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SYNTHESIS AND BIOLOGICAL EVOLUTION OF SULFONAMIDE FUSED AZITIDINONE AS ANTIBACTERIAL AND ANTIFUNGAL AGENTS

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ABSTRACT: A series of novel compounds 4-(3-(2-flourophenyl)-2-oxo-4-(substituted) arylazitidin-1-yl-N-(thiazol-2-yl)benzenesulfonamide **8a-8o** were synthesized in first reaction step by condensations of sulfathiazole (**STH) 4** and appropriate different aromatic aldehydes **5a-5o** in presence of catalytic amount of glacial acetic acid produced intermediate Schiff bases **6a-6o** with good to moderate yield. This Schiff base **6a-6o** further was followed by the react with 2-(4-fluorophenyl)acetyl chloride **7** in presence of toluene and triethylamine (TEA) as catalytic amount via cyclisation produced 4-member heterocyclic ring fused targeted compounds **8a-8o.** All newly synthesized fused heterocyclic compounds **8a-8o** were accepted by different spectral techniques and all final derivatives were examined for their antibacterial activity against gram +ve and gram -ve strains and antifungal activity. All results for scaffolds compare against the standard drug. Also studied their MIC (minimal inhibitory concentration).

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

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1.INTRODUCTION

The rapid investigation and improvement of the heterocyclic compounds have become the most leading areas of research and synthesis point of view in the field of medicinal chemistry because of compounds having efficacious biological properties [1]. The numbers of strategies are applying for finding new compounds possessing bacterial inhibitory action against organism and struggle to enhancement for drugs resistant strain, still require to discover novel antibacterial compounds [2]. After the examined the structure of sulfonamide and fact that known the first preventive exists

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chemotherapeutic agent, the researcher received much attention toward RSO_2NH_2 functionality. This most versatile moieties shown to demonstrate an broad range of activities such as Antibacterial and Antifungal [3–5], Carbonic anhydrase inhibitors (CAIs)[6][7], type-II diabetes[8], treating male erectile dysfunction[8], Anticancer[9], Anti HIV[10],[11], Cyclooxygenase-2 (COX-2) inhibitors [12], Antimalarial [13], cysteine protease[14], hypoglycemic[15], influenza[16], Antioxidant[5], [17–19], anti tuberculosis[20–22], etc. Beside the azitidine, another small fused 4-membered 'N' containing heterocyclic ring having carbonyl group at second position therefore also known as β-lactam and 2-azitidinone is one of the most potent pharmacophores showed famous drugs as cephalosporins, carbapenems, penicillin, monobactams, clavulanic acid, etc[23]. 2-azitidinone moieties mostly famous as Antibacterial but nowadays it's reported as numbers of biological applications such as anti-inflammatory[24], Antimicrobial[25], Anticancer[26], Anti Plasmodia[27], etc. The sulfonamides were fused with capped by four, five or six member heterocyclic ring resulted in these structural modification enhanced chemotherapeutic activity. Some of the reported sulfonamides clubbed 2-azitidinine compounds showed exhibit a diverse range of activity. B.B. Subudhi *et al.* developed a novel compound **1** having sulfonamide conjugate with 2-azitidinone and evaluated for their antimicrobial activity shown in **figure-1** [28]**,** I.K Bhat *et al.* investigated a novel series of N'-[3-chloro-4-substitutedphenyl-2-oxo-azitidin-1-yl]-2-(sulfanilamidooyrimidinyl) -acetamides using sulfadiazine and prepared β-lactam ring **2** and investigated their antimicrobial activity [29], Guanti *et al.* developed new derivatives of sulfonamide clubbed with azitidin-2-one **3** and found to exhibit good to moderate their antimicrobial activity is shown in **figure-1** [30]. We explored our ongoing work from the observations of these reported derivatives, it would be motivating to synthesized new series of sulfonamide fused 2-azitidinine, 4-(3-(2-flourophenyl) -2-oxo-4-(substituted)arylazitidin-1-yl-N-(thiazol-2-yl)benzenesulfonamide **8a-8o** that evaluated for their interesting 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.

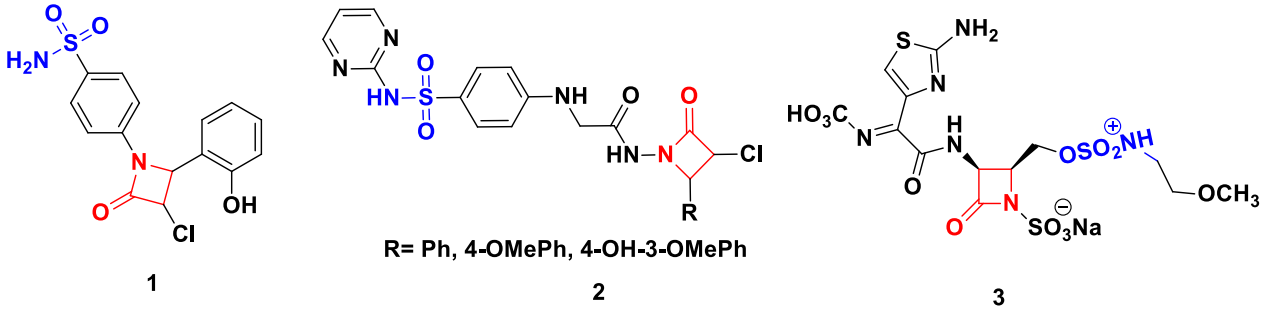

Figure-1 Some of reported sulfonamide bearing 2-azetidinone compounds

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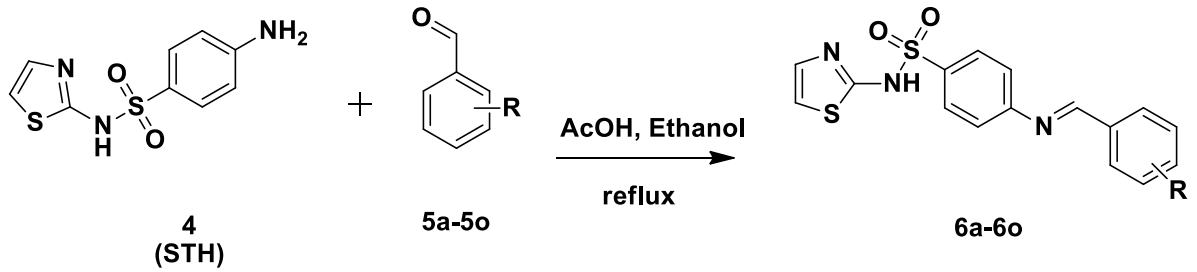
2. MATERIALS AND METHODS

