CHAPTER 4
SYNTHESIS, CHARACTERIZATION AND BIOLOGICAL STUDIES
OF SOME NEW 1,2,4-TRIAZOLE DERIVATIVES
4.1 Introduction

In the past decades, the problem of multi-drug resistant microorganisms has reached on alarming level around the world. For the treatment of microbial infections, the synthesis of new antiinfectious compounds has become an urgent need. According to the literature reports, triazole and its derivatives play a significant role in the therapy of diseases caused by microbial infections. The development of chemistry of 1,2,4-triazoles was triggered by Bladin\(^1\) in 1885. He synthesized the first 1,2,4-triazole (Fig. 4.1), represented by the cyclic structure and named the unknown parent compound as ‘triazole’.

\[
\begin{array}{c}
\text{Fig. 4.1: Structure of 1,2,4-Triazole}
\end{array}
\]

Triazoles are heterocyclic compounds featuring five member rings of two carbon atoms and three nitrogen atoms as part of the aromatic five-member ring (Fig. 4.2). Triazole refers either one of a pair of isomeric chemical compounds with molecular formula C\(_2\)H\(_3\)N\(_3\).

\[
\begin{array}{c}
\text{Fig: 4.2: Isomeric structure of 1,2,4-triazole}
\end{array}
\]

The chemistry of 1,2,4-triazoles and their fused structures with other heterocyclic systems has received considerable attention owing to their synthetic and effective
biological importance during the last two decades. In particular, triazoles and their heterocyclic derivatives have been reported to be used as drugs and to have considerable activities like fungicidal, antibacterial, anthelmintic, antiviral, anticancer, antitubercular, anticonvulsant, antifungal and plant growth regulating properties. Therefore it was thought worthwhile to synthesize substituted 1,2,4-triazoles derivatives.

4.1.1 Synthetic approaches and pharmacological activity of 1,2,4-triazole

Kalluraya et al, (1996) reported the synthesis and biological activities of 3-substituted-anilinomethyl-4-(5-substituted-2-furfurylidene)amino-1,2,4-triazole-5-thiones and their Mannich bases (249) (Fig. 4.3). Some of the synthesized compounds showed very good activity.

\[
\begin{align*}
R_1 & \quad R_2 \\
N & \quad R \\
N & \quad X \\
S & \quad Ar \\
HN & \quad N
\end{align*}
\]

\(Ar = 4-CH_3-C_6H_4, 2-OCH_3-C_6H_4; R = 4-Cl, 4-NO_2; X = O, S, N;\)

\(R_1R_2 = \text{morpholine, piperidine, diphenylamine.}\)

**Fig. 4.3:** 3-(substituted anilino methyl)-4, 5-(substituted-2-furfurylidene) amono-1,2,4-triazole-5-thione derivative

Holla et al, (2000) also reported the synthesis of Schiff bases starting from 3-substituted-4-amino-5-mercapto-1,2,4-triazoles (250) (Fig. 4.4). Some of the selected compounds were tested for their antibacterial, antifungal and herbicidal activities.
Where $R =$ Ph, 4-Chlorophenoxyethyl, 2-Chlorophenoxyethyl, 4-Chloro-3-methyl-phenoxyethyl, 2, 4-Dichlorophenoxyethyl, 3,4-Dimethyl-phenoxyethyl

**Fig. 4.4:** Mannich bases carrying 2, 4-dichlorophenylfurural moiety

Synthesis of some new pyridine substituted 1,2,4-Triazole (255) were attempted by Zamani et al, (2003)$^{14}$ by the intramolecular cyclization of 1,4-disubstituted thiosemicarbazide as shown in the **Scheme-4.1**.

**Scheme-4.1:** Pyridine containing 1,2,4-triazoles

Xu et al, (2004)$^{15}$ synthesized triazoles containing 1, 3-dioxolane rings (256) (Fig 4.5) were synthesized. The results of preliminary biological tests show that all of these compounds possess some fungicidal and plant growth regulant activities.
Fig. 4.5: Triazole compounds containing 1, 3-dioxolane rings

Abdel-Aziz *et al.*, (2007)\(^{16}\) synthesized a series of 1,2,4-Traizole containing Thiazolo [3, 2-a] benzimidazole Moiety (257) starting from 3-methylthiazolo [3, 2-a] benzimidazole-2-carboxylic acid ethyl ester (Fig 4.6).

Fig. 4.6: Thiazolo [3, 2-a] benzimidazole containing 1,2,4-traizole moiety

Mohammad *et al.*, (2008)\(^{17}\) synthesized 1,2,4-triazole derivatives of 4-hydroxyphenyl aceticacid (258) and evaluated for their anti-inflammatory activity by carrageenan induced rat paw edema method (Fig 4.7). The compounds, which showed good anti-inflammatory activity, were screened for their ulcerogenic and lipid peroxidation activities.
Where \( R = \) Phenyl, 2-Chlorophenyl, 4-Chlorophenyl, 4-Bromophenyl, 4-Fluorophenyl, 2-Methylphenyl, 4-Methyl phenyl, n-Butyl.

**Fig. 4.7:** 4-Hydroxyphenyl substituted 1,2,4-Triazole-3-thiol derivatives

Banday *et al*, (2009)\(^{18}\) synthesized a series of 4-phenyl-1,2,4-triazole-3-thiol (262). These compounds have been tested for their antibacterial activity against *Escherichia coli*, *Enterobacter aerogenes*, *Staphylococcus aureus* and *Salmonella typhi* by cup-plate method (Scheme-4.2).

![Scheme 4.2](image)

Where \( R = CH_3(CH_2)_7CH_2=CH_2(CH_2)_7 \)

\( CH_3(CH_2)_5CH(OH)CH_2CH_2=C(CH_2)_7 \)

**Scheme-4.2:** Fatty acids substituted 1,2,4-triazoles

Isloor *et al*, (2009)\(^{19}\) synthesized pyrazole containing 1,2,4-triazole derivatives (263). All the synthesized compounds (Fig 4.8) were screened for their antibacterial and antifungal activities by MIC method. It has found that among the tested compounds p-chloro substituted compound exhibit maximum inhibition.
Where $R = CH_3, C_3H_7, C_6H_5$

$R_1=CH_3, C_6H_5, p-ClC_6H_5, p-OCH_3C_6H_4$

$NR_1R_2=N$-methyl piperazine

**Fig. 4.8:** Mannich bases derived from Pyrazoles and 1,2,4-triazoles.

Murti *et al*, (2011) synthesized some new substituted 1,2,4-triazoles derivative (267) and evaluated their antimicrobial activity (*Scheme-4.3*).

