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Research Article

SYNTHESIS, SPECTRAL ANALYSIS, ANTIBACTERIAL ACTIVITY AND MOLECULAR DOCKING STUDIES OF SOME NOVEL DERIVATIVES OF COMBINED TETRAZOLE AND THIOSEMICARBAZIDE MOIETIES

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ABSTRACT

A few novel tetrazolyl thiosemicarbazide derivatives namely, 1-(1-(1-aryl-1*H*-tetrazol-5-yl)ethylidene) thiosemicarbazides (**5a-5g**) were synthesized and their structures were confirmed by FT-IR, ^{1}H-NMR and ^{13}C-NMR studies. The synthesized compounds were screened against various microbial strains for their antimicrobial activities and the results shows good activities. The compounds **5b** and **5f** were showing promising activity against *Staphylococcus aureus* and *Escherichia coli*. Additionally, Molecular docking studies were also carried out for these Tetrazolylthiosemicarbazide derivatives and were docked against Enoyl-[acyl-carrier-protein] reductase of *Staphylococcus aureus* (saFabI), obtained from Protein Data Bank (4ALI) as this structure was resolved in complex with NADP and triclosan. From the docking results, the compounds **5b, 5d** and **5f** are found to be strong binders with saFabI and having stronger binding affinity with saFabI than triclosan-saFabI complex. Therefore, it can be inferred that tetrazolylthiosemicarbazide derivatives, in specific, compounds **5f**, **5b** and **5d** could be taken up for further evaluation towards novel drug design against *Staphylococcus aureus*.

Keywords: Tetrazolylthiosemicarbazide, Spectral studies, Antimicrobial activities, Molecular docking studies, *Staphylococcus aureus*.

1. INTRODUCTION

Widespread incidence of antibiotic resistance among 5,00,000 people with suspected microorganism infections across twentytwo countries revealed by WHO's New Global Antimicrobial Surveillance System (GLASS). Generally, most of the reported microbials are *E. coli, K. pneumonia, S. aureus and S. pneumonia*. Thiosemicarbazides are a class of heterocyclic compounds which have general molecular structure R_1R_2C=N-NH-CS-NH_2. Thiosemicarbazide groups have more applications in pharmaceutical industry and medicinal chemistry and treat as antibacterial compounds [1]. Especially imine bond (-N=CH-) present in the thiosemicarbazide moieties are very useful in organic synthesis. Researchers published many number of articles with antibacterial activities of thiosemicarbazide derivatives [2]. Thiosemicarbazide derivatives showed attractive results against anti-tumor [3-4], heart disease [5], angiogenesis [6], vascular disease [7], antiamoebic [8], antitubercular [9], antiproliferative [10] and anti-cancer [11-12]. Thiosemicarbazides are the most powerful intermediate for the synthesis of several active pharmaceutical ingredients (API) and they are used significantly in the field of medicinal chemistry. Azoles are important drug moiety in medicinal chemistry. Recently, researchers focus on developing new drugs in pharmaceutical fields containing azoles especially imidazole, triazole and tetrazoles. These kinds of compounds have more applications in synthetic medicinal chemistry. Small molecules are the dependable supply for coming across novel biologically more active medicinally important compounds. Particularly, tetrazoles have much more applications in pharmaceutical and medicinal chemistry because of its unique structure. The improvement of tetrazole chemistry has been largely associated with wide scale of uses for this type of compounds in pharmaceutical and agricultural field of chemistry [13-25]. Tetrazole

and thiosemicarbazide based anti-microbial drugs are shown in Fig. 1.

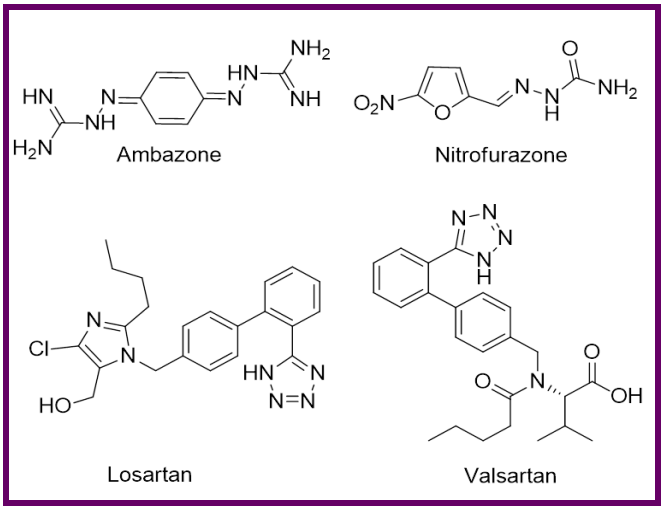


Fig. 1: Structure based thiosemicarbazide and tetrazole containing antimicrobial drugs.