The series of compounds 4-(3-(2-flourophenyl)-2-oxo-4-(substituted)arylazitidin-1-yl-N-(thiazol -2-yl)benzenesulfonamide **8a-8o** was synthesized and evaluated and this following chemical and reagents were used all sulfa drug (sulfathiazole-**STH**) were acquired from commercial sources (Sigma-Aldrich). Different aldehyde derivatives, Ethanol and toluene were purchased from Merck (Germany). Pre-coated aluminium sheets (silica gel 60 $F_{254,}$ Merck) were used for thin-layer chromatography (TLC) and spots were visualized under ultraviolet light. Melting point (M.P) were measured by using a Mel-temp instrument, and results are uncorrected. Infra-red spectra were recorded on Shimadzu spectrophotometer in the frequency range 4000-400 cm^{-1} using KBr pallet disc, ^{1}H NMR and ^{13}C NMR spectra 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. Advion expression CMS, USA were used for recorded mass spectra. The compound was analyzed for Carbon, Hydrogen, Nitrogen oxygen and Sulpher was estimated on CHNS analyzer serial NO. : 15084053

2.1 Synthesis



Scheme-1 Synthesis of Schiff base 6a-6o

General synthesis of derivatives of 4-(arylideneamino)-N-(thiazol-2-yl)benzensulfonamide (Schiff base)

A mixture of sulfathiazole (**STH) 4** (0.1 mol) and appropriate different aromatic aldehydes **5a-5o** (0.1 mol) in ethanol (50 ml) in the presence of the catalytic amount of glacial acetic acid (4 to 5 drops) was refluxed for 5 h. The solvent was removed under reduced pressure and the product cooled it. The solid product filtrated and washed with some hot ether and then allow to dried with air and product recrystallized from chloroform to get 4-((substituted)arylideneamino)-N-(thiazol-2-yl) benzensulfonamide **6a-6o** with light yellow coloured the reaction was continuously observed by thin layered chromatography (TLC) with using ethyl acetate: hexane (4:7). This following reaction steps of the Schiff bases shown in **scheme-1.**

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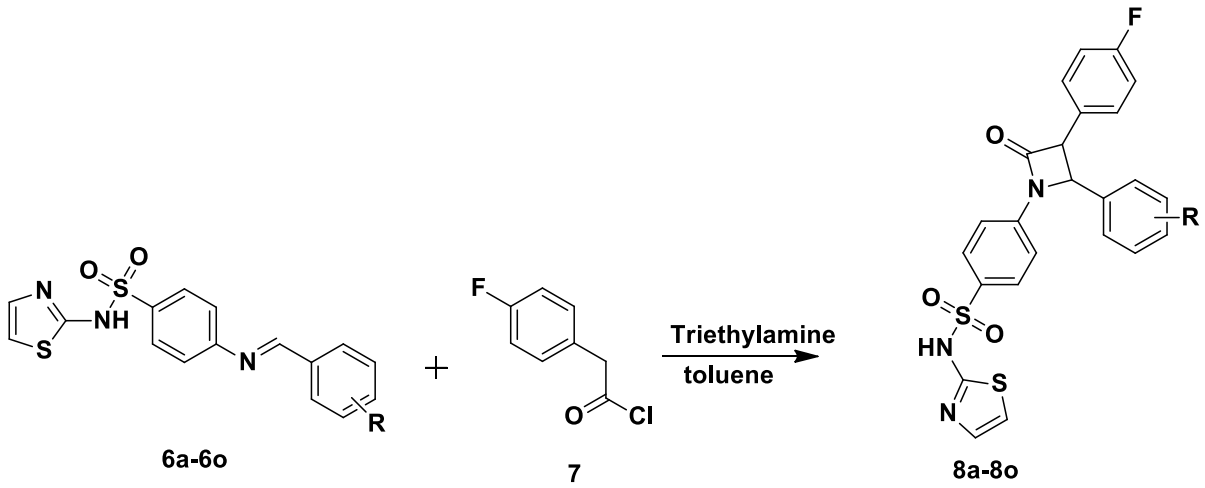

Where, R = p-H, p-Cl, 2,4-(Cl)2, o-OH, p-OH, p-CH_3, m-NO_2, o-OCH_3, p-OCH_3, p-F, o-CH_3, m-CH_3, p-$N(CH_3)2$, o-Cl, p-CH_2CH_3

Scheme-2 Synthesis of targeted compound 8a-8o

General synthesis of derivatives of 4-(3-(2-flourophenyl)-2-oxo-4-arylazitidin-1-yl-N-(thiazol-2-yl)benzenesulfonamide

A mixture of Schiff base **6a-6o** (0.02 mol) and triethylamine (TEA) (0.04 mol) was dissolved in toluene (100 ml), cooled near to 5ºC and stirred. To this well-stirred cooled solution 2-(4-fluorophenyl)acetyl chloride **7** (0.04 mmol) was added dropwise within a period of 20 min. The reaction mixture was then stirred for an additional 3-4 hrs and left at room temperature for 48 hrs. The resultant mixture was concentrated, cooled, poured into ice cold water, filter and then dried. The reaction was continuously observed by thin layered chromatography (TLC) with using The product thus obtained and recrystallization from n-hexane / EtOAc 8:2.gave derivatives of 4-(3-(2-flourophenyl)-2-oxo-4-(substituted) arylazitidin-1-yl-N-(thiazol-2-yl)benzenesulfonamide **8a-8o** yellow to light yellow coloured. **scheme-2**

Table 1: Physical data and substitutions of present synthetic compounds

Entry	AZi Compounds	M.P(ºC)	Molecular Weight	Molecular Formula	Yield%
a	C_6H_5	218-220	497.55	$C_{24}H_{18}FN_3O_3S_2$	75.3
b	4-Cl, C_6H_5	~249	513.99	$C_{24}H_{17}ClFN_3O_3S_2$	76.3
c	2,4-Cl, C_6H_5	288-291	548.44	$C_{24}H_{17}Cl_2FN_3O_3S_2$	69.5
d	2-OH, C_6H_5	~260	495.55	$C_{24}H_{18}FN_3O_4S_2$	72.4
e	4-OH, C_6H_5	~255	495.55	$C_{24}H_{18}FN_3O_4S_2$	68.5
f	4- CH_3, C_6H_5	>230	493.57	$C_{25}H_{20}FN_3O_3S_2$	72.1
g	3-NO_2, C_6H_5	~260	467.56	$C_{24}H_{17}FN_4O_5S_2$	73.4
h	2-O CH_3, C_6H_5	262-264	509.57	$C_{25}H_{20}FN_3O_4S_2$	70.3
i	4-O CH_3, C_6H_5	~275	509.57	$C_{25}H_{20}FN_3O_4S_2$	71.9

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j	4-F, C_6H_5	~249	497.54	$C_{24}H_{17}F_2N_3O_3S_2$	78.5
k	2- CH_3, C_6H_5	>250	493.57	$C_{25}H_{20}FN_3O_3S_2$	76.4
l	3- CH_3, C_6H_5	>250	493.57	$C_{25}H_{20}FN_3O_3S_2$	65.4
m	4-$N(CH_3)2$, C_6H_5	280-284	522.61	$C_{26}H_{23}FN_4O_3S_2$	70.3
n	2-Cl, C_6H_5	~241	513.99	$C_{24}H_{17}ClFN_3O_3S_2$	72.3
o	4-C_2H_5, C_6H_5	277-281	507.11	$C_{26}H_{22}FN_3O_3S_2$	77.2

4-(3-(2-flourophenyl)-2-oxo-4-phenylazitidin-1-yl)-N-(thiazol-2-yl)benzenesulfonamide (8a)

