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SYNTHESIS AND CHARACTERIZATION OF 4-(2-((SUBSTITUTED)2-CHLORO QUINOLIN-3-YL)-3-(4-FLUOROPHENYL)-4-OXOAZETIDIN-1-YL)-N-(THIAZOL-2-YL) BENZENESULFONAMIDE AS ANTIBACTERIAL AND ANTIFUNGAL AGENTS

Krupa P. Patel, Ganpat R. Patel*

Department of Chemistry, Sheth M. N. Science College, NGES campus, Patan, Gujarat - 384265, India.

ABSTRACT: In the present work synthesized functionalized a novel series of 4-(2-((substituted)2-chloroquinolin-3-yl)-3-(4-fluorophenyl)-4-oxoazetidin-1-yl)-N-(thiazol-2-yl)benzenesulfonamide **5a-j** were obtained via condensations of 2-chloroquinoline-3-carbaldehyde **1a-j** with sulfonamide (sulfathiazole **STH**) in presence of minimum amounts of ethanol that produced intermediate Schiff base **3a-j** with good yield. This Schiff base **3a-j** promote was followed by the react with 2-(4-fluorophenyl) acetyl chloride **4** in presence of toluene and triethylamine (TEA) as catalytic amount produced targeted compounds **5a-j** were recognized by physical study like melding point (M.P) and structural geometry characterized deliberate by elemental analysis (CHNS) also different recognition spectral studies for example FT-IR, ^{1}H NMR, ^{13}C NMR, and ESI-MS (Mass spectroscopic). The purities of synthesized all final derivatives were corrected by thin layer chromatography (TLC) the bioactivity of all final scaffolds have been investigated by such as anti-bacterial activity against gram +ve and gram -ve strains and antifungal activity.

Keywords: Sulfonamide, 2-Azetidinone, Antifungal, Anti-bacterial activity, Schiff base.

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Corresponding Author: Dr. Ganpat R. Patel* Ph.D.

Department of Chemistry, Sheth M. N. Science College, NGES campus, Patan, Gujarat - 384265, India.Email Address:babajnvv@gmail.com

1. INTRODUCTION

In the field of the medicinal chemistry heterocycles constituent considered as a significant role in the areas of research.[1] The function of the 2-Azetidinone (β-lactam) framework was recognized as unique structural synthetic target nucleus and important contribution in the pharmaceutical

research world for the reason that of their most attractive antibacterial drugs globally marketing (above 65%).[2] Since penicillin **1** finding during 1940s and cephalosporin **2** were identified most potent antibiotic include 2-Azetidinone (β-lactam) motif mainly consumed and prescribed drugs worldwide in 2010[3]. 2-Azetidinon have been most successive antibiotics having common structural characteristic ring framework system counting Carbapenems , monobactams, nocardicins, clavulanic acid, tazobactams, sulbactams, these molecules known as **PGPs** (penicillin binding proteins) or cellular permeability used in bacterial infection as most successful chemotherapeutic agents.[4-10]. Early 90's, mainly the researche deliberate on the synthesis of β-lactam (azetidin-2-ones) and study their core of the bacterial activity. Recent years, renewed attention and focused in modification, design and synthesis of novel β-lactam (azetidin-2-ones) containing sulfonamide derivatives and evaluated pharmacological active drugs that resist pathogenic bacterial growth. Other side Sulfonamides are comprise prominent class of structural skeletons established plentiful bioactive, natural and pharmaceutical products. They shows broad-range of biological activities and are working essentially in various pharmaceutical and therapeutic applications such as Anti bacterial[11-13], carbonic anhydrase inhibitors (CAIs)[14], anticancer agents[15], COX-II (Cyclooxygenase-II) specific inhibitors[16], anti oxidant activity[17], Cholesterol absorption inhibitor (CAI)[18] anti fungal[19] etc. The structural modification of sulfonamides group were enhanced therapeutic activity by united with easily four, five and six member heterocyclic rings like 2-Azetidinone (β-lactam). Researchers reported sulfonamide containing compounds shows potential antibacterial [20], antifungal activities [21-23], anti cancer [24], anti HIV[25] and anti-inflammatory[26]. We explored our continuing work from the previous our and some of reported derivatives (Figure 1, derivative 1), it would be inspiring to synthesized functionalized a novel series of 4-(2-((substituted) 2-chloroquinolin-3-yl)-3-(4-fluorophenyl)-4-oxoazetidin-1-yl) -N-(thiazol-2-yl)benzene sulfonamide **5a-j** that investigated for their attractive antibacterial activity against gram +ve and gram -ve strains with minimum inhibition concentration (MIC) and Antifungal activity with (MIC) were characterized by elemental analysis, spectral data.