Where $Ar = 4'$-Chlorophenyl, 3'-Hydroxyphenyl, 4'-Methoxyphenyl, 2'-Nitrophenyl 4'-Dimethylaminophenyl

**Scheme-4.3:** Pyridine containing Schiff base derived 1,2,4-triazoles

Faidallah *et al*, (2011) synthesized 3, 5-difluoromethyl substituted 1,2,4-triazole derivatives (271) and evaluated their antidiabetic and antimicrobial studies (*Scheme-4.4*).
Scheme-4.4: 3,5-di (Trifluoromethyl)-1,2,4-triazolesulfonylurea and thiourea derivatives

Zoumpoulakis et al, (2012)\textsuperscript{22} synthesized a series of sulphonamide substituted 1,2,4-traizole derivatives (274) and evaluated its antifungal studies (Scheme-4.5).

Scheme-4.5: Sulfonamide containing 1,2,4-triazoles

Pattan et al, (2012)\textsuperscript{23} synthesized a series of 1,2,4-triazole derivatives (276, 277) and studied its anti-tubercular and anti-inflammatory activity (Scheme-4.6) when compared with standard drug Norfloxacin, Griseofulvin, Streptomycin, and Diclofenac sodium respectively.
Fluorinated 3,5-disubstituted-4H-1,2,4-triazol-4-amines (Fig 4.9) was synthesized by Min Chen et al, (2012).²⁴ The preliminary bioassay results showed that these compounds exhibited certain fungicidal activities at the concentration of 100 μg/mL (278-280).

Fig. 4.9: Fluorine containing 3, 5-disubstituted-4H-1,2,4-triazol-4-amines.

A new class of sulfone linked bis heterocycles arylaminosulfonylmethyl 1,2,4-triazoles (281) (Fig: 4.10) were prepared and tested for antimicrobial activity and cytotoxicity by Muralikrishna et al, (2012).²⁵
Where $R=\text{H, Cl, Me}$

**Fig. 4.10:** Sulfone linked 1,2,4-triazole derivative

Synthesis of novel 1, 3, 5-trisubstituted-1,2,4-triazoles were prepared recently by Dalloul *et al.*, (2012)\(^{26}\) using nitrilimines by the 1, 3-dipolar cycloaddition reaction of C-phenyl-amino carbonyl-N-aryl nitritilimines with guanidine derivatives (**Scheme-4.7**) (284). Some of the synthesized compounds showed very good antimicrobial activity.

**Scheme-4.7:** Novel 1,3,5-trisubstituted 1,2,4-triazoles.

Recently Plech *et al.*, (2013)\(^{27}\) synthesized some 4-alkyl-1,2,4-triazoles and studied its anticonvulsant activity. Chromatographic tests showed that lack of anticonvulsant effect of two derivatives (287) with long alkyl chains at N-4 position of the 1,2,4-triazole ring was due to the inability to cross the blood–brain barrier (**Scheme-4.8**).
4.2. Results and discussion

The key intermediate in the present synthetic approach is 3, 4, 5-trimethoxyphenyl benzoic acid hydrazide (290) and was synthesized from the commercially available 3, 4, 5-trimethoxyphenyl benzoic acid (288) through esterification, and hydrazidation as per the literature.\(^{28,29}\) The compound (290) was then converted into (291) by reaction with different aliphatic and aromatic isothiocayante in ethanol. Cyclization of this intermediate with sodium hydroxide under reflux condition afford different 4-(substituted)-5-(3,4,5-trimethoxyphenyl)-4H-1,2,4-triazole-3-thiol derivatives 292 (a-n). Subsequently these thiol derivatives treated with 2,6-difluoro benzyl bromide to afford 3-(2,6-Difluoro-benzyl sulfanyl)-4-(substituted)-5-(3,4,5-trimethoxyphenyl)-4H-[1,2,4] triazole derivative 293 (a-n) (Scheme-4.9).
Scheme-4.9: Synthetic route for the title compounds 292 (a-l) and 293 (a-l)

Table 4.1: List of compounds synthesized from the scheme-4.9

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<th>293(a-n)</th>
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All the reactions were monitored by TLC. Melting point was determined on a Buchi Melting point B-545 apparatus. The IR spectra (in KBr pellets) were recorded on a Nicolet 6700 FT-IR spectrometry. $^1$H NMR spectra were recorded on Bruker (300 and 400MHz) spectrometer instruments, in CDCl$_3$ or DMSO solvent. Mass spectra were recorded on LCMS Agilent 1100 series using 0.1% aqueous TFA in acetonitrile system. Elemental analysis was performed on thermo Finningan Flash EA 1112 CHN analyzer. Chromatography was performed on silica gel (60-120 mesh) for compound purification.

Formation of 3-((2, 6-Difluoro-benzyl sulfanyl)-4-(substituted)-5-(3, 4, 5-trimethoxy phenyl)-4H-[1,2,4] triazole derivative was confirmed by recording their IR, $^1$H NMR and $^{13}$C NMR. Elemental analysis and mass spectral data. IR spectrum of (293a) shows absorption at 2935 cm$^{-1}$ which is due to aromatic stretching, an absorption band at 1586 cm$^{-1}$ is due to C=\(\text{N}\) group, band at 1470 cm$^{-1}$ is stretching of phenyl rings and absorption band observed at 1030 cm$^{-1}$ is due to C-F group. The $^1$H NMR of (293a) shows multiplet in the region of $\delta$ 7.65-7.53 due to phenyl ring protons, singlet 2H in the region of $\delta$ 6.64 show for trimethoxy phenyl protons, Similarly singlet at $\delta$ 4.3 shows 2H for –S benzyl protons and singlet at $\delta$ 3.69 and 3.64 shows 9 protons for trimethoxy group. The mass spectrum of (293a) showed molecular ion peak at m/z 504, which is agreement with the molecular formula C$_{24}$H$_{20}$ClF$_2$N$_3$O$_3$S. Similarly the spectral values for all the compounds and C, H, N analyses are given in the experimental part. Also single
crystal X-ray analysis of (293a) further confirmed the structure of synthesized compounds.\textsuperscript{30}

4.3 Synthesis

4.3.1 General procedure

4.3.1.1 Preparation of Methyl 3, 4, 5-trimethoxybenzoate (289)

To a mixture of 3, 4, 5-trimethoxy benzoic acid (288) (20 g, 0.095 mol) in methanol (200 mL) was added conc. sulphuric acid (2 mL) and refluxed for 5 h. The reaction was monitored through thin layer chromatography. The reaction mixture was concentrated and the solid separated was filtered, washed with water and recrystallized with ethanol to give title compound (289) as white crystalline solid. (20 g, 93%) Mp. 130-145\textdegree C.