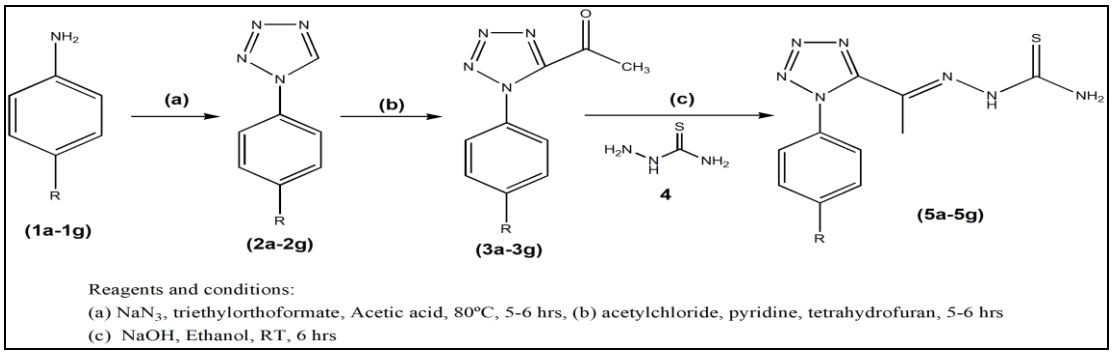
Complex structure is compared to their natural counterpart; those molecules are more easily synthesized. Generally, its soft structure optimization can lead to a potential candidate as drug compounds. Through utilization of combinatorial chemistry, massive libraries of small molecules had been generated and screened for specific biological activities. In view of the above considerations, the thiosemicarbazide and substituted tetrazoles were incorporated into a hybrid structure with enhanced antibacterial activity. The current work describes a novel new series of tetrazole containing hybrid thiosemicarbazide derivatives **(5a-5g)** which are synthesized with novel ideas.

2. MATERIAL AND METHODS

Melting points (°C, uncorrected) of the synthesized thiosemicarbazide compounds were checked in the open capillary tubes using the melting point apparatus (Contemp MEPOAP121, India) and reported as uncorrected. All the solvents and chemicals are purchased from Himedia and Sigma-Aldrich. The purity of all the thiosemicarbazide compounds was tested on a TLC silica gel 60 F-254 with thin layer chromatography using eluting solvents such as chloroform and ethyl acetate (1:1). Column chromatography is used for the purification of all the synthesized compounds, packing with 100-200 mesh silica gel and eluted with a mixture of chloroform and ethyl acetate. All the synthesized compounds have been characterized with an FT-IR spectrometer (Thermo Nicolet-Avatar-330 FT-IR spectrophotometer) by using of KBr pellets. ^{1}H-NMR and ^{13}C-NMR spectroscopy has been performed in DMSO-d6 with Bruker AMX-400 NMR Spectrometer at 293K operating with the frequencies of 100MHz and 400MHz respectively using tetra methyl silane (TMS) as an internal standard. The coupling constant (J values) is given in Hz. Elemental analyzes (C, H and N) were conducted using the organic elemental analyzer (Thermo Scientific Flash 2000).

3. RESULTS AND DISCUSSION

Seven novel derivatives of thiosemicarbazide containing hybrid tetrazoles namely 1-(1-(1-aryl-1*H*-tetrazol-5-yl) ethylidene) thiosemicarbazides (**5a-5g**) were synthesized by the reaction of 1-(1-phenyl-1*H*-tetrazol-5-yl) ethanone (**3a-3g**) and thiosemicarbazide **4**, with sodium hydroxide in refluxing ethanol (Scheme-1). Precipitation occurred after quenching the reaction with addition of ice cold water. The precipitate was filtered, washed with water thoroughly and dried under vacuum. For all the synthesized tetrazolylthiosemicarbazide derivatives, the structures (**5a-5g**) are confirmed by various spectral studies such as FT IR, ^{1}H NMR, ^{13}C NMR and Mass spectra.



Scheme 1: Synthetic route for the novel hybrid compounds containing tetrazole and thiosemicarbazide moiety (5a-5g).

3.1. Spectral analysis of synthesized compounds

Among the synthesized compounds, the compound 1-(1-(1-aryl-1*H*-tetrazol-5-yl)ethylidene) thiosemicarbazide (**5a**) is taken as a representative compound for the discussion for their spectral analyses of FT-IR, Mass, ^{1}H and ^{13}C NMR spectral values.

In the FT-IR spectrum of compound **5a**, a strong absorption appeared at 1613 cm^{-1} is attributed to thiosemicarbazide group's C=S stretching frequency. The absorptions observed at 3069 cm^{-1} reveals that the presence of aromatic C-H stretching frequency. The absorptions within the range of 2925-2807 cm^{-1} is because of the aliphatic C-H stretching frequency. The strong absorption observed at 1587 cm^{-1} is due to the frequency of stretching by the C=N group. The absorptions observed in the range of 3432 cm^{-1} is caused by N-H stretching frequency of the thiosemicarbazide moiety. The lack of stretching frequency for the C=O group and the existence of stretching frequency for the N-H group indicates the formation of the imine functionality.