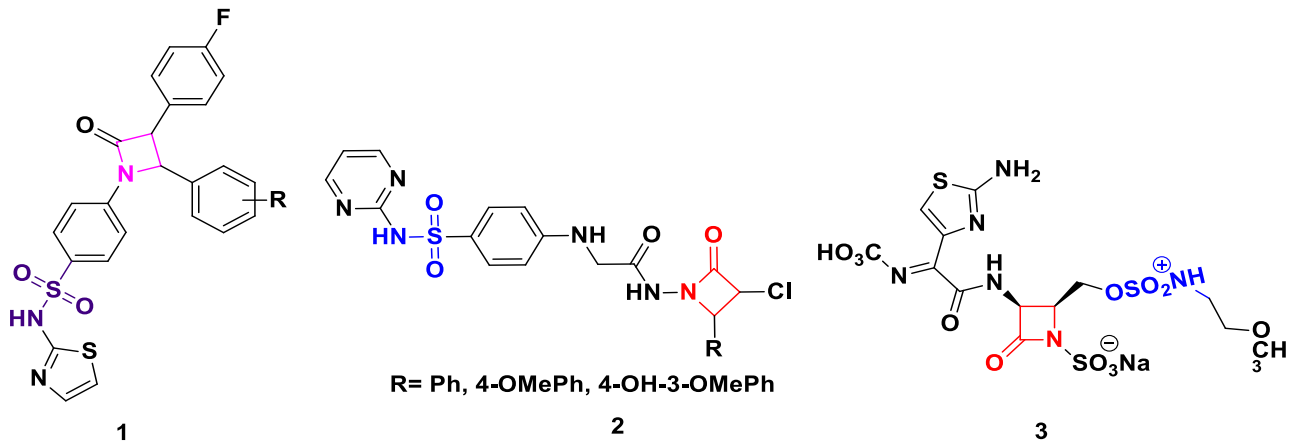


Figure-1 Some of reported sulfonamide bearing 2-azetidinone compounds

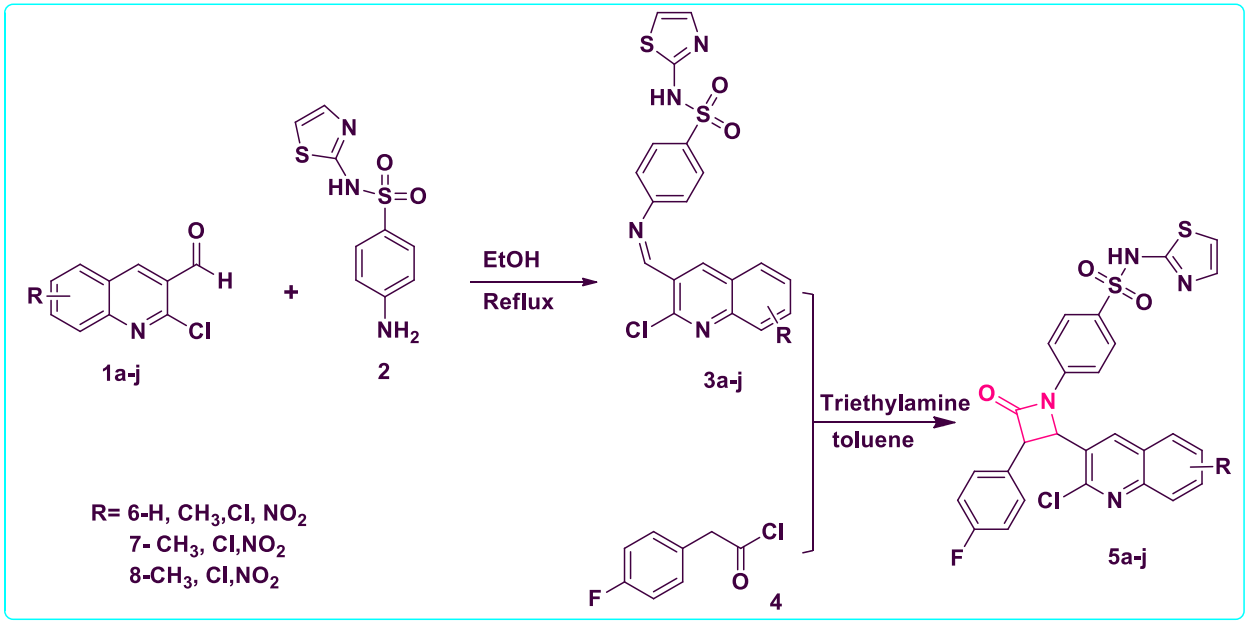
2. MATERIALS AND METHODS

In present work of the novel series of 4-(2-((substituted)2-chloroquinolin-3-yl)-3- (4-fluorophenyl)-4-oxoazetidin-1-yl)-N-(thiazol-2-yl)benzenesulfonamide which containing sulfonamide functionality united with 2-Azitidinone (Azitidin-2-one or β-lactam) group chemical and reagents were used all sulfonamides (sulfa drugs) **2** and 2-(4-flourophenyl)acetyl chloride **4** were acquired from commercial sources (Sigma-Aldrich). Different derivatives 2-chloroquinoline-3-carbaldehyde **1a-j,** Tri-ethylamine (TEA), ethanol and toluene were purchased from Merck (Germany). Pre coated aluminum sheets (silica gel 60 $F_{254,}$ Merck) were used as (TLC) thin-layer chromatography and spot were visualized underneath ultraviolet light. (M.P) Melting point was considered by using a Mel-temp apparatus, and consequences are uncorrected. Advion expression CMS, USA were used for recorded mass spectra. The compounds were analyzed for Carbon, Hydrogen, Nitrogen oxygen and Sulpher were estimated on CHNS analyzer serial NO. : 15084053. Infra-red spectra was recorded on Shimadzu spectrophotometer in the frequency range 4000-400 cm^{-1} using KBr pallet disc, ^{1}H NMR and ^{13}C NMR spectrum were recorded on bruker at 400 MHz and 100 MHz in DMSO solution and chemical shifts were recorded in parts per million (ppm) with TMS at the internal reference.