4.3.1.2 Preparation of 3, 4, 5-trimethoxybenzohydrazide (290)

A mixture of methyl 3, 4, 5-trimethoxybenzoate (289) (20 g, 0.095 mol) and hydrazine hydrate (9 mL, 0.18 mol) in ethanol (200 mL) was heated to reflux for 8 h. The reaction was monitored through thin layer chromatography. The reaction mixture was concentrated and allowed to cool. The solid product obtained was filtered, dried under vacuum, washed with water and recrystallized using ethanol to give (290) as white crystals.

4.3.1.3 General procedure for preparation of N-substituted-2-[(3, 4, 5 trimethoxy phenyl) carbonyl] hydrazinecarbothioamide 291 (a-n)

A mixture of 3, 4, 5-trimethoxybenzohydrazide (290) (0.0088 mol) and different aromatic isothiocyanate (R-NCS) (0.0096 mol) was refluxed with absolute ethanol (10 vol) for 2 h. The progress of the reaction was monitored through thin layer chromatography. The excess of solvent was distilled off and solid product obtained was
filtered, washed with cold ethanol, dried under vacuum to afford title compound 291(a-l) as white solid. (80-90%).

4.3.1.4 General procedure for preparation of 4-(N-substituted)-5- (3, 4, 5-trimethoxy phenyl) -4H-1,2,4-triazole-3-thiol 292(a-l)

A mixture of N-substituted-2-[(3, 4, 5-trimethoxyphenyl) carbonyl] hydrazine carbothio amide (0.005 mol) in 10 % NaOH (10 vol) was heated at 100 °C for 18h. Progress in the reaction was monitored through thin layer chromatography. After the completion of reaction, the reaction mixture was cooled to RT, acidified with conc. HCl to pH~4, the solid separated out was filtered and dried. The solid obtained was purified by column chromatography using silica gel 60-120 mesh size and petroleum ether: ethyl acetate as eluent to afford title compound 292 (a-l) as pale yellow solid.

4.3.1.5 General procedure for preparation of 3-(2, 6-Difluoro-benzyl sulfanyl)-4-(Substituted)-5-(3, 4, 5-trimethoxy phenyl)-4H-[1,2,4] triazole derivative 292 (a-l)

To a solution of 4-(N-substituted)-5- (3,4,5-trimethoxy phenyl) -4H-1,2,4-triazole-3-thiol 292 (a-l) (0.0039 mol) in dry acetonitrile (20 mL) was added potassium carbonate (0.0078 mol) followed by 2,6-difluorobenzyl bromide (0.0042 mol) at RT. After the addition, the reaction mixture was stirred at RT for 6h. Reaction mixture was monitored by TLC. After the completion, the reaction mixture was concentrated and purified by column chromatography using pet ether, ethyl acetate as an eluent to afford title compound as white solid. 292 (a-l) (80-85 %).
4.4 Characterization

4.4.1 Experimental data

4.4.1.1 3, 4, 5-trimethoxybenzohydrazide (290)

(18 g, 90%). \(^1\)H-NMR (DMSO-d\(_6\)): \(\delta\) 9.70 (s, 1H, -NH proton), 7.14 (s, 2H, Trimethoxy phenyl ring-H), 4.45 (s, 2H, -NH2 proton), 3.79 (s, 6H), 3.67 (s, 3H). IR (KBr) cm\(^{-1}\): -NH2, NH (3185), 3097, 2993 (Aryl-CH), C =C (phenyl-1552), C-O (1468); MS: m/z = 227 (M\(^+\)).

4.4.1.2 4-(3-Chloro phenyl)-5-(3, 4, 5-trimethoxyphenyl)-4H-1,2,4-triazole-3-thiol (292a)

Yield 57%; IR (KBr) cm\(^{-1}\): 3097, 2993 (Aryl-CH), C=N (1595-stretch of Triazole ring), -NH (3175), C=C (phenyl-1565), C-O (1400); MS: m/z = 378(M\(^+\)); \(^1\)H-NMR (DMSO-d\(_6\)): \(\delta\) 14.16 (s, 1H, Triazole -NH), 7.66 (s, 1H), 7.60-7.52 (m, 2H), 7.36-7.35 (d, 1H, \(J = 7.68\) Hz), 6.61 (s, 2H, Trimethoxy phenyl ring-H), 3.63 (s, 3H), 3.56 (s, 6H). \(^{13}\)C NMR(DMSO-d\(_6\))168, 153, 150, 139, 136, 133, 131, 130, 129, 128, 121, 106, 60, 55. Anal. Calcd. (Found) for C\(_{17}\)H\(_{16}\)ClN\(_3\)O\(_3\)S: C, 54.04 (54.07); H, 4.27 (4.32); N, 11.12 (11.12)

4.4.1.3 3-{(3,4,5-Trimethoxyphenyl)-5-mercapto-[1,2,4]triazol-4-ylf-phenyl-methanone: (292b)

Yield 78.9 %; IR (KBr) cm\(^{-1}\): 3084, 2922 (Aryl-CH), C=N (1600-stretch of Triazole ring), -NH (3150), C=C (phenyl-1515), C-O (1250); MS: m/z = 372 (M\(^+\)); \(^1\)H-NMR (DMSO-d\(_6\)): \(\delta\) 14.12 (s, 1H, Triazole -NH), 7.8-7.75 (m, 3H, Benzoyl-H), 7.74-7.2 (m, 2H, benzoyl-H), 6.65 (s, 2H, Trimethoxy phenyl ring-H), 3.67 (s, 3H), 3.62 (s, 6H). Anal. Calcd. (Found) for C\(_{18}\)H\(_{17}\)N\(_3\)O\(_4\)S: C, 58.21 (58.20); H, 4.61 (4.65); N, 11.31 (11.28).