Yellow solid, mp 218-220ºC; Anal. Calcd for $C_{24}H_{18}FN_3O_3S_2$: C, 60.11; H, 3.78; N, 8.76; O, 10.01; S, 13.37%; found C, 60.70; H, 3.82; N, 8.10; O, 10.02, S, 13.17%; IR (KBr) ($\upsilon_{max,}$ cm^{-1}); 3345 (NH), 3052 (C-H_{str} saturated hydrocarbon) 1770 (CO, β-lactam), 1620 (C=N_{str}) 1382 Asy., 1123 Syn., (O=S=O), 1511 (thiazole ring); ^{1}H NMR (400 MHz, DMSO) δ 4.14 (d, 1H, CH azi), 5.02 (d, 1H, CH azi), 7.11-8.99 (m, aromatic Protons), 7.02, 8.52 (d 1H and d 1$H_{thiazole}$), 11.89 (s, 1H -NH). ^{13}C NMR (100 MHz, DMSO-*d_6*) δ 172.01, 162.17, 160.30, 152.19, 145.15, 138.14, 136.25, 135.05, 132.15, 129.91, 129.14, 128.11, 128.06, 120.11, 114.24, 114.02, 60.99, 52.36. ESI-MS: *m/z* calculated 479.08, found $[M + H]^+$ 480.

4-(2-(4-chlorophenyl)-3-(4-flourophenyl)-4-oxaazitidin-1yl)-N-(thiazol-2-yl)benzenesulfonamide (8b)

Yellow solid, mp ~249ºC; Anal. Calcd for $C_{24}H_{17}ClFN_3O_3S_2$: C, 56.08; H, 3.33; N, 8.18; O, 9.34; S, 12.48%; found C, 56.15; H, 3.52; N, 8.10; O, 9.32, S, 12.47%; IR (KBr) ($\upsilon_{max,}$ cm^{-1}); 3350 (NH), 3050 (C-H_{str} saturated hydrocarbon) 1772 (CO, β-lactam), 1630 (C=N_{str}) 1320 Asy., 1128 Syn., (O=S=O), 1510 (thiazole ring); ^{1}H NMR (400 MHz, DMSO) δ 4.09 (d, 1H, CH azi), 4.80 (d, 1H, CH azi), 7.24-8.98 (m, aromatic Protons), 7.10, 8.39 (d 1H and d 1$H_{thiazole}$), 12.00 (s, 1H -NH).^{13}C NMR (100 MHz, DMSO-*d_6*) δ 169.93, 161.97, 161.36, 145.69, 136.04, 135.41, 133.05, 129.27, 129.05, 128.41, 128.13, 120.02, 115.41, 115.36, 114.21, 62.69, 56.92. ESI-MS: *m/z* calculated 513.04, found $[M + H]^+$ 514.1.

4-(2-(2,4-dichlorophenyl)-3-(4-flourophenyl)-4-oxaazitidin-1yl)-N-(thiazol-2-yl)benzenesulfonamide (8c)

Light Yellow solid, mp 288-291ºC; Anal. Calcd for $C_{24}H_{17}Cl_2FN_3O_3S_2$: C, 52.56; H, 2.94; N, 7.66; O, 8.75; S, 11.69%; found C, 52.45; H, 2.92; N, 7.70; O, 9.02, S, 11.57%; IR (KBr) ($\upsilon_{max,}$ cm^{-1}); 3340 (NH), 3053 (C-H_{str} saturated hydrocarbon) 1775 (CO, β-lactam), 1635 (C=N_{str}) 1388 Asy., 1125 Syn., (O=S=O), 1515 (thiazole ring); ^{1}H NMR (400 MHz, DMSO) δ 4.14 (d, 1H, CH azi), 4.92 (d, 1H, CH azi), 7.11-8.98 (m, aromatic Protons), 7.00, 8.44 (d 1H and d 1$H_{thiazole}$), 11.19 (s, 1H -NH). ^{13}C NMR (100 MHz, DMSO-*d_6*) δ 170.25, 161.22, 160.02, 151.20, 144.85, 138.25, 135.15, 134.25, 131.55, 129.10, 129.01, 128.33, 128.02, 120.14, 114.66, 114.22, 61.03, 53.25. ESI-MS: *m/z* calculated 547.00, found $[M + H]^+$ 548.01

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4-(3-(4-flourophenyl)-2-(2-hydroxyphenyl)-4-oxaazitidin-1yl)-N-(thiazol-2-yl)benzenesulfonamid (8d)

Yellow solid, mp 260ºC; Anal. Calcd for $C_{24}H_{18}FN_3O_4S_2$: C, 58.17; H, 3.83; N, 8.48; O, 12.91; S, 12.94%; found C, 58.45; H, 3.75; N, 8.48; O, 12.87, S, 12.97%; IR (KBr) ($\upsilon_{max,}$ cm^{-1}); 3590 (Ar-OH) 3355 (NH), 3045 (C-H_{str} saturated hydrocarbon) 1772 (CO, β-lactam), 1640 (C=N_{str}) 1355 Asy., 1135 Syn., (O=S=O), 1510 (thiazole ring); ^{1}H NMR (400 MHz, DMSO) δ 4.07 (d, 1H, CH azi), 4.97 (d, 1H, CH azi), 7.20-8.88 (m, aromatic Protons), 7.05, 8.34 (d 1H and d 1$H_{thiazole}$), 11.59 (s, 1H -NH). ^{13}C NMR (100 MHz, DMSO-d_6) δ 169.35, 161.11, 159.33, 148.11, 142.95, 138.11, 135.22, 133.40, 129.41, 129.31, 129.25, 128.82, 116.08, 115.66, 114.98, 59.26, 52.01. ESI-MS: *m/z* calculated 495.07, found $[M + H]^+$ 496.04

4-(3-(4-flourophenyl)-2-(4-hydroxyphenyl)-4-oxaazitidin-1yl)-N-(thiazol-2-yl)benzenesulfonamid (8e)

Yellow solid, mp ~255ºC; Anal. Calcd for $C_{24}H_{18}FN_3O_4S_2$: C, 58.17; H, 3.66; N, 8.48; O, 12.91; S,12.94%; found C, 58.44; H, 3.70; N, 8.48; O, 12.87, S, 12.99%; IR (KBr) ($\upsilon_{max,}$ cm^{-1}); 3592 (Ar-OH) 3356 (NH), 3044 (C-H_{str} saturated hydrocarbon) 1775 (CO, β-lactam), 1640 (C=N_{str}) 1355 Asy., 1136 Syn., (O=S=O), 1510 (thiazole ring); ^{1}H NMR (400 MHz, DMSO) δ 4.09 (d, 1H, CH azi), 4.92 (d, 1H, CH azi), 7.20-8.89 (m, aromatic Protons), 7.08, 8.32 (d 1H and d 1$H_{thiazole}$), 11.62 (s, 1H -NH). ^{13}C NMR (100 MHz, DMSO-d_6) δ 169.61, 162.02, 161.35, 157.34, 144.78, 137.12, 135.86, 132.53, 129.15, 129.01, 128.98, 128.43, 120.23, 114.66, 114.25, 62.33, 54.66. ESI-MS: *m/z* calculated 495.07, found $[M + H]^+$ 496.05