2.1 Synthesis

Synthesis of derivatives of schiff bases (SB) of (Z)-4-((((substuted)2-chloroquinolin-3-yl) methylene)amino)-N-(thiazol-2-yl)benzenesulfonamide (3a-j)

The all compounds of derivatives of schiff bases were prepared by our earlier method. (11-13) The following concentration among equimolar amounts (1:1) derivatives of the 2-chloroquinoline-3-carbaldehyde **1a-j** (0.1 mol) and sulfathiazole (**STH**), **2** (0.1 mol) in lowest amount amounts of Ethanol solution. The reaction mixture was refluxed to carry on for three to six-seven hours in oil bath and then cooled it. The solid product were filtrated and washed with some hot ethanol and then allow to dried with air and recrystallized from chloroform to get (Z)-4-((((substuted)2-chloroquinolin-3-yl)methylene)amino)-N-(thiazol-2-yl)benzenesulfonamide with light yellow colored. the reaction was continuously monitoring by thin layered chromatography (TLC) with using ethyl acetate : hexane (4:7). This subsequent reaction steps of the last product of schiff bases **3a-j** shown in scheme-**1.**



Scheme- 1 Synthesis route of compounds 5a-j (AZT)

Synthesis of 4-(2-((substituted)2-chloroquinolin-3-yl)-3-(4-fluorophenyl)-4-oxoazetidin-1-yl) -N-(thiazol-2-yl)benzenesulfonamide (5a-j)

The product mixture of Schiff base **3a-j** (0.02 mol) and triethyl amine (TEA) (0.04 mol) was dissolved in toluene (100 ml), cooled close to 5ºC and stirred. To this well-stirred cooled solution 2-(4-flourophenyl)chloroacetyl chloride (F-CAC) **4** (0.04 mmol) was added drop by drop with in a period of 15 min. The remain reaction mixture was then stirred for an supplementary 3-4 hrs and keep on at room temperature for 48 hrs. The consequential mixture was concentrated, cooled, poured in to beaker of ice cold water, sieve and then dried. Reaction was continuously monitoring by test of thin layered chromatography (TLC) with using The product thus obtained and recrystallization from n-hexane/EtOAc 8:2.gave derivatives of 4-(2-((substituted)2-chloroquinolin -3-yl)-3-(4-fluorophenyl)-4-oxoazetidin-1-yl)-N-(thiazol-2-yl)benzenesulfonamide **5a-j** One yellow to light yellow colored. (11-13)

Table- 1 Physical data and substitutions of present synthetic compounds

Entry	AZI Compounds	M.P(ºC)	Molecular Weight	Molecular Formula	Yield%
5a	**R= 6-H**	215-217	562.66	$C_{27}H_{19}FN_4O_3S_3$	69.98
5b	**8-CH_3**	~235	576.68	$C_{28}H_{21}FN_4O_3S_3$	65.73
5c	**7-CH_3**	212-215	576.68	$C_{28}H_{21}FN_4O_3S_3$	64.33
5d	**6,8-CH_3**	222	590.71	$C_{29}H_{23}FN_4O_3S_3$	63.85
5e	**8-NO_2**	>237	607.66	$C_{27}H_{18}FN_5O_5S_3$	62.24
5f	**7-NO_2**	>239	607.66	$C_{27}H_{18}FN_5O_5S_3$	62.20
5g	**6-NO_2**	~236.41	607.66	$C_{27}H_{18}FN_5O_5S_3$	63.55
5h	**8-Cl**	223-225	597.10	$C_{27}H_{18}ClFN_4O_3S_3$	63.10
5i	**7-Cl**	~225	597.10	$C_{27}H_{18}ClFN_4O_3S_3$	63.18
5j	**6-Cl**	~227	597.10	$C_{27}H_{18}ClFN_4O_3S_3$	62.9

4-(3-(4-fluorophenyl)-2-(2-mercaptoquinolin-3-yl)-4-oxoazetidin-1-yl)-N-(thiazol-2-yl)benzene sulfonamide (5a)

Yellow solid, mp 215-217ºC; Anal. Calcd for $C_{27}H_{19}FN_4O_3S_3$: C, 57.64; H, 3.40; N, 9.96; O, 8.53; S, 17.10%; found C, 58.01; H, 3.52; N, 10.02; O,9.05, S,18.11%; IR (KBr) ($\upsilon_{max,}$ cm^{-1}); 3340 (NH), 3032 (C-H_{str} saturated hydrocarbon) 1731 (C=O_{str} for azitidinone) 1541, 1510 and 1162 (for pyrazolin ring) 1330 Asy., 1184 Syn., (O=S=O), 1590 (thiazole ring); ^{1}H NMR (400 MHz, DMSO) δ 5.55 (d,CH-Cl_{lactam}), 4.98 (d, CH-N_{lactam}), 7.02-8.04 (m, aromatic Protons), 12.01 (s, 1H -NH). ESI-MS: *m/z* calculated 562.06, found $[M + H]^+$ 563.02.

