Chapter VI

Conclusion

This investigation was undertaken to design potential inhibitors against *Mycobacterium tuberculosis* (MTB) cell wall enzymes using *in-silico* and *in-vitro* methodologies. Specifically, the goal was to identify novel inhibitors that target enzymes within the Mtb cell wall and to develop new medications for antimycobacterial therapy. To achieve this, molecular docking and molecular dynamics simulations were employed to screen chemical databases such as ChemSpider, Drug Bank, and Zinc databases for potential inhibitors against *MmpL*, *GlfT2*, and *MurB* enzymes. In total, fourteen compounds were discovered, with seven identified as effective against *GlfT2* and another seven against *MurB*. However, none of the compounds were found to be effective against the target enzyme *MmpL*.

To investigate the behavior of the compounds targeting *GlfT2* and *MurB*, MDS studies were conducted. These investigations involved studying conformational changes in the ligand within the active site residues and analyzing their molecular interactions through molecular dynamics (MD) simulation. The results suggest that the compounds maintained stability within the active site of the target enzymes and exhibited consistent interactions throughout the simulation. Based on their stability, consistent interaction, and availability, the most stable compounds were selected for *in-vitro* validation, with two compounds each tested against *GlfT2* and *MurB*.

Notably, the identified compounds in this study had not been reported before, and the study represents the first report of these compounds against drug-resistant

Mycobacterium tuberculosis. These initial compounds with leading properties can lay the groundwork for subsequent alterations and extensive efficacy research, with the potential to lead to the development of novel medications for combating antimicrobial agents against resistant Mtb. Additionally, inhibitors designed for *GlfT2* and *MurB* may also prove effective against other MTB cell wall enzymes.

In conclusion, the results of the present study are promising and provide evidence for the efficacy of the identified compounds against virulent strains of *Mycobacterium tuberculosis* and highlight the potential of structure-based screening combined with *in-vitro* testing as an effective method for evaluating antitubercular compounds. For the development of future anti-mycobacterial medicines, further *in vivo* studies are needed.