4. SUMMARY

1. A series of novel hydrazinyl thiazole derivatives (46–70) have been synthesized [(Z)-4-phenyl-2-(2-(1 phenylethylidene)hydrazinyl) thiazoles (46–53), (Z)-2-(2-(1-furan-2-yl)ethylidene)hydrazinyl)-4-(4-methoxyphenyl)thiazole 54, (Z)-4-(4-methoxyphenyl)-2-(2-(1(thiophen-2-yl)ethylidene)hydrazinyl)thiazole 55, 2(2(diphenylmethylene)hydrazinyl)-4-phenylthiazoles (56–63), (Z)-4-phenyl-2-(2-(phenyl(pyridin-4-yl and pyridin-2-yl)methylene) hydrazinyl)thiazoles (64–68), (Z)-1-((2-(4 phenylthiazol-2-yl)hydrazono)methyl)naphthalen-2-ols (69 and 70)] and characterized by IR, $^1$H and $^{13}$C NMR spectra. To confirm that the D$_2$O exchange spectrum for 54 recorded. In addition two dimensional NMR spectra of $^1$H–$^{13}$C COSY have been recorded for compounds 52, 54 and 66. The Mass spectra also recorded for compounds 46, 48, 49 and 51–70 and their appropriate molecular ion peaks are also observed.

2. The compounds 46, 48, 54–56, 65 and 68–70 are tested for their antibacterial activity against Staphylococcus aureus, Escherichia coli, Klebsiella pneumoniae, salmonella typhi and P. aeruginosa From the zone of inhibition, it is clear that the compound 46, 68, 69 and 70 shows very good activity against Salmonella typhi and Staphylococcus aureus when compared to the standard.

3. The zone of inhibition of tested compound 48 it is inferred that they show very good activity against Aspergillus niger compared to the standard but they show very less activity against all other fungal strains when compared to the standard Amphotericin B.
4. Especially the NO$_2$ substituted compound 70 was found to be more potent among all and exhibit an enhanced activity than Amikacin and Amphotoricin B amidst the compounds 70 shows very good activity than 69.

5. Among the 25 newly synthesized thiazoles, nine compounds (46, 48, 54–56, 65 and 68–70) are chosen for molecular docking studies using rigid docking method. Autodock 4.2 is used to determine the orientation of the ligands bound in the active site of antifungal target protein (receptor) 3KRQ.

6. Similarly compound 68, 69 and 70 possess highest binding energy with estimated inhibition constant 921.82 nm, 843.01 and 576.13 nm respectively, also they are found to be good inhibitor of the antifungal target protein.

7. Presence of five membered heterocyclic ring and various substitutents at the nitrogen atom of hydrazinyl moiety and C-2 of thiazole ring shifts inhibitory activity spectrum towards 3KRQ.

8. Ethyl 1,4-dibenzyl-2,6-diphenyl-1,2,5,6-tetrahydropyridine-3-carboxylate (71–79) and Ethyl 1,2,6-triphenyl-4-(phenylamino)-1,2,5,6-tetrahydropyridine-3-carboxylate (80 and 81) have been synthesized and characterized by IR, $^1$H NMR, $^{13}$C NMR spectral techniques. $^1$H-$^1$H COSY, $^1$H-$^{13}$C COSY and DEPT spectra are recorded for the representative compound 76 and their 1D spectral assignments are ascertained. Further the methylene carbons are unambiguously ascertained using DEPT spectrum.

9. The mass spectra are recorded for the synthesized compounds 75, 78, 80 and 81 and their (M+H)$^+$ molecular
ion peaks are observed at 575.2322, 589.3071, 563.2910 and 715.1088 respectively.

10. Single crystal XRD is recorded for compound 75 and 80. The intermolecular interactions of F⋯H and O⋯H lead a network like architecture and F⋯H and O⋯H distances are within the van der Waals radii 75.

11. The flag pole positions 2 and 5 of the piperidine ring, the C=O group of the ester and the −NH are on the same side of the plane 75.