4-(3-(4-flourophenyl)-2-oxo-4-(p-tolyl)azitidin-1yl)-N-(thiazol-2-yl)benzenesulfonamid (8f)

Yellow solid, mp >230ºC; Anal. Calcd for $C_{25}H_{20}FN_3O_3S_2$: C, 60.84; H, 3.85; N, 8.51; O, 9.72; S, 12.99%; found C, 60.74; H, 3.75; N, 8.48; O, 9.83, S, 12.99%; IR (KBr) ($\upsilon_{max,}$ cm^{-1}); 3354 (NH), 3034 (C-H_{str} saturated hydrocarbon) 1765 (CO, β-lactam), 1642 (C=N_{str}) 1345 Asy., 1136 Syn., (O=S=O), 1515 (thiazole ring); ^{1}H NMR (400 MHz, DMSO) δ 2.22 (s, 3H, CH_3) 4.10 (d, 1H, CH azi), 4.99 (d, 1H, CH azi), 7.15-9.12 (m, aromatic Protons), 7.02, 8.42 (d 1H and d 1$H_{thiazole}$), 12.64 (s, 1H -NH). ^{13}C NMR (100 MHz, DMSO-d_6) δ 170.12, 161.15, 161.02, 156.14, 144.18, 136.15, 135.31, 131.55, 129.42, 129.12, 129.01, 128.40, 120.55, 114.22, 114.02, 62.17, 56.21. 23.15. ESI-MS: *m/z* calculated 493.57, found $[M + H]^+$ 494.4

4-(3-(4-flourophenyl)-2-(3-nitrophenyl)-4-oxaazitidin-1yl)-N-(thiazol-2-yl)benzenesulfonamid (8g)

Yellow solid, mp 260ºC; Anal. Calcd for $C_{24}H_{17}FN_4O_5S_2$: C, 54.95; H, 3.27; N, 10.68; O, 15.25; S, 12.23%; found C, 54.84; H, 3.55; N, 10.48; O,15.37, S, 12.29%; IR (KBr) ($\upsilon_{max,}$ cm^{-1}); 3350 (NH), 3037 (C-H_{str} saturated hydrocarbon) 1770 (CO, β-lactam), 1652 (C=N_{str}) 1345 Asy., 1138 Syn., (O=S=O), 1519 (thiazole ring); ^{1}H NMR (400 MHz, DMSO) δ 4.10 (d, 1H, CH azi), 4.98 (d, 1H, CH azi), 7.25-9.02 (m, aromatic Protons), 7.08, 8.32 (d 1H and d 1$H_{thiazole}$), 11.74 (s, 1H -NH). ^{13}C

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NMR (100 MHz, DMSO-d_6) δ 169.78, 160.84, 159.23, 146.48, 143.10, 137.91, 134.24, 132.47, 129.50, 129.28, 129.01, 128.79, 116.12, 115.23, 61.99, 53.32. ESI-MS: *m/z* calculated 524.06, found $[M + H]^+$ 525.0 4

4-(3-(4-flourophenyl)-2-(2-methoxyphenyl)-4-oxaazitidin-1yl)-N-(thiazol-2-yl)benzenesulfonamid (8h)

white solid, mp 262-264ºC; Anal. Calcd for $C_{25}H_{20}FN_3O_4S_2$: C, 58.93; H, 3.73; N ,8.25; O, 12.56; S, 12.59%; found C, 58.84; H, 3.65; N, 8.40; O, 12.77, S, 12.69%; IR (KBr) ($\upsilon_{max,}$ cm^{-1}); 3354 (NH), 3036 (C-H_{str} saturated hydrocarbon) 1775 (CO, β-lactam), 1642 (C=N_{str}) 1355 Asy., 1128 Syn., (O=S=O), 1512 (thiazole ring); ^{1}H NMR (400 MHz, DMSO) δ 3.71 (s,3H Ar-OCH_3) 4.12 (d, 1H, CH azi), 4.96 (d, 1H, CH azi), 7.15-8.92 (m, aromatic Protons), 7.07, 8.32 (d 1H and d 1$H_{thiazole}$), 11.64 (s, 1H -NH). ^{13}C NMR (100 MHz, DMSO-d_6) δ 169.81, 161.36, 160.89, 156.12, 146.17, 136.28, 135.96, 131.44, 129.48, 129.21, 129.08, 128.59, 120.13, 115.55, 114.25, 62.48, 55.88, 52.56. ESI-MS: *m/z* calculated 509.09, found $[M + H]^+$ 510.08

4-(3-(4-flourophenyl)-2-(4-methoxyphenyl)-4-oxaazitidin-1yl)-N-(thiazol-2-yl)benzenesulfonamid (8i)

white solid, mp 262-264ºC; Anal. Calcd for $C_{25}H_{20}FN_3O_4S_2$: C, 58.93; H, 3.96; N ,8.25; O, 12.56; S, 12.59%; found C, 58.82; H, 3.65; N, 8.42; O, 12.77, S, 12.59%; IR (KBr) ($\upsilon_{max,}$ cm^{-1}); 3355 (NH), 3030 (C-H_{str} saturated hydrocarbon) 1777 (CO, β-lactam), 1642 (C=N_{str}) 1355 Asy., 1128 Syn., (O=S=O), 1512 (thiazole ring); ^{1}H NMR (400 MHz, DMSO) δ 3.75 (s,3H Ar-OCH_3) 4.13 (d, 1H, CH azi), 4.97 (d, 1H, CH azi), 7.15-8.92 (m, aromatic Protons), 7.08, 8.32 (d 1H and d 1$H_{thiazole}$), 11.75 (s, 1H -NH).). ^{13}C NMR (100 MHz, DMSO-d_6) δ 169.58, 160.12, 159.56, 158.41, 145.22, 136.48, 134.88, 132.15, 129.47, 129.01, 128.75, 128.57, 120.14, 116.02, 115.98, 62.63, 54.99, 52.43. ESI-MS: *m/z* calculated 509.09, found $[M + H]^+$ 510.09

4-(2,3-bis(4-flourophenyl)-4-oxaazitidin-1yl)-N-(thiazol-2-yl)benzenesulfonamid (8j)

Light Yellow solid, mp ~249ºC; Anal. Calcd for $C_{24}H_{17}F_2N_3O_3S_2$: C, 57.94; H, 3.44; N, 7.66; O,8.45; S, 12.89%; found C, 57.85; H, 3.42; N, 8.60; O, 8.52, S, 12.87%; IR (KBr) ($\upsilon_{max,}$ cm^{-1}); 3344 (NH), 3050 (C-H_{str} saturated hydrocarbon) 1772 (CO, β-lactam), 1630 (C=N_{str}) 1387 Asy., 1128 Syn., (O=S=O), 1510 (thiazole ring);^{1}H NMR (400 MHz, DMSO) δ 4.08 (d, 1H, CH azi), 4.94 (d, 1H, CH azi), 7.29-8.83 (m, aromatic Protons), 7.10, 8.31 (d 1H and d 1$H_{thiazole}$), 11.90 (s, 1H -NH). ^{13}C NMR (100 MHz, DMSO-d_6) δ 169.69, 163.14, 161.97, 161.36, 145.69, 136.05, 135.41, 129.27, 129.21, 128.23,128.14, 114.21, 114.04, 66.69, 56.92; ESI-MS: *m/z* calculated 497.07, found $[M + H]^+$ 498.2