In the ^{1}H NMR spectrum of the compound, 1-(1-(1-phenyl-1*H*-tetrazol-5-yl)ethylidene) thiosemicarbazide **5a**, a sharp singlet peak observed at 1.71 ppm is due to the methyl group in the thiosemicarbazide moiety. The amino protons of the thiosemicarbazide part of the compound appeared at 2.54 ppm. Phenyl group aromatic protons appeared in the range between 7.09-7.61 ppm. The imino NH proton of the thiosemicarbazide moiety gives a peak at 10.06 ppm.

In the ^{13}C NMR spectrum of the compound, 1-(1-(1-phenyl-1*H*-tetrazol-5-yl)ethylidene) thiosemicarbazide, the methyl carbon gives a signal at 24.56 ppm. The aromatic carbons resonated in the range of 121.02-130.79 ppm. The *ipso* carbon of the tetrazole ring and ethylidene moiety appears respectively at 151.13 and 175.25 ppm. The thionyl carbon of the thiosemicarbazide moiety resonated and gives a signal at 181.45 ppm.

3.2. Antibacterial studies

The pharmacological importance of the different heterocyclic compounds paved the way for active synthetic and medicinal chemistry oriented research. In this way all the synthesized compounds have been screened against various microbial strains for their antimicrobial activities using a standard screening method [26]. Compounds with a variety of substitutions at para-positions were synthesized and screened to analyze and enhance the biological activity. The synthesized compounds (**5a-5g**) were screened for their antibacterial activity by disc diffusion method for their antibacterial activities against the bacterial strains viz., *Bacillus subtilis, Salmonella typhi, Vibrio cholerae, Escherichia coli, Klebsiella pneumonia* and *Staphylococcus aureus*. All the newly synthesized compounds show good antimicrobial activities against most of the bacterial strains analyzed using disc diffusion method and assessed the inhibition region. This tetrazolyl-thiosemicarbazide derivatives shows promising activity against *Staphylococcus aureus* and *Escherichia coli* utilizing methanol as solvent in various concentrations viz., 50µl/ml, 100µl/ml, 150µl/ml and 200µl/ml. Streptomycin was used as positive control. The results are presented in Table 1 & 2.

The activity data reveals that, the antibacterial activity of compound **5b** against *Escherichia coli* and *Staphylococcus aureus* is showing better than the control compound. Compound **5b** shows the inhibition zone of 24 mm against *S. aureus* and 20 mm against *E. coli* at 200 µl/ml concentration. For the compound **5d,** the zone of inhibition against *S.aureus* is 20 mm and the zone of inhibition against *E. coli* is 17 mm at 200 µl/ml concentration. Similarly the compound **5f** shows the inhibition zone of 22 mm against *S.aureus* and 18 mm against *E. coli* at 200 µl/ml concentration. In this present study, from the results, the compounds **5b** and **5f** were showing promising activity against *Staphylococcus aureus* and *Escherichia coli*.

Table 1: Antibacterial activity of tetrazole containing hybrid thiosemicabazide derivatives (5a-5g) against *Staphylococcus aureus*

Compound Name	Area of inhibition zone (mm)				
	*C	50 µl	100 µl	150 µl	200 µl
5a	10	10	11	12	12
5b	10	16	18	20	24
5c	10	12	13	13	15
5d	10	12	15	18	20
5e	10	12	13	15	17
5f	10	14	17	20	22
5g	10	13	15	16	18

Table 2: Antibacterial activity of tetrazole containing hybrid thiosemicabazide derivatives (5a-5g) against *Escherichia coli*

Compound Name	Area of inhibition zone (mm)				
	*C	50 µl	100 µl	150 µl	200 µl
5a	10	10	11	11	12
5b	10	11	13	17	20
5c	10	-	10	10	10
5d	10	11	13	15	17
5e	10	11	11	13	15
5f	10	10	12	15	18
5g	10	10	11	13	13

3.3. Molecular docking studies

Molecular docking experiments were carried out to verify the pharmacological data obtained and to provide clear evidence of the antibacterial action observed in the seven newly synthesized compounds. Tetrazole-thiosemicarbazide derivatives were docked against Enoyl-[acyl-carrier-protein] reductase of *Staphylococcus aureus* (saFabI). The atomic coordinates of crystal structure for saFabI were obtained from Protein Data Bank (**4ALI**) [27]. The protein was resolved by 2.10AO. Among many structures available for saFabI in protein data bank, '**4ALI**' was chosen for molecular docking as this structure was resolved in complex with NADP and triclosan. NADP (nicotinamide-adenine-dinucleotide phosphate) is a substrate of the FabI used in the chemical reaction of fatty acid biosynthesis in bacteria.