4-(3-(4-fluorophenyl)-2-(2-mercapto-8-methylquinolin-3-yl)-4-oxoazetidin-1-yl)-N-(thiazol-2-yl)benzene sulfonamide (5b)

Light Yellow solid, mp ~235ºC; Anal. Calcd for $C_{28}H_{21}FN_4O_3S_3$: C, 58.32; H, 3.67; N, 9.72; O, 8.32; S, 16.68%; found C, 59.22; H,3.95; N,10.60; O,8.90; S,15.65%; IR (KBr) ($\upsilon_{max,}$ cm^{-1}); 3340 (NH), 3044 (C-H_{str} saturated hydrocarbon) 1729 (C=O_{str} for azitidinone) 1560, 1511 and 1117 (for pyrazolin ring) 1342 Asy., 1160 Syn., (O=S=O), 1575 (thiazole ring); ^{1}H NMR (400 MHz, DMSO) δ 3.17 (t 3H, CH_3) 5.10 (d,CH-Cl_{lactam}), 4.98 (d, CH-N_{lactam}), 7.01-8.23 (m, aromatic Protons), 11.82 (s, 1H -NH). ESI-MS: *m/z* calculated 576.08, found $[M + H]^+$ 577.08.

4-(3-(4-fluorophenyl)-2-(2-mercapto-7-methylquinolin-3-yl)-4-oxoazetidin-1-yl)-N-(thiazol-2-yl)benzene sulfonamide (5c)

Light Yellow solid, mp 212-215ºC; Anal. Calcd for $C_{28}H_{21}FN_4O_3S_3$: ∶ C, 58.32; H, 3.67; N, 9.72; O, 8.32; S, 16.68%; found C, 59.23; H, 3.84; N, 10.57; O, 15.25; S, 17.09%; IR (KBr) ($\upsilon_{max,}$ cm^{-1}); 3350 (NH), 3050 (C-H_{str} saturated hydrocarbon) 1772 (C=O_{str} for azitidinone) 1520, 1026 (for pyrazolin ring) 1320 Asy., 1128 Syn., (O=S=O), 1630 (thiazole ring); ^{1}H NMR (400 MHz, DMSO)

δ 3.85 (t 3H, CH_3) 4.78 (d,CH-Cl_{lactam}), 5.32 (d, CH-N_{lactam}), 6.84-7.74 (m, aromatic Protons), 11.55 (s, 1H -NH). ^{13}C NMR (100 MHz, DMSO-d_6) δ 159.12, 149.53, 147.35, 133.23, 132.04, 130.28, 129.43, 128.69, 128.00, 126.88, 126.11, 114.76, 112.60, 77.20, 77.03, 76.77, 63.10, 43.69 ESI-MS: *m/z* calculated 576.08, found $[M + H]^+$ 578.08

4-(3-(4-fluorophenyl)-2-(2-mercapto-6,8-dimethylquinolin-3-yl)-4-oxoazetidin-1-yl)-N-(thiazol-2-yl)benzene sulfonamide (5d)

white solid, mp 222ºC; Anal. Calcd for $C_{29}H_{23}FN_4O_3S_3$: C, 58.96; H, 3.92;N, 9.48; O, 8.13; S, 16.28%; found C, 59.70; H, 4.00; N, 9.70 O, 8.42; S, 15.25%; IR (KBr) ($\upsilon_{max,}$ cm^{-1}); 3342 (NH), 3033 (C-H_{str} saturated hydrocarbon) 1740 (C=O_{str} for azitidinone) 1540, 1522,and 1144 (for pyrazolin ring) 1327 Asy., 1178 Syn., (O=S=O), 1595 (thiazole ring); ^1H NMR (400 MHz, DMSO) δ 3.12 (t 3H, CH_2CH_3) 5.12 (d,CH-Cl_{lactam}), 4.90 (d, CH-N_{lactam}), 6.98-8.14 (m, aromatic Protons), 12.05 (s, 1H -NH). ESI-MS: *m/z* calculated 590.09, found $[M + H]^+$ 591.03

4-(3-(4-fluorophenyl)-2-(2-mercapto-8-nitroquinolin-3-yl)-4-oxoazetidin-1-yl)-N-(thiazol-2-yl)benzene sulfonamide (5e)

white solid, mp >237ºC; Anal. Calcd for $C_{27}H_{18}FN_5O_5S_3$: C, 53.37; H, 2.99; F, 3.13; N, 11.53; O, 13.16; S, 15.83%; found C, 54.02; H, 3.55; N, 12.50; O, 12.12; S, 16.22%; IR (KBr) ($\upsilon_{max,}$ cm^{-1}); 3348 (NH), 3029 (C-H_{str} saturated hydrocarbon) 1734 (C=O_{str} for azitidinone) 1544, 1512,and 1159 (for pyrazolin ring) 1342 Asy., 1165 Syn., (O=S=O), 1588 (thiazole ring); ^1H NMR (400 MHz, DMSO) δ 5.10(d,CH-Cl_{lactam}), 4.78 (d, CH-N_{lactam}), 7.00-8.15 (m, aromatic Protons), 12.10 (s, 1H -NH). ESI-MS: *m/z* calculated 607.05, found $[M + H]^+$ 606.01