4-(3-(4-flourophenyl)-2-oxo-4-(o-tolyl)azitidin-1yl)-N-(thiazol-2-yl)benzenesulfonamid (8k)

Yellow solid, mp >250ºC; Anal. Calcd for $C_{25}H_{20}FN_3O_3S_2$: C, 60.84; H, 4.08; N, 8.51; O, 9.72; S, 12.99%; found C, 60.74; H, 3.75; N, 8.48; O, 12.97, S, 12.99%; IR (KBr) ($\upsilon_{max,}$ cm^{-1}); 3354 (NH), 3034 (C-H_{str} saturated hydrocarbon) 1765 (CO, β-lactam), 1642 (C=N_{str}) 1345 Asy., 1136 Syn.,

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(O=S=O), 1515 (thiazole ring); ^{1}H NMR (400 MHz, DMSO) δ 2.24 (s, 3H, CH_3) 4.10 (d, 1H, CH azi), 4.99 (d, 1H, CH azi), 7.15-9.12 (m, aromatic Protons), 7.02, 8.42 (d 1H and d 1H$_{thiazole}$), 12.64 (s, 1H -NH). ^{13}C NMR (100 MHz, DMSO-d_6) δ 170.14, 160.22, 160.02, 154.23, 146.20, 134.12, 133.12, 131.98, 129.22, 129.03, 128.22, 128.01, 120.17, 114.31, 114.20, 61.93, 54.24. 22.17.ESI-MS: *m/z* calculated 493.57, found $[M + H]^+$ 494.4

4-(3-(4-flourophenyl)-2-oxo-4-(m-tolyl)azitidin-1yl)-N-(thiazol-2-yl)benzenesulfonamid (8l)

Yellow solid, mp >250ºC; Anal. Calcd for $C_{25}H_{20}FN_3O_3S_2$: C, 60.84; H, 4.08; N, 8.51; O, 9.72; S, 12.99%; found C, 60.75; H, 3.74; N, 8.49; O, 12.96, S, 12.98%; IR (KBr) ($\upsilon_{max,}$ cm^{-1}); 3352 (NH), 3033 (C-H$_{str}$ saturated hydrocarbon) 1760 (CO, β-lactam), 1641 (C=N$_{str}$) 1345 Asy., 1131 Syn., (O=S=O), 1520 (thiazole ring); ^{1}H NMR (400 MHz, DMSO) δ 2.27 (s, 3H, CH_3) 4.15 (d, 1H, CH azi), 4.96 (d, 1H, CH azi), 7.15-8.99 (m, aromatic Protons), 7.12, 8.42 (d 1H and d 1H$_{thiazole}$), 12.64 (s, 1H -NH). ^{13}C NMR (100 MHz, DMSO-d_6) δ 169.25, 162.10, 161.89, 158.11, 146.12, 135.69, 134.12, 132.15, 129.41, 129.22, 129.01, 128.13, 120.25, 115.10, 114.23, 61.87, 54.65. 23.35. ESI-MS: *m/z* calculated 493.09, found $[M + H]^+$ 494.1

4-(2-(4-dimethylamino)phenyl)-3-(4-flourophenyl)-4-oxaazitidin-1yl)-N-(thiazol-2-yl)benzenesulfonamid (8m)

Yellow solid, mp 280-284ºC; Anal. Calcd for $C_{26}H_{23}FN_4O_3S_2$: C, 59.75.; H, 4.44; N, 10.72; O, 9.18; S, 12.27%; found C, 59.74; H, 4.45; N, 10.78; O, 12.30, S, 12.29%; IR (KBr) ($\upsilon_{max,}$ cm^{-1}); 3352 (NH), 3042 (C-H$_{str}$ saturated hydrocarbon) 1775 (CO, β-lactam), 1632 (C=N$_{str}$) 1342 Asy., 1130 Syn., (O=S=O), 1520 (thiazole ring); ^{1}H NMR (400 MHz, DMSO) δ 2.94 (s, 6H, N-2(CH_3)) 4.12 (d, 1H, CH azi), 5.05 (d, 1H, CH-Ar azi), 7.12-8.82 (m, aromatic Protons), 7.04, 8.44 (d 1H and d 1H$_{thiazole}$), 11.64 (s, 1H -NH). ^{13}C NMR (100 MHz, DMSO-d_6) δ 169.36, 161.45, 160.58, 156.12, 145.35, 135.27, 134.55, 132.08, 129.52, 129.13, 129.02, 128.81, 120.25, 115.21, 115.03, 62.33, 56.14. 42.35.ESI-MS: *m/z* calculated 522.12, found $[M + H]^+$ 513.10

4-(2-(2-chlorophenyl)-3-(4-flourophenyl)-4-oxaazitidin-1yl)-N-(thiazol-2-yl)benzenesulfonamide (8n)

White solid, mp ~241ºC; Anal. Calcd for $C_{24}H_{17}ClFN_3O_3S_2$: C, 56.08; H, 3.33; N, 8.18; O, 9.34; S, 12.48%; found C, 56.14; H, 3.50; N, 8.13; O, 9.31, S, 12.48%; IR (KBr) ($\upsilon_{max,}$ cm^{-1}); 3350 (NH), 3050 (C-H$_{str}$ saturated hydrocarbon) 1776 (CO, β-lactam), 1632 (C=N$_{str}$) 1388 Asy., 1128 Syn., (O=S=O), 1512 (thiazole ring); ^{1}H NMR (400 MHz, DMSO) δ 4.02 (d, 1H, CH azi), 4.90 (d, 1H, CH azi), 7.21-8.98 (m, aromatic Protons), 7.07, 8.40 (d 1H and d 1H$_{thiazole}$), 11.56 (s, 1H -NH). ^{13}C NMR (100 MHz, DMSO-d_6) δ 169.83, 161.21, 161.01, 146.79, 136.14, 135.40, 133.12, 129.21, 129.14, 128.33, 128.17, 120.12, 115.14, 115.06, 114.10, 61.99, 55.92. ESI-MS: *m/z* calculated 513.04, found $[M + H]^+$ 514.1

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4-(2-(2-ethylphenyl)-3-(4-flourophenyl)-4-oxaazitidin-1yl)-N-(thiazol-2-yl)benzenesulfonamide (8o)

