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ABSTRACT

The present research work deals with the synthesis, biological evaluation and docking studies of some novel heterocyclic compounds. The thesis comprises of five chapters.

Chapter-1 deals with the general introduction, literature reviews of heterocyclic compounds. The biological importance of heterocyclic compounds has been discussed.

Chapter-2 deals with the designing and synthesis of diketo esters, diketo acids, and their amino acid/dipeptidic analogues. Thirty-two compounds were synthesized and characterized by various spectroscopic techniques. The results of *in vitro* antibacterial screening of synthesized compounds revealed fifteen compounds (**1a–c**, **1e–h**, **1j**, **1l**, **2a–c**, **3d**, **5c** and **5e**) as potent against different bacterial strains. By using the MTT assay on human cell line (HepG2), the viability of cell proliferation was evaluated and nine compounds (**1c**, **1e**, **1j**, **1l**, **2a**, **2b**, **3d**, **5c** and **5e**) showed no cytotoxic effect at the concentration range of 50–450 µg/mL. In the biochemical evaluation against purified methionine aminopeptidase (MetAPs) from *Streptococcus pneumonia* (*Sp*MetAP), *Mycobacterium tuberculosis* (*Mt*MetAP), *Enterococcus faecalis* (*Ef*MetAP) and human *(Hs*MetAP), compounds displayed differential behavior against these four enzymes.

Chapter-3 deals with designing and synthesis of amino acid-triazole hybrids as anti-leishmanial agents. The synthesized compounds were screened *in vitro* against the promastigote form of *Leishmania donovani* (Dd8 strain). Among the eighteen synthesized compounds, three compounds **6d, 6g** and **6q** were found to be most potent growth inhibitors with IC_{50} = 88.83 ± 2.93, 96.88 ± 12.88,

and 94.45 ± 6.51 μM respectively and displayed no cytotoxicity towards macrophage cells. Supported by docking studies, the lead inhibitors (**6d**, **6g** and **6q**) showed interactions with key residues in the catalytic site of trypanothione reductase.

Chapter-4 deals with the synthesis, characterization and antimicrobial evaluation of 2,4-disubstituted thiazoles. The structure of the compounds was established using various spectroscopic techniques and X-ray crystallography was performed for compound **1**. The synthesized compounds were screened for their *in vitro* antimicrobial activity. Out of twenty-three compounds, nine compounds (**2a, 2b, 2f, 4a**, **4c**, **4d**, **4e** and **4f**) showed comparatively lower IC_{50} values against the tested microbial strains. The three compounds (**2f**, **4c** and **4e**) were selected as promising inhibitors among the synthesized compounds and hemolysis as well as i*n vitro* cytotoxicity results of the lead compounds revealed their non-toxic nature. The docking studies of lead inhibitors (**2f**, **4c** and **4e**) showed good binding interactions with bacterial methionine aminopeptidase (MetAP). The significant antimicrobial activity of some of the synthesized compounds and good *in silico* ADME properties highlights them as promising molecules for further synthetic and biological exploration.

Chapter-5 deals with the synthesis of thirty-four 1,2,3-triazole-quinazolinone conjugates. The structural analysis was further confirmed by X-ray crystallographic studies for compounds **2** and **5c**. Compounds, **5g**, **5n** and **6e** show activity against all the three strains of Candida, viz. *C. albicans, C. glabrata* and *C. tropicalis* with IC_{50} values in the range 8.36 ± 1.31 μg/mL to 65.58 ± 3.20 μg/mL. The compound **5n** emerged as a most potent inhibitor among compounds (**5a–5q**) and **6e** among compounds (**6a–6q**). The hemolysis results of compounds **5e**, **5g**, **5n**, **6c**, **6e** and **6n** revealed non-toxic nature of these compounds. The docking studies of compounds (**5e**, **5n** and **6e)** with lanosterol 14α-demethylase (CYP51) of *C. glabrata* (PDB ID: 5JLC) showed good binding interactions. Further, *in silico* ADME prediction of synthesized compounds indicated that compounds have a potential to develop as good oral drug candidate.