4.4.1.4 4-{(Trifluoromethyl) phenyl]-5-(3, 4, 5-trimethoxyphenyl)-4H-1,2,4-triazole-3-thiol (292c)
Yield 78.9 %; IR (KBr) cm⁻¹: 3085, 2932 (Aryl-CH), C=N (1587-stretch of Triazole ring), -NH (3150), C=C (phenyl-1589), C-O (1350); MS: m/z = 411 (M⁺); ¹H-NMR (DMSO-d₆): δ 14.13 (s, 1H, Triazole-NH), 7.30-7.32 (m, 2H, phenyl-H), 7.68-7.66 (d, 1, J = 7.8 Hz, phenyl-1H), 7.53-7.51 (d, 1H, J = 7.9 Hz, phenyl-1H), 6.5 (s, 2H, Trimethoxy phenyl ring-H), 3.59 (s, 3H), 3.50 (s, 6H); ¹³C NMR (DMSO-d₆), 168, 152, 149, 137, 133, 130, 129, 126, 125, 124, 122, 106, 105, 60, 55. Anal. Calcd. (Found) for C₁₈H₁₆F₃N₃O₃S: C, 52.55 (52.60); H, 3.92 (3.99); N, 10.21 (10.25).

4.4.1.5 4-(2, 4-Dichlorophenyl)-5-(3, 4, 5-trimethoxyphenyl)-4H-1,2,4-triazole-3-thiol (292d)

Yield 73%; IR (KBr) cm⁻¹: 3065, 2962 (Aryl-CH), C=N (1577-stretch of Triazole ring), -NH (3160), C=C (phenyl-1599), C-O (1390); MS: m/z = 412(M⁺); ¹H-NMR (DMSO-d₆): δ 14.27 (s, 1H, Triazole-NH), 7.93-7.92 (s, 1H), 7.82-7.80 (d, 1H, J = 8.56 Hz, 1H), 7.70-7.68 (d, 1H, J = 10.84 Hz), 6.63-6.60 (s, 2H, Trimethoxy phenyl ring-H), 3.64 (s, 3H), 3.59 (s, 6H); ¹³C NMR (DMSO-d₆), 168, 152, 149, 137, 133, 130, 129, 126, 125, 124, 122, 106, 105, 60, 55. Anal. Calcd. (Found) for C₁₇H₁₆Cl₂N₃O₃S: C, 49.52 (49.58); H, 3.67 (3.65); N, 10.19 (10.20).

4.4.1.6 4-tert-Butyl-5-(3, 4, 5-trimethoxyphenyl)-4H-1,2,4-triazole-3-thiol (292e)

Yield 77 %; IR (KBr) cm⁻¹: 3095, 2952 (Aryl-CH), C=N (1597-stretch of Triazole ring), -NH (3130), C=C (phenyl-1559), C-O (1380); MS: m/z = 268(M⁺) [corresponds to tert-butyl cleaved fragment]. ¹H-NMR (DMSO-d₆): δ 12.96 (s, 1H, Triazole-NH), 7.20 (s, 2H, Trimethoxy phenyl ring-H), 3.81 (s, 6H), 3.71 (s, 3H), 1.5 (s, 9H); ¹³C NMR (DMSO-d₆), 164, 151, 149, 137, 120, 106, 60, 56, 46. Anal. Calcd. (Found) for C₁₅H₂₁N₃O₃S: C, 55.71 (55.78); H, 6.54 (6.50); N, 12.99 (13.01).

4.4.1.7 4-(4-Bromo phenyl)-5-(3, 4, 5-trimethoxyphenyl)-4H-1,2,4-triazole-3-thiol (292f)
Yield 63%; IR (KBr) cm\(^{-1}\): 3045, 2952 (Aryl-CH), C=N (1567-stretch of Triazole ring), -NH (3170), C=C (phenyl-1539), C-O (1340); MS: m/z = 422(M\(^{+}\)); \(^{1}\)H-NMR (DMSO-d\(_6\)): \(\delta\) 14.16 (s, 1H, Triazole -NH), 7.75-7.73 (d, 2H, J = 8.68 Hz), 7.37-7.35 (d, 2H, J = 8.7 Hz), 6.58 (s, 2H, Trimethoxy phenyl ring-H), 3.64 (s, 3H), 3.56 (s, 6H). Anal. Calcd. (Found) for C\(_{17}\)H\(_{16}\)BrN\(_3\)O\(_3\)S:  C, 48.35 (48.38); H, 3.82 (3.85).

4.4.1.8 4-(2, 5-Dimethoxy phenyl)-5-(3, 4, 5-trimethoxyphenyl)-4H-1,2,4-triazole-3-thiol (292g)

Yield 75%; IR (KBr) cm\(^{-1}\): 3098, 2983 (Aryl-CH), C=N (1585-stretch of Triazole ring), -NH (3195), C=C (phenyl-1555), C-O (1410); MS: m/z = 404(M\(^{+}\)); \(^{1}\)H-NMR (DMSO-d\(_6\)): \(\delta\) 14.04 (s, 1H, Triazole -NH), 7.13-7.05 (m, 3H), 6.62 (s, 2H, Trimethoxy phenyl ring-H), 3.71 (s, 3H), 3.62 (s, 3H), 3.53 (s, 9H). Anal. Calcd. (Found) for C\(_{19}\)H\(_{21}\)N\(_3\)O\(_5\)S:  C, 56.56 (56.58); H, 5.25 (5.28); N, 10.42 (10.55).

4.4.1.9 4-(4-Methoxy benzyl)-5-(3, 4, 5-trimethoxyphenyl)-4H-1,2,4-triazole-3-thiol (292h)

Yield 68%; IR (KBr) cm\(^{-1}\): 3093, 2953 (Aryl-CH), C=N (1583-stretch of Triazole ring), -NH (3184), C=C (phenyl-1585), C-O (1346); MS: m/z = 387(M\(^{+}\)); \(^{1}\)H-NMR (DMSO-d\(_6\)): \(\delta\) 14.12 (s, 1H, Triazole -NH), 7.04-7.02 (d, 2H, J = 8.64 Hz), 6.83-6.81(d, 2H, J = 8.68 Hz), 6.63 (s, 2H, Trimethoxy phenyl ring-H), 5.2 (s, 2H, benzyl –CH2 proton), 3.69 (s, 3H), 3.65 (s, 3H) 3.6 (s, 6H). \(^{13}\)C NMR(DMSO-d\(_6\)) 169, 158, 153, 152, 150, 137, 130, 127, 125, 114, 105, 60, 55, 46. Anal. Calcd. (Found) for C\(_{19}\)H\(_{21}\)N\(_3\)O\(_4\)S:  C, 58.90 (58.92); H, 5.46 (5.48); N, 10.85 (10.85).