4-(3-(4-fluorophenyl)-2-(2-mercapto-7-nitroquinolin-3-yl)-4-oxoazetidin-1-yl)-N-(thiazol-2-yl)benzene sulfonamide (5f)

yellow solid, mp >239ºC; Anal. Calcd for $C_{27}H_{18}FN_5O_5S_3$: C, 53.37; H, 2.99; F, 3.13; N, 11.53; O, 13.16; S, 15.83%; found C, 54.30; H, 2.01; N, 12.23; O, 14.90; S, 16.99%; IR (KBr) ($\upsilon_{max,}$ cm^{-1}); 3333 (NH), 3037 (C-H_{str} saturated hydrocarbon) 1736 (C=O_{str} for azitidinone) 1548, 1510 and 1170 (for pyrazolin ring) 1330 Asy., 1187 Syn., (O=S=O), 1584 (thiazole ring); ^1H NMR (400 MHz, DMSO) δ 5.10 (d,CH-Cl_{lactam}), 4.70 (d, CH-N_{lactam}), 6.78-8.01 (m, aromatic Protons), 11.77 (s, 1H -NH). ESI-MS: *m/z* calculated 607.05, found $[M + H]^+$ 606.03.

4-(3-(4-fluorophenyl)-2-(2-mercapto-6-nitroquinolin-3-yl)-4-oxoazetidin-1-yl)-N-(thiazol-2-yl)benzene sulfonamide (5g)

Yellow solid, mp 236-41ºC; Anal. Calcd for $C_{27}H_{18}FN_5O_5S_3$: C, 53.37; H, 2.99; F, 3.13; N, 11.53; O, 13.16; S, 15.83%; found C, 53.72; H, 3.31; N, 12.62; O, 12.60; S, 16.61%; IR (KBr) ($\upsilon_{max,}$ cm^{-1}); 3355 (NH), 3033 (C-H_{str} saturated hydrocarbon) 1727 (C=O_{str} for azitidinone) 1542, 1519,and 1170 (for pyrazolin ring) 1336 Asy., 1188 Syn., (O=S=O), 1568 (thiazole ring); ^1H NMR (400 MHz, DMSO) δ 5.17 (d,CH-Cl_{lactam}), 4.99 (d, CH-N_{lactam}), 7.10-8.15 (m, aromatic Protons), 12.00 (s, 1H -NH). ESI-MS: *m/z* calculated 607.05, found $[M + H]^+$ 606.02.

4-(2-(8-chloro-2-mercaptoquinolin-3-yl)-3-(4-fluorophenyl)-4-oxoazetidin-1-yl)-N-(thiazol-2-yl)benzene sulfonamide (5h)

Yellow solid, mp 223-225ºC; Anal. Calcd for $C_{27}H_{18}ClFN_4O_3S_3$: C, 54.31; H, 3.04; Cl, 5.94; N, 9.38; O, 8.04; S, 16.11%; found C, 55.30; H, 3.93; N, 10.20; O, 7.25; S, 17.27%; IR (KBr) ($\upsilon_{max,}$ cm^{-1});3340 (NH), 3058 (C-H_{str} saturated hydrocarbon) 1725 (C=O_{str} for azitidinone) 1551, 1487,and 1106 (for pyrazolin ring) 1351 Asy., 1174 Syn., (O=S=O), 1620 (thiazole ring); ^{1}H NMR (400 MHz, DMSO) δ 5.34(d,CH-Cl_{lactam}), 4.40 (d, CH-N_{lactam}), 7.00-7.75 (m, aromatic Protons), 11.77 (s, 1H -NH). ^{13}C NMR (100 MHz, DMSO-d_6) δ 149.55, 147.39, 138.24, 137.85, 132.01, 130.20, 130.06, 129.44, 128.77, 128.05, 126.12, 125.58, 112.50, 77.27, 77.06, 63.38, .43.71, 21.10; ESI-MS: *m/z* calculated 596.02, found $[M + H]^+$ 596.12

4-(2-(7-chloro-2-mercaptoquinolin-3-yl)-3-(4-fluorophenyl)-4-oxoazetidin-1-yl)-N-(thiazol-2-yl)benzene sulfonamide (5i)

Yellow solid, mp ~225ºC; Anal. Calcd for $C_{27}H_{18}ClFN_4O_3S_3$: C, 54.31; H, 3.04; Cl, 5.94; N, 9.38; O, 8.04; S, 16.11%; found C, 55.86; H, 3.92; N, 10.21; O, 7.16; S, 17.11%; IR (KBr) ($\upsilon_{max,}$ cm^{-1}); 3361 (NH), 3028 (C-H_{str} saturated hydrocarbon) 1731 (C=O_{str} for azitidinone) 1542, 1521,and 1172 (for pyrazolin ring) 1330 Asy., 1168 Syn., (O=S=O), 1578 (thiazole ring); ^{1}H NMR (400 MHz, DMSO) δ 5.10 (d,CH-Cl_{lactam}), 4.88 (d, CH-N_{lactam}), 7.01-8.08 (m, aromatic Protons), 11.88 (s, 1H -NH). ESI-MS: *m/z* calculated 596.02, found $[M + H]^+$ 596.88.