12. The 1, 2, 5, 6-tetrahydropyridine ring exhibits a flat boat conformation (compound 75).

13. It shows strong hydrogen bonding interactions between H2O and the carbonyl oxygen of neighbouring molecules 75.

14. The flag pole positions 31 and 34 of the piperidine ring, as well as the CO group of the ester and the −NH are on the same side of the plane 80.

15. The piperidine ring adopts a twisted chair 75 and boat 80 conformations.

16. Antibacterial and antifungal activities have been studied for compounds 71–81 against a panel of pathogenic bacterial and fungal strains. Especially the fluoro substituted compounds 75 and 81 are found to be more potent among all and exhibit an enhanced activity than amikacin and Amphotericin B amidst the compound 81 shows very good activity when compared to 75. The decreased activity of the compound 80 compared to 78 might be due to the presence of methyl and methoxy groups.
17. Compounds (71–81) produces good dock score of -5.2, -5.4, -4.8, -5.2, -5.2 and -4.2 kcal/mole indicate high binding affinity of the ligand toward the target protein 1YWN–1031. The maximum dock score is -11.3 kcal/mole produced by compounds 72 and is found to possess less number of interaction with target protein, 74, 79 and 81 are found to be more active. As far as dock score and H–bond interaction are concerned

18. 3-(phenyl(phenylamino)methyl)-1H-indole-5-carbonitrile 82–86 and 3,3’-(phenylmethylene)bis(1H-indole-5-carbonitrile) 87 and 88 have been synthesized. All these compounds have been characterized by IR, 1H NMR, 13C NMR and Mass spectra. In addition two dimensional NMR spectra of 1H-13C COSY and Single crystal XRD and have also been recorded for compound 82.

19. Mass spectrum also recorded for compounds 82, 84–88 and their appropriate molecular ion peaks are also observed at 383.1517 (M+H)+, 367, 383, 396 (M-2H)+, 403.1583 (M+H)+ and 391.1353 (M+H)+respectively.

20. Antibacterial and antifungal activities have been studied for compounds 82–86 against bacterial and fungal strains.

21. These antimicrobial studies concluded that para nitro substituted compounds 82, 84 and 86 showed better antimicrobial activities against Aspergillus niger.

22. In this series introduction of both electron donating (-OCH3) 84 and electron withdrawing group (-CH3) group in the phenyl ring 85, insignificantly reduces their antimicrobial characters.
23. The inhibitors (83–87) are found to be interacting with active site of residues like MET 816, PHE 786, and PHE 820.

24. The inhibitors 82 with dock score -10.5 kcal/mole possess three kinds of interaction.

25. Inhibitor 84 and 85 (dockscore -10.5 and -9.7 respectively) are showing two π–π stacking interactions with PHE 786 and PHE-820.

26. Inhibitor 83 [dock score -10.8 kcal/mole] shows only hydrophobic interaction with MET 816 but in case of ligand 86 (dock score -10.6 kcal/mole) there is only one hydrogen bond interaction between nitrogen atom of nitrile group on the indolyl moiety and hydrogen atom of water molecule.

27. Synthesis of 3-acetyl-2H-benzo[g]chromen-2-one (89) and hydrazinyl carbothioamide derivative (90–92), have been synthesized. All the compounds have been characterized by IR, 1H and 13C NMR spectra. In addition two dimensional NMR spectra of 1H–13C COSY have been recorded for compound 90. The mass spectra are also recorded for compounds 90 and 91 and their appropriate molecular ion peaks are also observed at 460.1253 and 468.

28. Compounds 90–92 exhibit excellent activity compared to the standard Amphotoricin B. Especially compound 90 having the coumarinyl moiety was found to be more potent among all and exhibits an enhanced activity than Amikacin and Amphotoricin B.

29. All the compounds studied are found to form three strong hydrogen bonds with the protein 1JNX compounds 90–92.
30. The \((E)\)-N-(2-(4-methoxyphenyl)-2-oxoethyl)-2-(1-(2-oxo-2H-benzo[g] chromen-3-yl)ethylidene)hydrazine carbothioamide (91) with the best antibacterial activity shows a very good binding energy of -8.40 kcal/mol and it may be considered as a good inhibitor of the protein 1JNX.