Triclosan is a biocide used against various microorganisms and used in certain food and personal health care items, such as oral and dermal goods, including mouthwashes, toothpastes, soaps, deodorants and hand sanitizers and household items like dish detergents, plastics and textiles. Further, triclosan has been reported to disrupt bacterial cell wall functions of bacteria [28]. Triclosan has been reported to target different bacterial fatty acid biosynthetic enzymes, enoyl-[acyl-carrier protein] reductase, Gram-negative and Gram-positive bacteria and Mycobacteria [29]. Atomic coordinates for protein structure that is in complex with both substrate and an inhibitor could facilitate help us to perform the docking specifically at substrate/inhibitor binding sites. Therefore, '4ALI' was chosen over other structures for saFabI for molecular docking. While docking substrate and triclosan were removed from the atomic coordinate file of the protein to target the binding site for substrate/tetrazole derivatives. Molecular docking was carried out using CLC Drug Discovery Workbench (version 1.5).

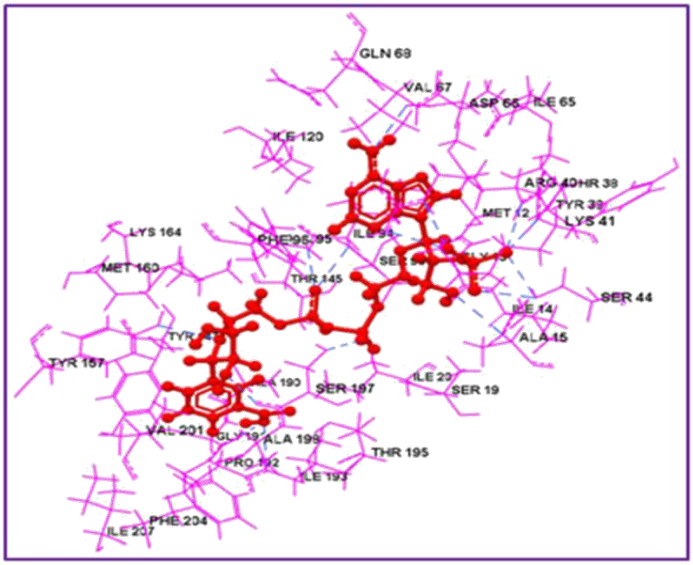


Fig. 2: The molecular docking of Compound Triclosan nto FabI

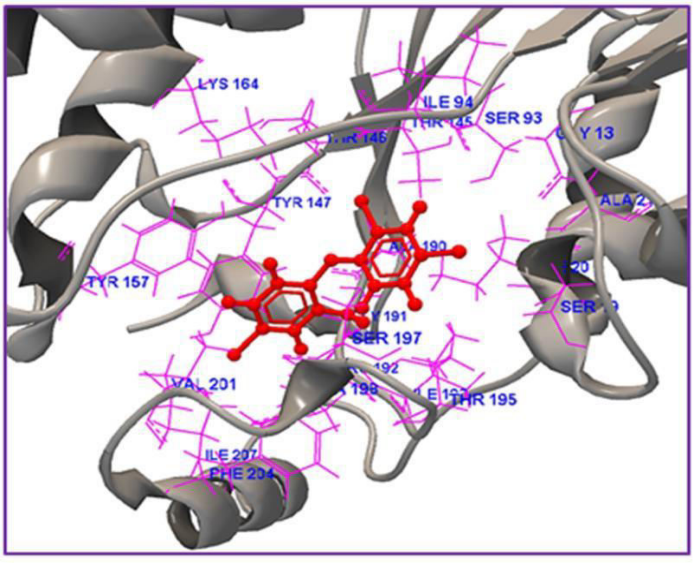


Fig. 3: The molecular docking of NADP into FabI

All the seven tetratzolethiosemicarbazide derivatives were docked successfully on Enoyl-[acyl-carrier-protein] reductase of *Staphylococcus aureus* (saFabI). Further, all of them were docked onto the substrate /inhibitor binding site of (active site) of the saFabI. Therefore, it can be inferred as FabI of *S. aureus* could be a potential drug target for tetrazole derivatives. Tetratzole thiosemicarbazide derivatives **5b, 5d** and **5f** are strong binders with saFabI. The crystal structure given in PDB ID: **4ALI** was resolved in complex with NADP and triclosan. Therefore, both NADP and triclosan were also docked in the saFabI in order to use binding energy of them in complex with saFabI as controls shown in Fig. 2 & 3.