4-(2-(6-chloro-2-mercaptoquinolin-3-yl)-3-(4-fluorophenyl)-4-oxoazetidin-1-yl)-N-(thiazol-2-yl)benzene sulfonamide (5j)

Light Yellow solid, mp ~227ºC; Anal. Calcd for $C_{27}H_{18}ClFN_4O_3S_3$: C, 54.31; H, 3.04; N, 9.38; O, 8.04; S, 16.11%; found C, 55.29; H, 3.98; N, 10.35; O, 7.34; S, 16.40%; IR (KBr) ($\upsilon_{max,}$ cm^{-1}); 3350 (NH), 3032 (C-H_{str} saturated hydrocarbon) 1736 (C=O_{str} for azitidinone) 1550, 1480,and 1177 (for pyrazolin ring) 1340 Asy., 1185 Syn., (O=S=O), 1580 (thiazole ring);; ^{1}H NMR (400 MHz, DMSO) δ 5.25 (d,CH-Cl_{lactam}), 5.01 (d, CH-N_{lactam}), 7.12-8.10 (m, aromatic Protons), 12.03 (s, 1H -NH). ESI-MS: *m/z* calculated 596.02, found $[M + H]^+$ 597.01.

2.2 BIOLOGICAL ACTIVITY

2.2.1. Determination of antibacterial activity (zone inhibition and MIC)

$$\textbf{Activity index}(\textbf{A.I}) = \frac{\textbf{mean of the zone of inhibition of derivatives}}{\textbf{zone of inhibition obtained for standard antibiotic drug}}$$

This activity is done by in vitro agar well diffusion our reported process (11-13). Plates inoculated with the bacteria (two Gram-negative and two Gram-positive) (MTCC No.8558 Enterobacter aerogens, Escherichia coli MTCC No.1610, Micrococcus luteus MTCC No.11948 and Bacillus cereus MTCC No.8558). The inhibitions zone was measured were the microorganism inhibited after the incubation was done and were compared with standard streptomycin (1000µg/ml). shown in

table-2

The minimum Inhibitory concentration (MIC)of all synthesized compounds were tested by broth micro dilution method with against standard bacterial strains (MTCC No.8558 Enterobacter aerogens, Escherichia coli MTCC No.1610, Micrococcus luteus MTCC No.11948 and Bacillus cereus MTCC No.8558) were dilution to make desire concentration of compounds. The serially two fold dilutions of tested compounds and control inoculated with actively bacterial cell which were the nutrient broth. These nutrient maintaining inoculated for 37 ºC for 24 hour the spectrophotometer was used for monitoring and also visually. The minimum concentration or maximum dilution which was required for kill bacterial growth regard as minimum Inhibitory concentration (MIC). MIC values shown in **table-3**

2.2.2. Determination of antifungal activity (zone inhibition and MIC)

According previous our reported process, (11-13) all synthesized new series of 4-(2-((substituted)2-chloroquinolin-3-yl)-3-(4-fluorophenyl)-4-oxoazetidin-1-yl)-N-(thiazol-2-yl)benzenesulfonamide **5a-j** were screened for their antifungal activity against and *Candida albicans* and *Aspergillus niger* in DMF, the activity conduct by using in vitro agar well diffusion process. Mixture of Pepton (1g), D-glucose (4g) and agar (2g) were mix to prepared Saubourauds agar media and the medium was maintained 5.7 pH by adding 100 ml of distill water and make a suspension for fungal strain. Every Petri dish of suspension of corresponding species were made by using 20ml of fungal with 3ml salin in dish which dried by using incubator at 37 ºC for 1 day. A equipped control was permitted for 3 to 4 day at 37 ºC and the fungal inhibitions zone was calculated were the microorganism inhibited subsequent to the incubation was completed. The results compare with standard voriconazole (table-**4)**

MIC values of finalized derivatives **5-a-j** were evaluated and the spectrophotometer was used for observing data and visually also. (Table-**5**)

3. RESULTS AND DISCUSSION

In these present work synthesis targeted compounds **5a-j** were modified with initially prepared potent intermediate Schiff base **3a-j** via reaction between sulfathaizole (**STH) 4** and different 2-chloroquinoline-3-carbaldehyde **1a-j** with good yield. These Schiff base **3a-j** supplementary utilized for production these new of 4-(2-((substituted)2-chloro quinolin-3-yl)-3-(4-fluorophenyl) -4-oxoazetidin-1-yl)-N-(thiazol-2-yl)benzenesulfonamide **5a-j** were established by physical properties like melding point (M.P) and characterized done by elemental analysis (CHNS) also various detection spectral techniques such as FT-IR, ^{1}H NMR, ^{13}C NMR, and ESI-MS (Mass spectroscopic). The FT-IR of all compounds showed stretching band ~1725-1770 cm^{-1} for CO, β-lactam, strong asymmetric starching vibrations band for (O=S=O) within the range 1320-1351 cm^{-1} and second symmetric starching vibrations within the range of 1120-1188 cm^{-1}. ^{1}H NMR (400 MHz, DMSO) for all compounds showed doublet for two CH β-lactam of at δ 4.78-4.99 and δ 5.01-5.34.