4.4.1.10 4-Cyclopentyl-5-(3, 4, 5-trimethoxyphenyl)-4H-1,2,4-triazole-3-thiol (292i)

Yield 57%; IR (KBr) cm\(^{-1}\): 3043, 2943 (Aryl-CH), C=N (1543-stretch of Triazole ring), -NH (3154), C=C (phenyl-1565), C-O (1376); MS: m/z = 336 (M\(^{+}\)); \(^{1}\)H-NMR (DMSO-d\(_6\)): \(\delta\) 13.81 (s, 1H, Triazole -NH), 6.83 (s, 2H, Trimethoxy phenyl ring-H), 4.66-4.62 (t, 1H,
\[ J = 8.72 \text{ Hz}, 1H), \ 3.8 \text{ (s, 6H), 3.787 (s, 3H), 2.56-2.49 (m, 2H), 1.84-81 \text{ (m, 4H), 1.77-1.75 (m, 2H)}; ^{13}\text{C NMR(DMSO-d\text{6}) 165, 152, 151, 147, 139, 121, 107, 60, 57, 56, 28, 24.} \]

Anal. Calcd. (Found) for C\text{16}H\text{21}N\text{3}O\text{3}S: C, 57.29 (57.30); H, 6.31 (6.31); N, 12.53 (12.51).

4.4.1.11 4-(4-methoxyphenyl)-5-(3,4,5-trimethoxyphenyl)-4H-1,2,4-triazole-3-thiol (292j)

Yield 70%; IR (KBr) cm\text{1}: 3087, 2943 (Aryl-CH), C=N (1593-stretch of Triazole ring), -NH (3174), C=C (phenyl-1555), C-O (1396); MS: m/z = 374(M\text{+}); ^{1}H-NMR (DMSO-d\text{6}): \delta 14.07 \text{ (s, 1H, Triazole -NH), 7.29-7.27 \text{ (t, 2H, J = 6.9Hz), 7.06-7.05 \text{ (t, 1H, J = 7.04 Hz), 6.60 \text{ (s, 2H, Trimethoxy phenyl ring-H)}, 3.78 \text{ (s, 3H)}, 3.6 \text{ (s, 3H)}, 3.5 \text{ (s, 6H).}} \]

Anal. Calcd. (Found) for C\text{18}H\text{21}N\text{3}O\text{4}S: C, 57.89 (58.80); H, 5.13 (5.15); N, 11.25 (11.30).

4.4.1.12 4-(4-Chloro benzyl)-5-(3, 4, 5-trimethoxyphenyl)-4H-1,2,4-triazole-3-thiol (292k)

Yield 87%; IR (KBr) cm\text{1}: 3098, 2958 (Aryl-CH), C=N (1588-stretch of Triazole ring), -NH (3180), C=C (phenyl-1589), C-O (1340); MS: m/z = 391(M\text{+}); ^{1}H-NMR (DMSO-d\text{6}): \delta 14.12 \text{ (s, 1H, Triazole -NH), 7.377-7.35 \text{ (d, 1H, J = 8.40 Hz), 7.10-7.08 \text{ (d, 2H, J = 8.36 Hz), 6.68 \text{ (s, 2H, Trimethoxy phenyl ring-H)}, 5.3 \text{ (s, 2H, benzyl –CH2 proton)}, 3.67 \text{ (s, 3H)}, 3.65 \text{ (s, 6H).}} \]

Anal. Calcd. (Found) for C\text{18}H\text{18}ClN\text{3}O\text{3}S: C, 55.17 (55.20); H, 4.63 (4.65); N, 10.72 (10.75).

4.4.1.13 4-(4-bromo-2, 6-dimethyl phenyl)-5-(3, 4, 5-trimethoxyphenyl)-4H-1,2,4-triazole-3-thiol (292l)

Yield 71%; IR (KBr) cm\text{1}: 3098, 2800 (Aryl-CH), C=N (1610-stretch of Triazole ring), -NH (3187), C=C (phenyl-1600), C-O (1456); MS: m/z = 450(M\text{+}); ^{1}H-NMR (DMSO-d\text{6}): \delta 14.09 \text{ (s, 1H, Triazole -NH), 7.02 \text{ (s, 2H)}, 6.62 \text{ (s, 2H, Trimethoxy phenyl ring-H)}, 3.62
(s, 3H), 3.53 (s, 6H). 2.35 (s, 6H, dimethyl group). Anal. Calcd. (Found) for C_{19}H_{20}BrN_{3}O_{3}S: C, 50.67 (50.66); H, 4.48 (4.5); N, 9.33 (9.21).

4.4.1.14 4-(3-Chlorophenyl)-3-(2, 6-difluoro-benzyl sulfonyl)-5-(3,4,5-trimethoxy-phenyl)-4H-[1,2,4]-triazole (293a)

Yield 66.66 %; IR (KBr) cm\(^{-1}\): 3051, 2935, 2834 (Aryl-CH), 3051, 2935, 2834 (Aryl-CH), C=N (1586-stretch of Triazole ring), C=C (phenyl-1565, 1625), C-O (1470); MS: m/z = 504(M\(^{+}\)); \(^{1}\)H-NMR (DMSO-d\(_{6}\)): \(\delta\) 7.63-7.53 (m, 3H, phenyl-H), 7.44-7.32 (m, 4H, phenyl-H), 6.64 (s, 2H, trimethoxy phenyl ring –H), 4.32 (s, 2H, benzyl –H), 3.64 (s, 3H, methoxy-H), 3.57 (s, 6H, methoxy-H). \(^{13}\)C NMR(DMSO-d\(_{6}\))161.8, 161.7, 159.3, 159.2, 154.3, 152.6, 149.8, 138.68, 135.3, 133.8, 131.4, 130.5, 130.45, 130.3, 130.1, 128.03, 126.9, 121.3, 112.6, 112.4, 111.2, 111.8, 111.7, 111.63, 111.5, 105.4, 60, 55, 24.