Three compounds namely **5f**, **5b** and **5d** were found to have stronger binding affinity (-52.12, -51.16 and -50.27 kcal/mol respectively) with saFabI than triclosan -saFabI complex (-49.93 kcal/mol). Therefore, it can be inferred that tetratzole thiosemicarbazide derivatives, **5f**, **5b** and **5d** could be taken up further evaluation towards novel drug design against *Staphylococcus aureus*. The docking models of compound **5f** shown in Fig. 4-9.

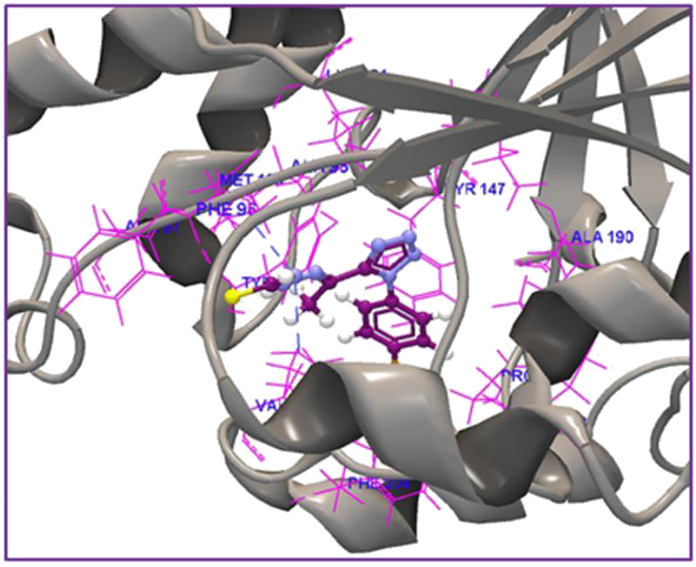


Fig. 4: The molecular docking of compound 5f into 4ALI protein

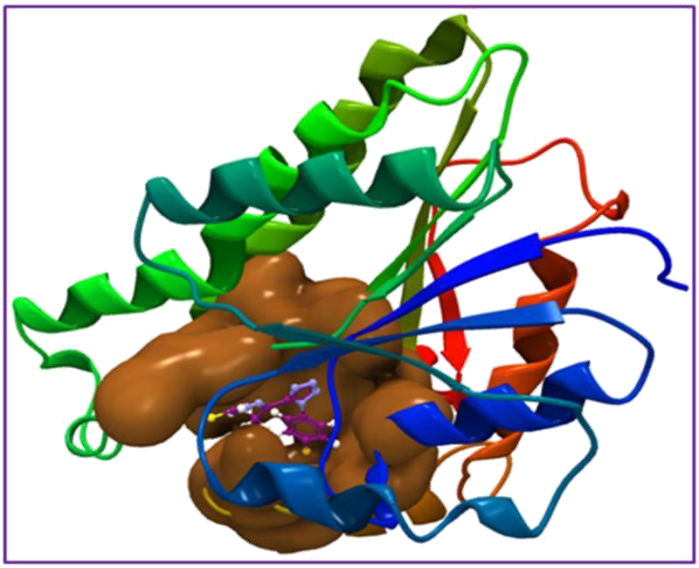


Fig. 5: The surface cavity of compound 5f into 4AL protein

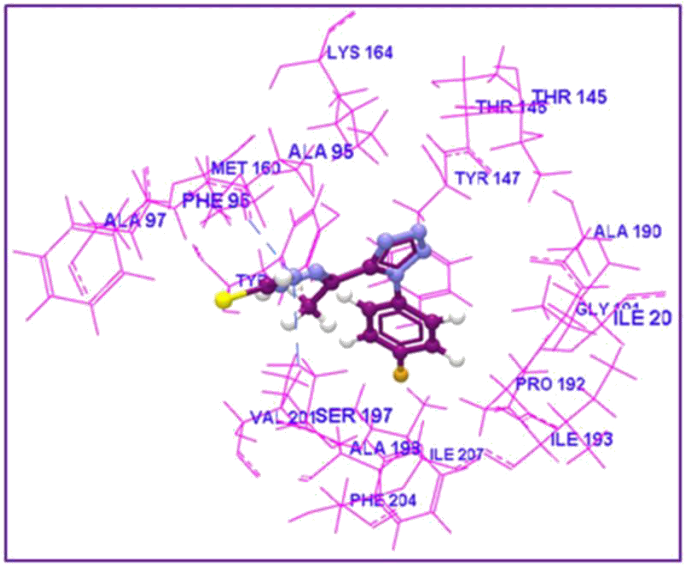


Fig. 6: Stick model of compound 5f into 4ALI protein

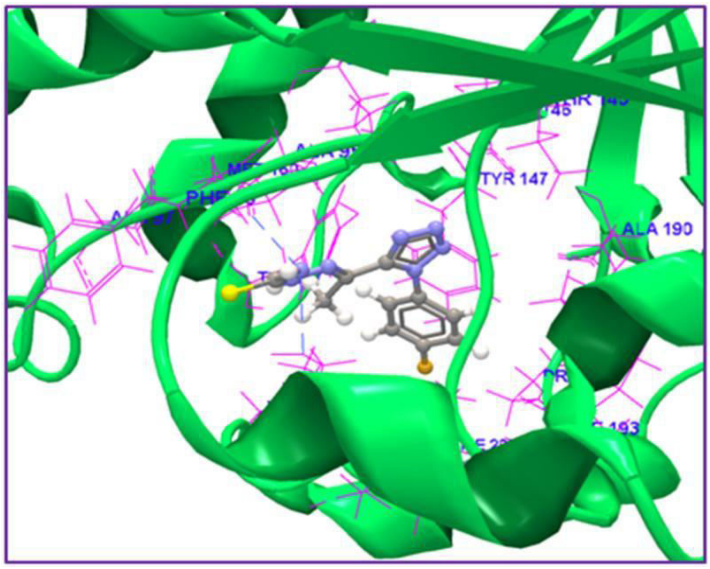


Fig. 7: Solid and ribbon model of compound 5f nto 4ALI protein

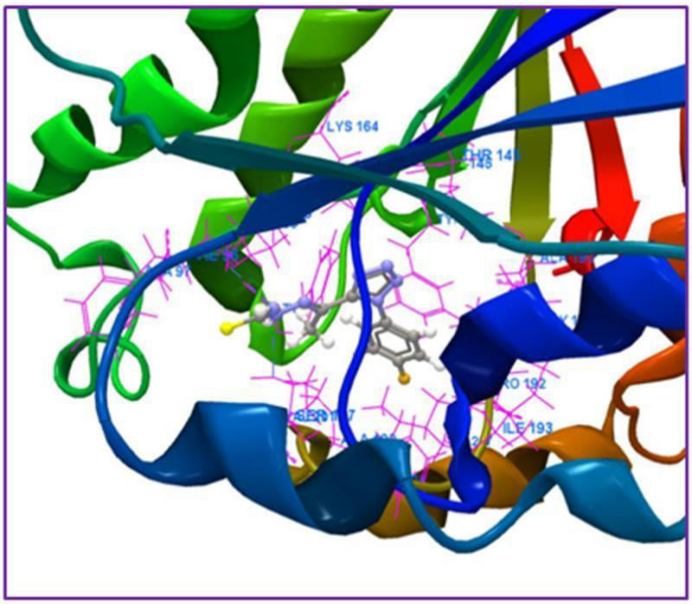


Fig. 8: The interaction of saFabI and Compound 5f in ribbon model

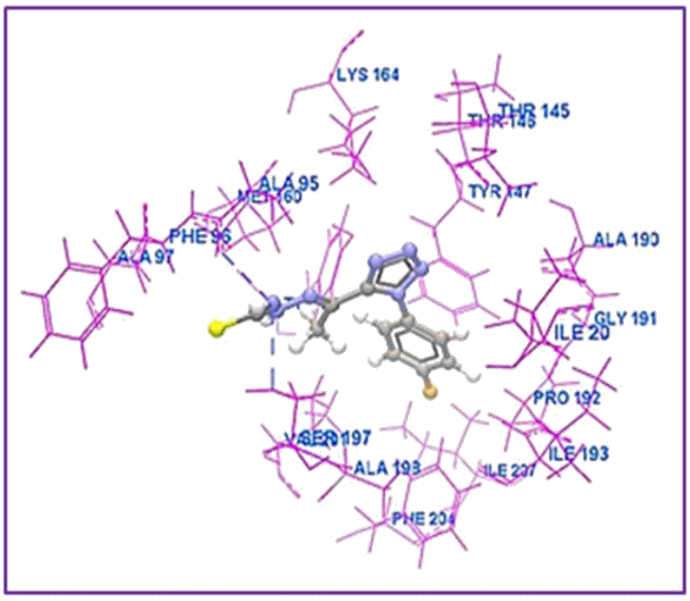


Fig. 9: The interaction of saFabI and Compound 5f n solid model

3.3.1. Possible mechanism of biological action of Thiosemicarbazide derivatives (5a-5g)

The binding interactions between the top most compound (compound **5f**) and the saFabI were analyzed. Using molecular docking, it was found that totally 19 amino acids residues from saFabI to fall in the substrate binding site. Though 3 of the 7 research derivatives were found as strong binders with saFabI than triclosan, using CLC Drug Discovery Workbench the binding energy of the complex containing saFabI and NADP were calculated to be -81.62 kcal/mol. This might be due to the fact the NADP is a far bigger molecule (containing 72 atoms and molecular weight of 739.37) than all of the derivatives (containing total of 28-32 atoms and molecular weight between 260.30 to 339.19) as well as triclosan (total number of atom: 24 and molecular weight 289.54). As per the Lipinsky's rule of five, a molecule should have its molecular weight lesser than 500 is preferred for any orally active molecule to be a drug. Thus, all the synthesized derivatives are having molecular weight less than 500 and three of them binding to triclosan-binding region which is overlapping with NADP binding site, would potentially alter the NADP binding conformation of the saFabI. Such conformational change would potentially block the natural reaction with NADP and therefore the fatty acid biosynthesis. Such block in fatty acid biosynthesis would destruct the bacterial cell wall that would be lethal to the bacteria.