The concentration of standard drug streptomycin was 1000 µg/ml. All compounds **5a-j** excellent exhibited significant antibacterial action measure up to to control. compound **5e** and **5h** showed highest zone of inhibition against ***Enterobacter aerogens*** **MTCC No. 8558** and ***Micrococcus luteus*** **MTCC No. 11948.** Activity of **5g** and **5i** was better against **E.coli** and **B. cereus** compared to streptomycin**.** All compounds exhibited equivalent or improved active against Gram positive and negative bacteria. Analysis of structural features reveals that the more electronegative like NO_2 and Cl group linked with ring has increased antibacterial potential of compounds.

Table 2: Antibacterial activity of 5a-j derivatives

Derivatives	***Enterobacter aerogens*** **MTCC No. 8558**		***Escherichia coli*** **MTCC No. 1610**		***Micrococcus luteus*** **MTCC No. 11948**		***Bacillus cereus*** **MTCC No. 8558**	
	Mean value for Zone of Inhibition (mm)	Activity Index (A.I.)	Mean value for Zone of Inhibition (mm)	Activity Index (A.I.)	Mean value for Zone of Inhibition (mm)	Activity Index (A.I.)	Mean value for Zone of Inhibition (mm)	Activity Index (A.I.)
5a	15	0.625	17	0.708	29	1.208	15	0.625
5b	22	0.917	22	0.917	22	0.917	30	1.250
5c	22	0.917	22	0.917	24	1.000	30	1.250
5d	22	0.917	24	1.000	22	0.917	24	1.000
5e	36	1.500	34	1.417	36	1.500	34	1.417
5f	29	1.208	34	1.417	30	1.250	36	1.500
5g	30	1.208	36	1.500	30	1.250	34	1.417
5h	36	1.500	30	1.250	36	1.500	34	1.417
5i	29	1.208	36	1.500	30	1.250	36	1.500
5j	30	1.250	27	1.125	25	1.041	27	1.125
Std	24	-	24	-	24	-	24	-

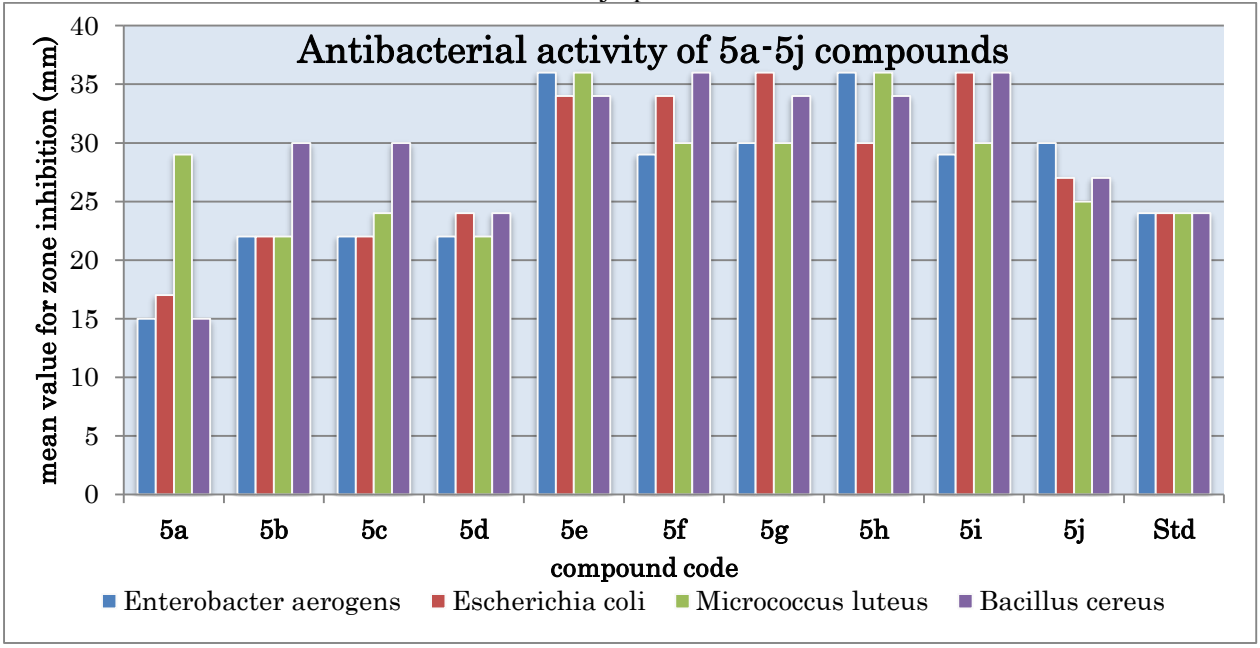


Figure- 2 zone inhibition Antibacterial activity of compounds 5a-j

Compounds **5e** and **5h** exhibited most potential zone inhibition activity as well as in MIC for all bacterial strains compared to standard while other compounds also showed moderate to good inhibitions action of MIC values.

Table 3: MIC results of 5*a-j* compounds

Derivatives	***Enterobacter aerogens* MTCC No. 8558**	***Escherichia coli* MTCC No. 1610**	***Micrococcus luteus* MTCC No. 11948**	***Bacillus cereus* MTCC No. 8558**
	MIC(µg/ml)	**MIC(µg/ml)**	**MIC(µg/ml)**	**MIC(µg/ml)**
5a	400	100	200	200
5b	400	200	-	200
5c	200	400	200	200
5d	200	-	400	200
5e	25	50	25	12.5
5f	50	25	50	50
5g	100	50	100	50
5h	50	25	25	25
5i	100	100	50	100
5j	100	100	50	200
Std	6.25	3.125	3.125	6.25

It has been shown that the antifungal results of inhibition mechanism for synthesized compounds **5a-j** considered as low to high inhibitory action against *Aspergillus nigar* and *Candida albicans*.