4.4.1.15 4-(Benzoyl)-3-(2, 6-difluoro-benzyl sulfonyl)-5-(3,4,5-trimethoxy-phenyl)-4H [1,2,4]-triazole (293b)

Yield 75 %; IR (KBr) cm\(^{-1}\): 3055, 2940, 2890 (Aryl-CH), C=N (1586-stretch of Triazole ring), C=C (phenyl-1565, 1625), C-O (1470); MS: m/z = 498(M\(^{+}\)); \(^{1}\)H-NMR (DMSO-d\(_{6}\)): \(\delta\) 7.8-7.75 (m, 3H, Benzoyl-H), 7.74-7.2 (m, 2H, benzoyl-H), 7.20-7.12 (m, 3H), 6.65(s, 2H, Trimethoxy phenyl ring-H), 4.32(s, 2H, benzyl –H), 3.69(s, 3H), 3.67(s, 6H). \(^{13}\)C NMR(DMSO-d\(_{6}\))161.5, 161.3, 159.3, 159.6, 154.3, 152.7, 149.8, 138.68, 135.3, 133.8, 131.4,130.3, 130.1, 128.03, 126.9, 121.3, 112.6, 112.4, 111.2, 111.8, 111.7, 111.63, 111.5, 105.4, 60, 55, 24.

4.4.1.16 4-(3-(Trifluoro methyl) phenyl)-3-(2, 6-difluoro-benzyl sulfonyl)-5-(3,4,5 trimethoxy-phenyl)-4H-[1,2,4]-triazole (293c)

Yield 66.66 %; IR (KBr) cm\(^{-1}\): 3046, 2938, 2836 (Aryl-CH stretch), C=N (1589-stretch of Triazole ring), C=C (phenyl-1497, 1472), C-O (1470); MS: m/z = 538(M\(^{+}\)); \(^{1}\)H-NMR (DMSO-d\(_{6}\)): \(\delta\) 7.94-7.92 (d, 2H, J = 7.28 Hz), 7.77-7.74 (t, 1H, J = 7.8 Hz), 7.64-7.62 (d,
1H, \( J = 7.72\) Hz), 7.41-7.35 (m, 1H), 7.09-7.04 (t, 2H, \( J = 8.0\) Hz), 6.60 (s, 2H, trimethoxy phenyl ring –H), 4.31 (s, 2H, benzyl –H), 3.62 (s, 3H, methoxy-H), 3.53 (s, 6H, methoxy-H). \(^{13}\)C NMR(DMSO-d\(_6\)), 161.8, 161.73, 159.33, 159.2, 154.5, 152.6, 149.7, 138.6, 134.8, 132.2, 131.2, 130.5, 130.4, 130.3, 130.2, 126.8, 125.2, 124.6, 121.9, 121.3, 112.3, 111.8, 111.7, 111.63, 111.5, 105.5, 60.06, 55.5, 24.96.

4.4.1.17 4-(2, 4-Dichlorophenyl)-3-(2, 6-difluoro-benzyl sulfanyl)-5-(3, 4, 5 trimethoxy-phenyl)-4H-[1,2,4]-triazole (293d)

Yield 91 %; IR (KBr) cm\(^{-1}\): 3065, 2962 (Aryl-CH), C=N (1577, 1569-stretch of Triazole ring), C=C (phenyl-1599, 1568), C-O (1390); MS: m/z = 538(M\(^+\)); \(^1\)H-NMR (DMSO-d\(_6\)): \( \delta \) 7.93-7.92 (s, 2H), 7.43-7.25 (m, 2H), 7.82-7.80 (d, 1H, \( J = 8.56\) Hz), 7.70-7.68 (d, 1H, \( J = 10.84\) Hz), 6.63-6.60 (s, 2H, Trimethoxy phenyl ring-H), 4.39 (s, 2H, benzyl –H), 3.64 (s, 3H), 3.59 (s, 6H). \(^{13}\)C NMR(DMSO-d\(_6\))162.8, 161.9, 159.9, 158.2, 155.3, 155.6, 145.8, 134.68, 134.3, 134.1, 131.4, 130.5, 130.45, 130.3, 128.03, 126.9, 121.3, 112.6, 112.4, 111.2, 111.8, 111.7, 111.63, 111.5, 105.4, 60, 55, 24.

4.4.1.18 4-(tert-Butyl)-3-(2, 6-difluoro-benzyl sulfanyl)-5-(3, 4, 5 trimethoxy-phenyl)-4H-[1,2,4]-triazole (293e)

Yield 82 %; IR (KBr) cm\(^{-1}\): 3095, 2952, 2900 (Aryl-CH), C=N (1577, 1569-stretch of Triazole ring), C=C (phenyl-1559, 1567), C-O (1380, 1389); MS: m/z = 450(M\(^+\)); \(^1\)H-NMR (DMSO-d\(_6\)): \( \delta \) 7.64-7.59 (m, 3H), 7.20 (s, 2H, Trimethoxy phenyl ring-H), 4.29 (s, 2H, benzyl-H), 3.71 (s, 3H), 3.70 (s, 6H), 1.5 (s, 9H). \(^{13}\)C NMR(DMSO-d\(_6\)), 164, 161, 159, 158, 154, 151, 149, 137, 120, 106, 60, 56, 24, 18

4.4.1.19 4-(4-Bromo phenyl)-3-(2,6-difluoro-benzyl sulfanyl)-5-(3,4,5 trimethoxy-phenyl)-4H-[1,2,4]-triazole (293f)
Yield 80 %; IR (KBr) cm$^{-1}$: 3051, 2935, 2834 (Aryl-CH), C=N (1586-stretch of Triazole ring), C=C (phenyl-1565, 1625), C-O (1470); MS: m/z = 548(M$^+$); $^1$H-NMR (DMSO-d$_6$): $\delta$ 7.73-7.71 (d, $J = 6.80$ Hz, 2H), 7.5-7.409 (m, 1H), 7.19-7.15 (m, 2H), 6.5 (s, 2H, trimethoxy phenyl ring-H), 4.29 (s, 2H, benzyl-H), 3.62 (s, 3H), 3.3 (s, 6H).

4.4.1.20 4-(2, 5-Dimethoxy phenyl)-3-(2, 6-difluoro-benzyl sulfanyl)-5-(3,4,5 trimethoxy-phenyl)-4H-[1,2,4]-triazole (293g)

Yield 86 %; IR (KBr) cm$^{-1}$: 3051, 2935, 2834 (Aryl-CH), C=N (1586-stretch of Triazole ring), C=C (phenyl-1565, 1625), C-O (1470); MS: m/z = 530(M$^+$); $^1$H-NMR (DMSO-d$_6$): $\delta$ 7.42-7.20 (m, 1H), 7.18-7.00 (m, 1H), 7.12-7.00 (m, 3H), 7.01-7.00 (d, 1H, $J = 4.0$ Hz), 6.68 (s, 2H, Trimethoxy phenyl ring-H), 4.34 (s, 2H, benzyl-H), 3.68 (s, 3H), 3.63 (s, 3H), 3.59 (s, 3H), 3.57 (s, 6H). $^{13}$C NMR(DMSO-d$_6$) 161.88, 161.81, 159.41, 159.3, 154.35, 153.28, 152.67, 150.43, 148.60, 138.57, 130.47, 130.37, 130.26, 122.79, 121.87, 116.82, 114.97, 113.92, 112.8, 112.61, 112.4, 111.7, 111.7, 111.6, 111.5, 104.4, 60, 56, 55.8, 55.5, 24.