Further, Schiebel *et al* [27] reported 9 amino acids from saFabI to interact with triclosan using crystal structure. It was observed in the present study that out of 9 amino acids 8, namely ALA95, ALA97, TYR147, TYR157, MET160, SER197, ALA198 and VAL201 to be present in the interacting regions of compound **5f**. These results appear to be very convincing as compound **5f** could be binding with FabI in the target region and with stronger affinity than triclosan. Further, Schiebel *et al.* [27] reported 24 amino acids from saFabI to interact with NADP. Eight of these residues namely ILE20, ALA95, THR145, THR146, LYS164, GLY191, PRO192 and SER197 were also found to fall in the binding region with compound **5f** in the present study. Finally, 2 amino acids, ALA95 and SER197 were observed in the docking analysis to interact with compound **5f** by hydrogen bonds. Both of these amino acids were already demonstrated in the crystallography study performed by Schiebel *et al.* as interacting with both NADP as well as triclosan. Therefore, the present study holds evidence to suggest that compound **5f** could be potentially an inhibitor of saFabI and it could be taken up forward for further evaluation towards drug discovery.

3.4. Synthetic procedure and spectral data for the synthesized compounds

Compounds **2a-2g** have already been reported [30-31] and as part of our ongoing research, a mixture of

1-aryl-1*H*-tetrazole (**2a-2g**), acetylchloride and pyridine in tedrahydrofuran (25 mL) at 0°C was prepared. The reaction mixture was then refluxed for six hours. The flow of the reaction was monitored by TLC using ethyl acetate and hexane as eluting solvent mixture. After the completion of the reaction, the reaction mixture was quenched with crushed ice and the solid thrown out was separated, washed with water and dried under vacuum to get 1-(1-aryl-1*H*-tetrazol-5-yl)ethanones (**3a-3g**). The compounds (**3a-3g**) were further treated to react with thiosemicarbazide **4** in the presence of sodium hydroxide in refluxing ethanol to obtain novel 1-(1-(1-aryl-1*H*-tetrazol-5-yl)ethylidene) thiosemicarbazides (**5a-5g**). The flow of this reaction was monitored by TLC and after completion, the reaction mixture was quenched with crushed ice, filtered the solid separated and dried under vacuum. The crude product obtained was then purified by column chromatography. Thus, the tetrazole containing hybrid semicarbazide derivatives (**5a-5g**) were synthesized with excellent yields.

3.4.1. Spectral Data

3.4.1.1. 1-(1-(1-phenyl-1H-tetrazol-5-yl) ethylidene)thiosemicarbazide (5a)

White solid; mp: 122-126°C; IR (KBr): 1587, 1613, 2807-2925, 3069, 3432 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ: 1.71 (s, 3H), 7.09-7.61 (m, 5H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 24.56, 121.02-130.79, 181.45; MS (*m/z*): 261.08 (M^+). Anal. Calcd.for $C_{10}H_{11}N_7S$ (%): C, 45.96; H, 4.24; N, 37.52; Found (%): C, 45.56; H, 4.00; N, 37.12.

3.4.1.2. 1-(1-(1-p-tolyl-1H-tetrazol-5yl)ethylidene)thiosemicarbazide (5b)

White solid; mp: 134-136°C; IR (KBr): 1578, 1607, 2964-2805, 3068, 3427 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ: 1.73 (s, 3H),2.29 (s, 3H), 7.24 -7.26 (d, 2H, J = 8 Hz),7.41 -7.43 (d, 2H, J = 8 Hz); ^{13}C NMR (100 MHz, DMSO-d_6): δ 23.38, 25.51, 114.47-138.60, 180.44; MS (*m/z*): 275.1 (M^+). Anal. Calcd. for $C_{11}H_{13}N_7S$ (%): C, 47.98; H, 4.76; N, 35.61; Found (%): C, 47.68; H, 4.46; N, 35.21.