Taking these consequences into considerations, merely **5e** and **5h** were considered as promising high potency inhibitory derivatives antifungal activity against to standard, whereas others derivatives showed moderate to average.

Table 4: Antifungal activity of 8*a-8o* compounds

Derivatives	*Aspergillus niger*		*Candida albicans*	
	Mean value for Zone of Inhibition (mm)	Activity Index (A.I.)	Mean value for Zone of Inhibition (mm)	Activity Index (A.I.)
5a	17	0.607	18	0.643
5b	18	0.643	19	0.679
5c	18	0.643	18	0.643
5d	21	0.75	22	0.75
5e	31	1.071	31	1.071
5f	22	0.786	22	0.75
5g	24	0.857	26	0.929
5h	31	1.071	30	1.071
5i	21	0.75	25	0.893
5j	22	0.786	23	0.821
Std	28	-	24	-

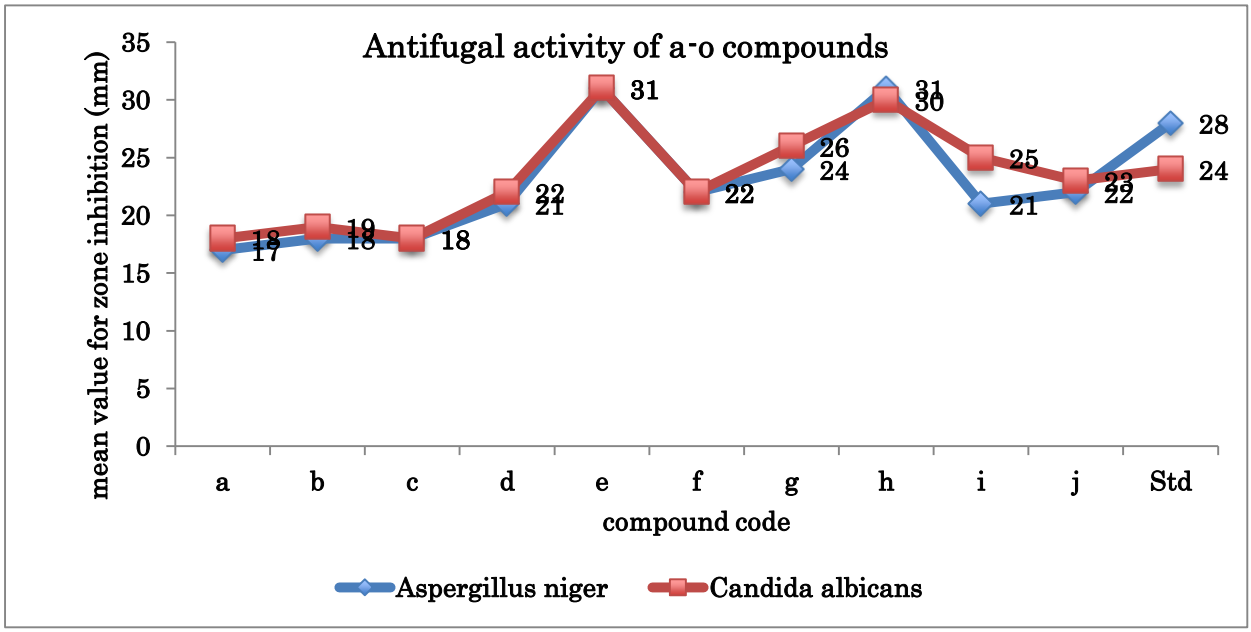


Figure- 3 zone inhibition Antifungal activity of compounds **5a-j**

Derivatives **5e** and **5h** exhibited most potential MIC values of antifungal compared to standard in addition to other compounds also showed moderate to good inhibitions action of MIC values.

Table 5: MIC results of compounds 5a-j

Derivatives	*Aspergillus niger*	*Candida albicans*
	MIC (µg/ml)	MIC (µg0/ml)
5a	200	100
5b	200	200
5c	-	400
5d	100	400
5e	25	25
5f	100	100
5g	50	100
5h	25	12.5
5i	100	100
5j	100	100
Std	6.25	6.25

4. CONCLUSION

In this present work we prepared a novel series of 4-(2-((substituted)2-chloro quinolin-3-yl)-3-(4-fluorophenyl)-4-oxoazetidin-1-yl)-N-(thiazol-2-yl)benzenesulfonamide **5a-j** was synthesized and evaluated for antibacterial activity against gram +ve and gram -ve strains and antifungal activity. The significant results shown for compounds **5e** and **5h** scaffold showed excellent potential antibacterial activity as well as in MIC, they also significant derivatives showed more potent compared to standard against *Aspergillus nigar* and *Candida albicans* as antifungal agents.

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ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Not applicable.

HUMAN AND ANIMAL RIGHTS

No Animals/Humans were used for studies that are base of this research.

CONSENT FOR PUBLICATION

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CONFLICT OF INTEREST

The authors have declared that they have no any conflict of interest.

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