂ F ₃ N ₆ O ₂ S	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 ₃ N ₇ O ₄ S	52.67 (52.68)	4.09 (4.06)	25.02 (25.04)
5(f)	CF ₃	S	210	57%	C ₂₈ H ₂₂ ClN ₇ O ₄ S	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)			
			<i>staphylococcus aureus</i> NCCS 2079	<i>Bacillus cereus</i> NCCS 2106	<i>Escherichia coli</i> NCCS 2065	<i>Pseudo-manas aeruginosa.</i> 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)	
	<i>Aspergillus niger</i> NCCS 1196	<i>Candida albicans</i> 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 antibacterial 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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