White solid, mp 277-281ºC; Anal. Calcd for $C_{26}H_{22}FN_3O_3S_2$: C, 61.52; H, 4.37; N, 8.28; O, 9.46; S, 12.63%; found C, 61.54; H, 4.50; N, 8.13; O, 9.39, S, 12.55%; IR (KBr) ($\upsilon_{max,}$ cm^{-1}); 3357 (NH), 3052 (C-H_{str} saturated hydrocarbon) 1779 (CO, β-lactam), 1631 (C=N_{str}) 1388 Asy., 1120 Syn., (O=S=O), 1510 (thiazole ring); ^{1}H NMR (400 MHz, DMSO) δ 1.8 (t, 3H, CH_3), 2.47 (m, 3H, CH_3) 4.10 (d, 1H, CH azi), 4.85 (d, 1H, CH azi), 7.21-8.98 (m, aromatic Protons), 7.10, 8.40 (d 1H and d 1$H_{thiazole}$), 11.56 (s, 1H -NH). ^{13}C NMR (100 MHz, DMSO-d_6) δ 169.35, 161.15, 161.02, 156.42, 144.20, 136.12, 134.02, 132.27, 129.50, 129.22, 129.12, 128.86, 120.30, 115.12, 114.93, 62.14, 55.25. 29.35, 15.23. ESI-MS: *m/z* calculated 507.11, found $[M + H]^+$ 508.15

2.2 Biological Activity

Determination of antibacterial activity (zone inhibition and MIC)

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

This activity is done by in vitro agar well diffusion method [31]. 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 microdilution 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 the actively bacterial cell which were the nutrient broth. This nutrient maintaining inoculated for 37 ºC for 24 hours the spectrophotometer was used for monitoring and also visually. The minimum concentration or maximum dilution which was required to kill bacterial growth regard as minimum Inhibitory concentration (MIC). MIC values are shown in **table-3**

Determination of antifungal activity (zone inhibition and MIC)

Antibacterial activities of synthesized new of series 4-(3-(2-flourophenyl)-2-oxo-4-(substituted) arylazitidin-1-yl-N-(thiazol-2-yl)benzenesulfonamide **8a-8o** were screened for their antifungal activity against *Aspergillus niger* and *Candida albicans* in DMF, this activity is done by in vitro agar well diffusion method. Pepton (1g) D-glucose (4g) and agar (2g) were used to prepared Saubourauds agar media and maintained 5.7 pH by adding 100 ml of distilling water and make a suspension for fungal strain. However The making suspension of corresponding species, the fungal

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transferred into 3ml salin and make a disc by adding 20 ml of fungal media for each Petri dish. and the plate was dried by using incubator at 37 ºC for 1 day. A prepared control was allowed for three to four day at 37 ºC and the fungal inhibitions zone was measured was the microorganism inhibited after the incubation was done and were compared with standard voriconazole shown in **table-4.** The minimum inhibitory concentration (MIC) of all synthesized compounds were tested by broth microdilution method with against standard fungal strains *Aspergillus niger* and *Candida albicans* were dilutions to make desire concentration of compounds. The serially two-fold dilutions of tested compounds and control inoculated with an active cell which was the nutrient broth. These nutrient cultures were maintaining inoculated for 35 ºC for 48 hours. and spectrophotometer was used for monitoring and also visually. The minimum concentration or maximum dilution which was required to kill the inoculums growth regard as minimum Inhibitory concentration (MIC). MIC values are shown in **table-5**

3. RESULTS AND DISCUSSION

In these present work, synthesis targeted sulfonamide containing 2-azetidinone compounds **8a-8j** were customized with initially prepared potent intermediate Schiff base **6a-6o** via the reaction between sulfathaizole (**STH) 4** and different aromatic aldehydes **5a-5o** with good yield. These Schiff base **6a-6o** auxiliary utilized for production of 4-(3-(2-flourophenyl)-2-oxo-4-(substituted)arylazitidin -1-yl-N-(thiazol-2-yl)benzenesulfonamide **8a-8o** were established by physical properties like melting 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 ~1770-1775 cm^{-1} for CO, β-lactam, strong asymmetric starching vibrations band for (O=S=O) within the range 1340-1387 cm^{-1} and second symmetric starching vibrations within the range of 1123-1188 cm^{-1}. ^{1}H NMR (400 MHz, DMSO) for all compounds showed doublet for two CH β-lactam of at δ 4.05-4.15 and δ 4.80-4.97

Table 2: Antibacterial activity of 8*a-8o* compounds

Derivatives	***E.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.)
a	28	1.167	22	0.917	24	1.000	24	1.000
b	19	0.791	20	0.833	19	0.791	16	0.667
c	16	0.667	15	0.625	15	0.625	15	0.625

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d	20	0.833	23	0.958	20	0.833	19	0.791
e	19	0.791	23	0.958	19	1.125	27	1.125
f	36	1.500	30	1.250	26	1.083	27	1.125
g	24	1.000	24	1.000	26	1.083	19	0.791
h	30	1.250	30	1.250	24	1.000	36	1.500
i	30	1.250	20	0.833	16	0.667	27	1.125
j	16	0.667	16	0.667	15	0.625	19	1.125
k	30	1.208	27	1.125	30	1.250	24	1.000
l	22	0.917	17	0.708	29	1.208	15	0.625
m	36	1.500	30	1.250	30	1.250	36	1.500
n	16	0.667	27	1.125	15	0.625	19	0.791
o	30	1.250	27	1.125	25	1.041	24	1.000
Std	24	-	24	-	24	-	24	-

The concentration of standard drug streptomycin was 1000 µg/ml. All synthesized compounds **8a-8o** displayed very good, good and moderately active against Gram-positive and gram-negative bacteria. The significant results are shown for **8f, 8h, 8i, 8k, 8m** and **8o** scaffold shown very good increased antibacterial activity compared to streptomycin while compounds **8b, 8c, 8j** and **8n** shown leaser active antibacterial compared to standard, shown in **table-2** and other compound exist moderate active. However, the antibacterial activity of 4-(3-(2-flourophenyl)-2-oxo-4-arylazitidin -1-yl-N-(thiazol-2-yl)benzenesulfonamide could be considerable.

