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Topic of Research: **Rationale Design and Synthesis of Some Heterocyclic Compounds as Potent Antimicrobial Agents**

Keywords: Heterocyclic, antimicrobial azole, sulfonamide, bacterial infections, synergistic effect.

FINDING

The present Ph.D. thesis work focuses on the structure-based design of new therapeutic and non-toxic small molecules using computational biology (in-silico) tools followed by chemical synthesis and biological evaluations. For drug design, in-silico tools such as AutoDock Vina, Discovery Studio, PyMol, etc. were used. The designed compounds were synthesized using multi-step organic synthetic protocols. The thesis successfully delivered new structurally diverse small molecules based on azoles and sulphonamide. The developed molecules demonstrated their potential therapeutic ability as antimicrobials. The present research work, published in peer reviewed journals of scientific repute such *Journal of Molecular Structure* and *Chemistry Select*. The thesis comprises five chapters including the first chapter as an introduction Second chapter includes the material and method used to carry out this research work. and the rest are experimental works.

Chapter 1 summarizes the general introduction, causes and treatment of bacterial infection. Besides heterocyclic compounds as antimicrobial agents are discussed in detail.

Chapter 2 includes the material and method used to carry out this research work. This chapter describes the details of chemicals and instruments used along with the details of the synthetic procedures used in reaction scheme are also included in this chapter.

Chapter 3 discusses synthesis and antimicrobial evaluation of isoxazole-triazole conjugates. A series of novel isoxazole-1,2,3-tiazole conjugates (8a-q) was synthesized through azide alkyne Huisgen cycloaddition reaction. The proposed structures were confirmed by elemental

analysis, FT-IR, 1H, 13C NMR and mass spectral data. 8b and 8m exhibited better antibacterial activity towards particular bacterial strains and showed no cytotoxicity against human cells (HEK293) even at higher concentrations. Compound 8m showed significant inhibition potential against E. coli biofilm formation. Compound 8m was further evaluated for DNA binding ability to probe its possible mode of action. Various spectroscopic, and electrochemical further corroborated with the experimental results. Furthermore, in silico ADME profiling of all the final compounds and molecular docking of the potent compound was performed with DNA to support in-vitro data.

Chapter 4 comprises synthesis, characterization and antimicrobial evaluation of 1,2.4 oxadiazole-sulfonamide conjugates. The title compounds 8a-8m were obtained through a multistep synthetic approach. Among them, compound 8d displayed notable inhibitory activity, with minimum inhibitory concentration (MIC) values of 64 µg/ml /ml observed against the Gram-positive bacteria *Staphylococcus aureus* and *Enterococcus faecalis.*

Chapter 5 discusses design, synthesis and biological evaluation of compounds 5a-5j Benzimidazole-sulfonamide conjugates inhibited bacterial strains with the zone of inhibition values ranging from 8-11 µg/ml at MIC value. Notably, the most significant ZOI measurements were obtained against B. subtilis and E. coli with the test compound. It was found compound 5f has remarkable antimicrobial activity.

Overall, these chapters highlight the development of various novel molecules with significant potential for the treatment of bacterial infections.