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ABSTRACT

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

CHAPTER 1: This chapter deals with the general introduction, synthesis and biological importance of nitrogen-containing heterocyclic compounds viz. β-lactams and 1,2,3-triazoles.

CHAPTER 2: This chapter deals with the synthesis of β-lactams 1,3-oxazin-4-one derivatives as antibacterial agents. Antibacterial evaluation results revealed moderate to fair antibacterial efficacy of compounds **4d**, **4h, 4k** and **4l** which was well supported by molecular docking studies. Non-toxic nature as well as ADMET profiling advocated the further structural optimization of this class of compounds.

CHAPTER 3: This chapter deals with a novel series of 1,2,3-triazole-amino acid hybrids and screened *in vitro* against the sensitive strains of *Candida* species. Among all, twelve compounds (**10a**, **10c-g**, **10i-j**, **10o**, **10r-s** and **10u**) showed comparatively lower IC_{50} values against various standard *Candida* strains as well as against FLC-sensitive and resistant clinical *C. albicans* isolates and identified two lead compounds **10d** and **10f** for further biological studies. These were found to be non-toxic on HEK293 cell line. Time kill kinetics study, ergosterol inhibition study and *in vivo* efficacy in *G. mellonella* larvae model also demonstrated potency of **10d** and **10f.**

CHAPTER-4: This chapter deals with the synthesis, characterization and biological evaluation of *N*-substituted 1,2,3-triazolyl appended indole-chalcone hybrids. Compound **4b** exhibited potent DPPH radical scavenging as well as anticancer activity against SiHa and SW-620 cancer cells without affecting normal cells (HEK293) at similar concentration. Selected compounds were further evaluated for their DNA binding ability of this compound as possible mode of action was also explored by various spectroscopic techniques.

CHAPTER 5: This chapter deals with the synthesis of a series of thirty-four 1,2,3-triazole and sulfonate derivatives from readily available natural bioactive alcohols and evaluated for *in vitro* antimicrobial activity. Triazole derivatives (**5e** and **5u)** emerged as potent antibacterial agents against *S. pneumoniae*, *E. faecalis* and *E. coli* bacterial strains as well as against multidrug resistant *E. coli* strains. Growth kinetics analysis, TEM micrographs, anti-biofilm activity and *in vivo* study on the larvae of *G. mellonella* for **5e** and **5u** exhibited their antibacterial potency.

CHAPTER 6: This chapter deals with the synthesis of ferulic acid-triazole (**7a-q**) and ferulic hydroxamic acid-triazole hybrids (**8a-p**). Antibacterial activity results indicated that hydroxamic acid analogues (**8a-p**) exhibited better activity as compared to the acid analogues (**7a-q**). These results clearly emphasizing on the role of hydroxamic acid functionality in imparting the antibacterial potential. Furthermore, MTT and hemolytic assays on the selected compounds, **8d**, **8j**, **8l** and **8p** indicated their non-toxic nature. Based on the role of hydroxamic acid as PDF inhibitors, we performed molecular docking study of one of the lead compound **8j** with bacterial peptide deformylase which indicated that the these compounds might serve as potential peptide deformylase inhibitors.

CHAPTER 7: This chapter deals with synthesis, characterization and antimicrobial evaluation of 7-chloroquinoline-triazole hybrids connected through piperazine linker. It was found that none of sixteen compounds exhibited potent antibacterial potential against any of the strains tested. However, most of the compounds exhibited good to moderate antifungal potential against *Candida* strains while compounds **7g** and **7j** emerged as potent antifungal agents against sensitive as well as resistant *Candida* strains. Non-toxic nature as well as preliminary antifungal data advocates the potential of these compounds to be carried forward for further structural optimization and pharmacological investigations.

CHAPTER 8: This chapter deals with the synthesis of isatin-triazole hydrazones and evaluation of their antimicrobial potential. It was found that these compounds did not exhibit potent antifungal potential against any of the strains tested. Moreover, four compounds (**9a, 9c, 9g** and **9i**) exhibited potent antibacterial activity against *S. pneumoniae*, *E. faecalis* and *K. pneumoniae* strains. ADME profiling of these compounds indicated their drug-like characteristics. Further, non-toxic nature and potency of these compounds indicated that these compounds can be carried forward for further structural optimization.

In summary, It can be concluded that a total of **One hundred fifty-three (153)** compounds have been synthesized, characterized and evaluated for antimicrobial activities. Out of all these compounds, twenty-one compounds were endowed with remarkable biological activity which can be carried forward for further structural optimization and pharmacological investigations.