3.4.1.3. 1-(1-(1-(4-methoxyphenyl)-1H-tetrazol-5yl) ethylidene)thiosemicarbazide (5c)

White solid; mp: 146-148°C; IR (KBr): 1581, 1609, 2964-2927, 3074, 3426 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ: 1.74 (s, 3H), 3.72 (s, 3H), 6.89-6.91 (d, 2H, J = 8 Hz), 7.41 -7.43 (d, 2H, J = 8 Hz); ^{13}C NMR (100 MHz, DMSO-d_6): δ 23.74, 55.15, 114.04-130.38, 183.04; MS (*m/z*): 291.09 (M^+). Anal.Calcd. for $C_{11}H_{13}N_7OS$ (%): C, 45.35; H, 4.50; N, 33.65; Found (%): C, 45.05; H, 4.10; N, 33.15

3.4.1.4. 1-(1-(1-(4-chlorophenyl)-1H-tetrazol-5-yl) ethylidene)thiosemicarbazide (5d)

White solid; mp: 112-116°C; IR (KBr): 1581, 1609, 2887-2959, 3075, 3423 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ: 1.74 (s, 3H), 7.59-7.61 (d, 2H, J = 8 Hz), 7.84 -7.86 (d, 2H, J = 8 Hz); ^{13}C NMR (100 MHz, DMSO-d_6): δ 22.75, 118.13-133.72, 182.55; MS (*m/z*): 295.05 (M^+). Anal. Calcd. for $C_{10}H_{10}ClN_7S$ (%): C, 40.61; H, 3.41; N, 33.15; Found (%): C, 40.11; H, 3.01; N, 32.90.

3.4.1.5. 1-(1-(1-(4-bromophenyl)-1H-tetrazol-5-yl) ethylidene)thiosemicarbazide (5e)

White solid; mp: 154-158°C; IR (KBr): 1581,1609, 2852-2958, 3073, 3445 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ: 1.70 (s, 3H), 7.49-7.51 (d, 2H, J = 8 Hz), 7.33 (s, 2H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 23.38, 115.33-136.93, 180.93; MS (*m/z*): 338.99 (M^+). Anal. Calcd. for $C_{10}H_{10}BrN_7S$ (%):C, 35.30; H, 2.96; N, 28.82; Found (%):C, 34.90; H, 2.68; N, 28.42.

3.4.1.6. 1-(1-(1-(4-fluorophenyl)-1H-tetrazol-5-yl) ethylidene)thiosemicarbazide (5f)

White solid; mp: 138-142°C; IR (KBr): 1579, 1608, 2898-2964, 3074, 3431 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ: 1.65 (s, 3H), 7.51 (s, 4H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 23.63, 119.59-137.54, 181.67; MS (*m/z*): 279.07 (M^+). Anal. Calcd. for $C_{10}H_{10}FN_7S$(%):C, 43.00; H, 3.61; N, 35.10; Found (%):C, 42.70; H, 3.35; N, 34.82

3.4.1.7. 1-(1-(1-(4-nitrophenyl)-1H-tetrazol-5-yl) ethylidene)thiosemicarbazide (5g)

Pale yellow solid; mp: 130-134°C; IR (KBr): 1578, 1606, 2893-2964, 3070, 3423 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ: 1.65 (s, 3H), 8.07-8.09 (s, 2H, J=8 Hz), 8.19-8.21 (d, 2H, J=8 Hz); ^{13}C NMR (100 MHz, DMSO-d_6): δ 23.74, 115.47-132.60, 181.44; MS (*m/z*): 306.06 (M^+). Anal.Calcd.for $C_{10}H_{10}N_8O_2S$ (%): C, 39.21; H, 3.29; N, 36.58; Found (%): C, 38.61; H, 3.23; N, 36.50

4. CONCLUSION

A series of novel tetrazolylthiosemicarbazide derivatives namely, 1-(1-(1-aryl-1*H*-tetrazol-5-yl) ethylidene) thiosemicarbazides (**5a-5g**) were synthesized. Their structures were confirmed by FT-IR, ^{1}H-NMR, ^{13}C-NMR and Mass spectral studies. The synthesized compounds were screened against various microbial strains for their antimicrobial activities and the compounds **5b** and **5f** were showing promising activity against *Staphylococcus aureus* and *Escherichia coli*. Additionally, Molecular docking studies were also carried out for these Tetrazolylthiosemicarbazide derivatives and were docked against Enoyl-[acyl-carrier-protein] reductase of *Staphylococcus aureus* (saFabI), obtained from Protein Data Bank (4ALI) as this structure was resolved in complex with NADP and triclosan. The docking results show, the compounds **5b, 5d** and **5f** are found to be strong binders with saFabI and having stronger binding affinity with saFabI than triclosan-saFabI complex. Hence, the docking results confirm the experimental antimicrobial results and reveals that the compounds **5f, 5b** and **5d** could be taken up for further evaluation towards novel drug design against *Staphylococcus aureus*.

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Conflict of interest

The authors declare that there is no conflict of interests regarding the publication of this paper.

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