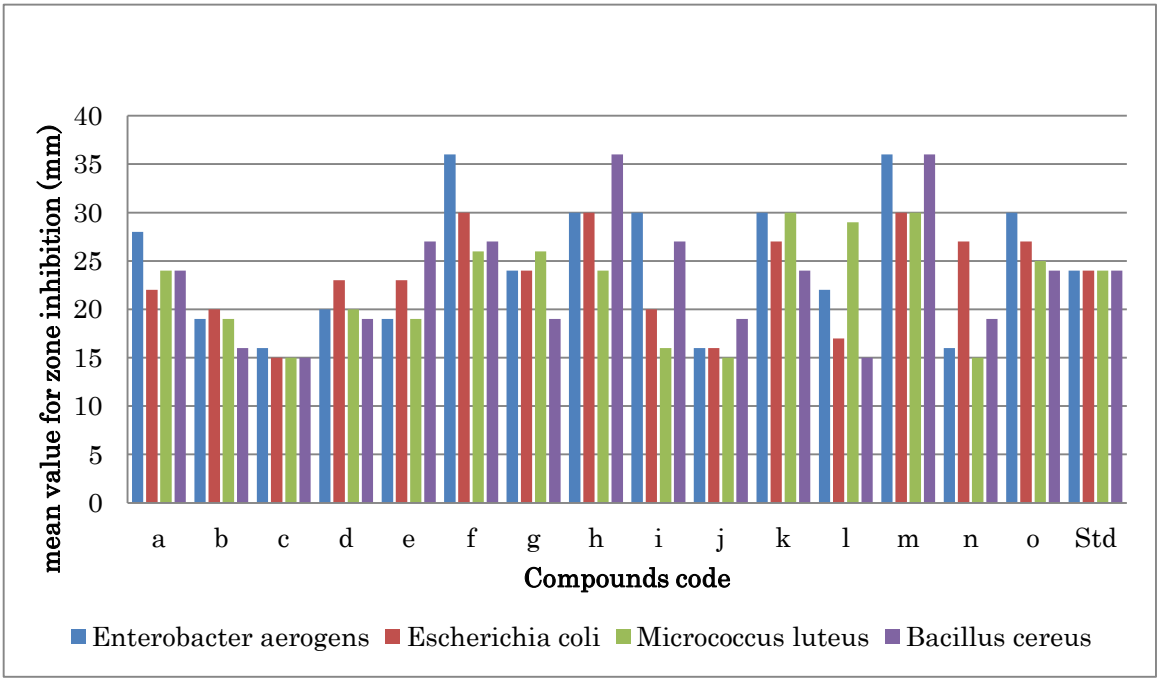

Figure 2: zone inhibition Antibacterial activity of compounds 8a-8o

For all synthesized compounds **8a**, **8f, 8m** and **8o** scaffold showed very good MIC values near to

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streptomycin shown in **table-3** and other compound showed good, moderate and leaser MIC values. However, the compound **8m** showed very good zone inhibition activity as well as in MIC for all bacterial strains.

Table 3: MIC results of 8*a-8o* 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)
a	25	50	50	50
b	100	200	200	200
c	200	400	400	200
d	400	100	200	200
e	200	100	200	200
f	12.5	25	25	50
g	100	100	200	100
h	100	50	100	100
i	100	200	200	100
j	400	-	-	400
k	100	100	100	50
l	100	200	100	200
m	12.5	12.5	25	12.5
n	200	100	100	400
o	100	100	100	50
Std	6.25	6.25	3.125	6.25

The antifungal screening results for synthesized sulfonamides **8a-8o** indicate that compounds showed good, moderate to average active against *Aspergillus nigar* and *Candida albicans*, The significant results are shown for **8f, 8m** and **8o** scaffold showed more potent compared to standard while other compounds showed average active antifungal compared to standard, shown in **table-4** However, the antifungal activity of 4-(3-(2-flourophenyl)-2-oxo-4-arylazitidin-1-yl-N- (thiazol-2-yl)benzenesulfonamide could be considerable.

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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.)
a	21	0.75	22	0.786
b	22	0.786	20	0.714
c	18	0.643	16	0.666
d	22	0.786	21	0.75
e	24	0.857	23	0.821
f	30	1.071	31	1.291
g	22	0.786	20	0.714
h	25	0.893	26	0.929
i	20	0.714	21	0.75
j	15	0.536	17	0.607
k	27	0.964	18	0.643
l	27	0.964	25	0.893
m	34	1.214	32	1.333
n	25	0.893	21	0.75
o	29	1.036	25	1.041
Std	28	-	24	-

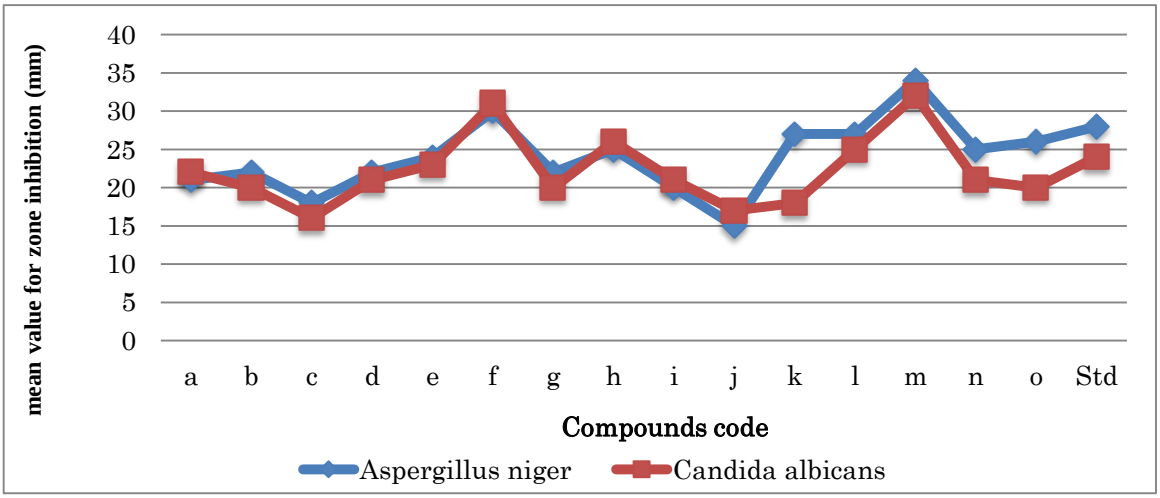

Figure 3: zone inhibition Antifungal activity of compounds 8a-8o

Minimum inhibition concentration (MIC) of antifungal For all synthesized compounds the **8f 8m** and **8o** scaffold showed moderate MIC values compared to standard drug voriconazole showed in **table-4** and other compound showed average MIC values. However, the compound **8m** showed very

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good zone inhibition activity as well as in MIC for all fungal strains.

Table 5: MIC results of compounds 8a-8o

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

4. CONCLUSION

In this Current work a series of 4-(3-(2-flourophenyl)-2-oxo-4-(substituted)arylazitidin-1-yl -N-(thiazol-2-yl)benzenesulfonamide **8a-8o** was synthesized and tested for antibacterial activity against gram +ve and gram -ve strains and antifungal activity. The significant results shown for compounds **8f, 8h, 8i, 8k, 8m** and **8o** scaffold showed very good increased antibacterial activity as well as in MIC, compound **8m** exhibited outstanding zone inhibition as Antibacterial, While compounds **8f, 8m** and **8o** scaffold showed more potent compared to standard against *Aspergillus nigar* and *Candida albicans* as antifungal agents.

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CONFLICT OF INTEREST

The author has declared that they have no conflict of interest.