4.4.1.21 4-(4-Methoxy benzyl)-3-(2,6-difluoro-benzyl sulfanyl)-5-(3,4,5 trimethoxy-phenyl)-4H-[1,2,4]-triazole (293h)

Yield 91 %; IR (KBr) cm$^{-1}$: 3051, 2935, 2834 (Aryl-CH), C=N (1586-stretch of Triazole ring), C=C (phenyl-1565, 1625), C-O (1470); MS: m/z = 514(M$^+$); $^1$H-NMR (DMSO-d$_6$): $\delta$ 7.3-7.28 (m, 3H), 7.06-7.04 (d, 1H, $J = 8.6$ Hz), 6.83-6.83 (d, 2H $J = 8.38$ Hz), 6.63(s, 2H, Trimethoxy phenyl ring-H), 5.2 (s, 2H, benzyl –CH2 proton), 4.28(s, 2H, benzyl –H), 3.69 (s, 3H), 3.65(s, 3H) 3.6 (s, 6H). $^{13}$C NMR(DMSO-d$_6$), 168, 161.8, 161.7, 159.3, 152, 149, 137, 133, 130, 130.5, 130.4, 130.35, 130.16, 128.03, 129, 126, 125, 124, 122, 112.6, 112.47, 112.2, 111.8, 111.7, 111.6, 105.4 60, 55, 46, 23.
4.4.1.22 4-(Cyclopentyl)-3-(2, 6-difluoro-benzyl sulfanyl)-5-(3,4,5 trimethoxy-phenyl)-4H-[1,2,4]-triazole (293i)

Yield 89 %; IR (KBr) cm\(^{-1}\): 3043, 2943 (Aryl-CH), C=N (1543-stretch of Triazole ring), C=C (phenyl-1565), C-O (1376); MS: m/z = 462(M\(^{+}\)); \(^1\)H-NMR (DMSO-d\(_6\)): \(\delta 7.46-7.40\) (m, 1H), 7.17-7.12 (m, 2H), 6.77(s, 2H, Trimethoxy phenyl ring-H), 4.60-4.62 (t, 1H, \(J = 8.72\) Hz), 4.5 (s, 2H), 3.8 (s, 6H), 3.787 (s, 3H), 1.97-1.92 (m, 2H), 1.76-1.56 (m, 2H).

4.4.1.23 4-(4-Methoxy phenyl)-3-(2, 6-difluoro-benzyl sulfanyl)-5-(3, 4, 5 trimethoxy-phenyl)-4H-[1,2,4]-triazole (293j)

Yield 92 %; IR (KBr) cm\(^{-1}\): 3087, 2943 (Aryl-CH), C=N (1593, 1612-stretch of Triazole ring), C=C (phenyl-1555, 1560), C-O (1396); MS: m/z = 500(M\(^{+}\)); \(^1\)H-NMR (DMSO-d\(_6\)): \(\delta 7.46-7.48\) (m, 1H), 7.19-7.17 (m, 2H), 7.29-7.27 (t, 2H, \(J = 6.9\) Hz), 7.06-7.05 (t, 2H, \(J = 7.04\) Hz), 6.60 (s, 2H, Trimethoxy phenyl ring-H), 4.39(s, 2H, benzyl-H) 3.78 (s, 3H), 3.6 (s, 3H), 3.5 (s, 6H).

4.4.1.24 4-(4-Chloro benzyl)-3-(2,6-difluoro-benzyl sulfanyl)-5-(3, 4, 5 trimethoxy-phenyl)-4H-[1,2,4]-triazole (293k)

Yield 85 %; IR (KBr) cm\(^{-1}\): 3098, 2958 (Aryl-CH), C=N (1593, 1612-stretch of Triazole ring), C=C (phenyl-1555, 1560), C-O (1396); MS: m/z = 518(M\(^{+}\)); \(^1\)H-NMR (DMSO-d\(_6\)): \(\delta 7.48\) (m, 3H), 7.38-7.36 (d, 1H, \(J = 8.40\) Hz), 7.13-7.09 (d, \(J = 8.36\) Hz, 2H), 6.68 (s, 2H, Trimethoxy phenyl ring-H), 5.3 (s, 2H, benzyl –CH2 proton), 4.32 (s, 2H, benzyl-H), 3.67(s, 3H), 3.65 (s, 6H). Anal. Calcd. (Found) for C\(_{25}\)H\(_{22}\)ClN\(_3\)O\(_3\)S:  C, 57.85 (57.97); H, 4.29 (4.28); N, 7.36 (7.34).

4.4.1.25 4-(4-Bromo-2, 6-dimethylphenyl)-3-(2, 6-difluoro-benzyl sulfanyl)-5-(3,4,5 trimethoxy-phenyl)-4H-[1,2,4]-triazole (293l)
Yield 86 %; IR (KBr) cm\(^{-1}\): 3098, 2800(Aryl-CH), C=N (1610-stretch of Triazole ring), C=C (phenyl-1600), C-O (1456); MS: m/z = 576 (M\(^{+}\)); \(^1\)H-NMR (DMSO-d\(_6\)) : δ 7.02-7.05 (m, 3H), 7.34-7.45 (m, 2H), 6.62 (s, 2H, Trimethoxy phenyl ring-H), 4.29 (s, 2H, benzyl-H), 3.62 (s, 3H), 3.53 (s, 6H, methoxy group), 2.35 (s, 6H, dimethyl group).