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REFERENCES

1. Nasr T, Bondock S, Eid S. Design, synthesis, antimicrobial evaluation and molecular docking studies of some new thiophene, pyrazole and pyridone derivatives bearing sulfisoxazole moiety. Eur J Med Chem. 2014;84:491–504.
2. Krátký M, Vin J, Volková M, Buchta V. European Journal of Medicinal Chemistry Antimicrobial activity of sulfonamides containing 5-chloro-2- hydroxybenzaldehyde and 5-chloro-2-hydroxybenzoic acid scaffold. 2012;50.
3. Nasr T, Bondock S, Eid S. Design, synthesis, antimicrobial evaluation and molecular docking studies of some new 2,3-dihydro thiazoles and 4-thiazolidinones containing sulfisoxazole. J Enzyme Inhib Med Chem. 2016;31(2):236–46.
4. Wang XL, Wan K, Zhou CH. Synthesis of novel sulfanilamide-derived 1,2,3-triazoles and their evaluation for antibacterial and antifungal activities. Eur J Med Chem [Internet]. 2010;45(10):4631–9.
5. Variya HH, Panchal V, Patel GR. Synthesis and characterization of 4- ((5-bromo-1 H -pyrazolo [3 , 4- b] pyridin-3- yl) amino) - N - (substituted) benzenesulfonamide as Antibacterial , and Antioxidant. 2019;8:1–10.
6. Supuran CT. Carbonic anhydrases: Novel therapeutic applications for inhibitors and activators. Nat Rev Drug Discov. 2008;7(2):168–81.
7. Garaj V, Puccetti L, Fasolis G, Winum J-Y, Montero J-L, Scozzafava A, et al. Carbonic anhydrase inhibitors: synthesis and inhibition of cytosolic/tumor-associated carbonic anhydrase isozymes I, II, and IX with sulfonamides incorporating 1, 2, 4-triazine moieties. Bioorg Med Chem Lett. 2004;14(21):5427–33.
8. Bunyapraphatsara N, Yongchaiyudha S, Rungpitarangsi V, Chokechaijaroenporn O. Antidiabetic activity of Aloe vera L. juice II. Clinical trial in diabetes mellitus patients in combination with glibenclamide. Phytomedicine. 1996;3(3):245–8.
9. Ghorab MM, Alsaid MS, Al-Dosari MS, Nissan YM, Al-Mishari AA. Novel chloroquinoline derivatives incorporating biologically active benzenesulfonamide moiety: Synthesis, cytotoxic activity and molecular docking. Chem Cent J. 2016;10(1):1–13.
10. Thaisrivongs S, Skulnick HI, Turner SR, Strohbach JW, Tommasi RA, Johnson PD, et al. Structure-based design of HIV protease inhibitors: Sulfonamide- containing 5,6-dihydro-4-hydroxy-2-pyrones as non-peptidic inhibitors. J Med Chem. 1996;39(22):4349–53.
11. Zhao Z, Wolkenberg SE, Lu M, Munshi V, Moyer G, Feng M, et al. Novel indole-3-sulfonamides as potent HIV non-nucleoside reverse transcriptase inhibitors (NNRTIs). Bioorganic Med Chem Lett. 2008;18(2):554–9.
12. Unsal-Tan O, Ozadali K, Piskin K, Balkan A. Molecular modeling, synthesis and screening of some new 4-thiazolidinone derivatives with promising selective COX-2 inhibitory activity. Eur

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J Med Chem. 2012;57:59–64.

13. Schultz LJ, Steketee RW, Macheso A, Kazembe P, Chitsulo L, Wirima JJ. The efficacy of antimalarial regimens containing sulfadoxine-pyrimethamine and/or chloroquine in preventing peripheral and placental Plasmodium falciparum infection among pregnant women in Malawi. Am J Trop Med Hyg. 1994;51(5):515–22.
14. Shenai BR, Lee BJ, Alvarez-Hernandez A, Chong PY, Emal CD, Neitz RJ, et al. Structure-activity relationships for inhibition of cysteine protease activity and development of Plasmodium falciparum by peptidyl vinyl sulfones. Antimicrob Agents Chemother. 2003;47(1):154–60.
15. Loubatières A. The hypoglycemic sulfonamides: history and development of the problem from 1942 to 1955. Ann N Y Acad Sci. 1957;71(1):4–11.
16. Harford CG, Smith MR, Wood Jr WB. Sulfonamide chemotherapy of combined infection with influenza virus and bacteria. J Exp Med. 1946;83(6):505.
17. Saeedi M, Goli F, Mahdavi M, Dehghan G. Synthesis and Biological Investigation of some Novel Sulfonamide and Amide Derivatives Containing Coumarin Moieties. 2014;13(January 2013):881–92.
18. Öztas N. Full Paper Synthesis, Antioxidant, and Antiacetylcholinesterase Activities of Sulfonamide Derivatives of Dopamine-Related Compounds. 2013;783–92.
19. Behbehani GR, Sadr MH, Nabipur H, Barzegar L. A Comparative Study on the Interaction of Sulfonamide and Nanosulfonamide with Human Serum Albumin. 2013;2013.
20. Salunke SB, Azad AK, Kapuriya NP, Balada-llasat J, Pancholi P, Schlesinger LS, et al. Bioorganic & Medicinal Chemistry Design and synthesis of novel anti-tuberculosis agents from the celecoxib pharmacophore. Bioorg Med Chem. 2015;23(9):1935–43.
21. Macingwana L. Investigation of the activity of sulfonamide anti-bacterial drugs in Mycobacterium tuberculosis and the role of oxidative stress on the efficacy of these drugs. 2014;(April).
22. Zohar Y, Einav M, Chipman DM, Barak Z. Acetohydroxyacid synthase from Mycobacterium avium and its inhibition by sulfonylureas and imidazolinones. 2003;1649:97–105.
23. Solankee A, Tailor R. Rapid and efficient synthesis of newer heterocyclic 2-azetidinone and 5-benzylidine-4-oxo-thiazolidine compounds and their pharmacological studies. Chem Int . 2017;3(2):123–34.
24. Kumar A, Rajput CS, Bhati SK. Synthesis of 3-[4′-(p-chlorophenyl)-thiazol-2′-yl]-2-[(substitutedazetidinone/thiazolidinone)-aminomethyl]-6-bromoquinazolin-4-ones as anti-inflammatory agent. Bioorg Med Chem. 2007;15(8):3089–96.
25. Rajasekaran A, Periasamy M, Venkatesan S. Synthesis, characterization and biological activity of some novel azetidinones. J Dev Biol Tissue Eng. 2010;2(1):5–13.

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26. Noolvi M, Agrawal S, Patel H, Badiger A, Gaba M, Zambre A. Synthesis, the antimicrobial and cytotoxic activity of novel azetidine-2-one derivatives of 1H-benzimidazole. Arab J Chem. 2014;7(2):219–26.
27. Singh P, Sachdeva S, Raj R, Kumar V, Mahajan MP, Nasser S, et al. Antiplasmodial and cytotoxicity evaluation of 3-functionalized 2-azetidinone derivatives. Bioorg Med Chem Lett. 2011;21(15):4561–3.
28. Subudhi BB, Ghosh G. Synthesis and antibacterial activity of some heterocyclic derivatives of sulfanilamide. Bull Chem Soc Ethiop. 2012;26(3):455–60.
29. Bhat IK, Mishra SK, James JP, Shastry CS. Antimicrobial studies of synthesized azetidinone derivatives from sulfamethoxazole moiety. J Chem Pharm Res. 2011;3(3):114–8.
30. Guanti G, Riva R, Cascio G, Manghisi E, Morandotti G, Satta G, et al. A new class of cis-monobactam derivatives bearing a sulfamoyloxymethyl or an N-alkylsulfamoyloxymethyl group at position 4: Synthesis and antibacterial activity. Farm. 1998;53(3):173–80.
31. Bhoi MN, Borad MA, Pithawala EA, Patel HD. Novel benzothiazole containing 4 H -pyrimido [2, 1- b] benzothiazoles derivatives : One pot, solvent-free microwave assisted synthesis and their biological evaluation. Arab J Chem. 2016.

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