4.4.2 Spectral data

Fig. 4.11: \(^1\)H NMR spectrum of 4-(3-chloro phenyl)-5-(3, 4, 5-trimethoxyphenyl)-4H-1,2,4-triazole-3-thiol (292a)
Fig. 4.12: $^{13}$C NMR spectrum of 4-(3-chloro phenyl)-5-(3, 4, 5-trimethoxyphenyl)-4H-1,2,4-triazole-3-thiol (292a)

Fig. 4.13: IR spectrum of 4-(3-chloro phenyl)-5-(3,4,5-trimethoxyphenyl)-4H-1,2,4-triazole-3-thiol (292a)
Fig. 4.14: $^1$H NMR spectrum of 4-(2, 5-dimethoxy phenyl)-5-(3,4,5-trimethoxyphenyl)-4H-1,2,4-triazole thiol (292g)
Method info:
A: 0.1% TFA IN H2O  
B: 0.1% TFA IN ACN  
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Inactivity Code: AC/AD/10-003  
Page 1 of 2
Fig. 4.15: LCMS spectrum of 4-(2, 5-dimethoxy phenyl)-5-(3,4,5-trimethoxyphenyl)-4H-1,2,4-triazole-3-thiol (292g)

Fig. 4.16: $^1$H NMR spectrum of 4-(3-Chlorophenyl)-3-(2, 6-difluoro-benzyl sulfonyl)-5-(3,4,5-trimethoxy-phenyl)-4H-[1,2,4]-triazole (293a)
Fig. 4.17: $^{13}$C NMR Spectrum of 4-(3-Chlorophenyl)-3-(2, 6-difluoro-benzyl sulfanyl)-5-(3,4,5-trimethoxy-phenyl)-4H-[1,2,4]-triazole (293a)
Fig. 4.18: LCMS spectrum of 4-(3-Chlorophenyl)-3-(2, 6-difluoro-benzyl sulfanyl)-5-(3, 4,5-trimethoxy-phenyl)-4H-[1,2,4]-triazole (293a)
Fig. 4.19: X-ray crystal structure for 293a

Fig. 4.20: IR Spectrum of 4-(3-Chlorophenyl)-3-(2, 6-difluoro-benzyl sulfanyl)-5-(3,4,5-trimethoxy-phenyl)-4H-[1,2,4]-triazole (293a)
Fig. 4.21: $^1$H NMR spectrum of 4-(3-(trifluoro methyl) phenyl)-3-(2, 6-difluoro-benzyl sulfanyl)-5-(3, 4, 5 trimethoxy-phenyl)-4H-[1,2,4]-triazole (293c)

Fig. 4.22: $^{13}$C NMR spectrum of 4-(3-(trifluoro methyl) phenyl)-3-(2,6-difluoro-benzyl sulfanyl)-5-(3,4,5 trimethoxy-phenyl)-4H-[1,2,4]-triazole (293c)
**Fig. 4.23:** LCMS spectrum of 4-(3-(trifluoro methyl) phenyl)-3-(2,6-difluoro-benzyl sulfanyl)-5-(3,4,5 trimethoxy-phenyl)-4H-[1,2,4]-triazole (293c)
4.5 Biological activity

4.5.1 Antibacterial studies

The *in vitro* antibacterial activity of newly synthesized compounds 292 (a-l) and 293(a-l) were determined by well plate method.\textsuperscript{31,32} In this work, *Escherichia coli*, *Staphylococcus aureus*, *Pseudomonas aeruginosa* were used for investigation. The test compounds were dissolved in DMSO at concentrations of 1 and 0.5 µg/mL. Ceftriaxone, Amoxycillin with Potassium Clavulanate were used as standard drugs. The antibacterial screening revealed that some of the tested compounds showed good inhibition against various tested microbial strains.

**Table-4.2** Antibacterial data for the newly synthesized triazole derivatives 292 (a-l) in MIC (µg/mL)

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<th><em>Escherichia coli</em></th>
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<td>292g</td>
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<td>Growth in all Concentrations</td>
<td>Growth in all Concentrations</td>
<td>Growth in all Concentrations</td>
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</tr>
<tr>
<td>292h</td>
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</tr>
<tr>
<td>292i</td>
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</tr>
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<tr>
<td></td>
<td>Staphylococcus aureus</td>
<td>Bacillus cereus</td>
<td>Escherichia coli</td>
<td>Psuedomonas aeruginosa</td>
<td>Drug Control</td>
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<td>--------------------------</td>
<td>--------------------------</td>
<td>------------------------</td>
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<tr>
<td>293a</td>
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<tr>
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<td>Growth in all Concentrations</td>
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Table-4.3: Antibacterial data for the newly synthesized Triazole derivatives 293 (a-l) in MIC (µg/mL)
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<th>293I</th>
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<th>Growth in all Concentrations</th>
<th>Growth in all Concentrations</th>
<th>No growth</th>
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<tbody>
<tr>
<td>Ceftriaxone (Standard)</td>
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<td>No growth in any of the concentrations</td>
<td>No growth in any of the concentrations</td>
<td>No growth in any of the concentrations</td>
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<tr>
<td>Inoculum Control</td>
<td>Growth</td>
<td>Growth</td>
<td>Growth</td>
<td>Growth</td>
<td>-</td>
</tr>
<tr>
<td>Media/ Broth control</td>
<td>No growth</td>
<td>No growth</td>
<td>No growth</td>
<td>No growth</td>
<td>-</td>
</tr>
</tbody>
</table>

**Note:** Antimicrobial activity tested at 50µg/mL, 25µg/mL, 12.5µg/mL, 6.25µg/mL, 3.125 µg/mL and 1.56 µg/mL concentrations of the compound.

### 4.6 Conclusions

A new series of novel 3-(2,6-difluoro-benzyl sulfanyl)-4-(substituted)-5-(3,4,5-trimethoxy phenyl)-4H-[1,2,4] triazole derivatives were synthesized in reasonably good yields. They were characterized by $^1$H NMR, $^{13}$C NMR, mass spectrometry, IR studies and antimicrobial property by well plate method. The antibacterial screening revealed that, few of the tested compounds showed good inhibition against various tested microbial strains. Compound (292d) showed significant antibacterial activity against *B. cereus* at concentrations of 1.0 and 0.5 µg/mL compared to standard drug Streptomycin. Compound (293g) showed similar activity against *S. aureus* and *B.cereus* respectively at 1.0 and 0.5 µg/mL concentrations. The remaining compounds showed moderate activity against all of the four tested bacterial strains compared to standard Ceftriaxone. Results of antibacterial studies have been presented in **Table-4.2** and **Table-4.3**. The active compound (292d) has 2,4-dichlorophenyl substituent and (293g) has 2,5-dimethoxy substituent respectively along with 2,6-difluorobenyl group. The presence of dichloro and dimethoxy group contributes the net biological activity.
Fig. 4.24: Most potent compounds among the synthesized compounds

4.7 References

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6 Holla, B. S., Akberali, P. M., Shivananda, M. K. “Studies on nitrophenylfuran
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