Abstract No: PP-02

Computational investigation of novel Curcumin derivatives as anti -Tuberculosis agents

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Tuberculosis (TB) remains a major global health burden, necessitating the development of novel and effective anti-TB drugs. Curcumin a naturally occurring compound found in turmeric has shown potential as an antimicrobial agent, including activity against *Mycobacterium tuberculosis* the causative agent of TB. In this computational study, the potential of natural derivatives of curcumin as anti-TB drugs was investigated using molecular docking studies and molecular dynamics (MD) simulations. Bedaquiline was used as the reference drug. Using Auto Dock 4.2, molecular docking studies were performed to predict the binding affinities and binding modes of a library of curcumin derivatives with the selected TB targets. The outcomes of the molecular docking studies showed that numerous curcumin derivatives have high affinity for the targeted proteins: Decaprenylphosphoryl-β-D-ribose oxidase protein, Dihydrofolate reductase protein, Enoyl- {acyl-carrier protein} reductase (NADH) protein, InhA 4,3-oxoacyl-(Acyl-carrier-protein) reductase protein, Pantothenatekinaseprotein, UDP-N-Acetylmuramoyl-L-Alanyl-D-Glutamate-2,6 Diaminopimelateligase protein. Insights into prospective curcumin derivatives' modes of action as long-term control drugs were offered by the docking scores and interaction profiles. The key interactions influencing the binding process were also understood by investigation of the binding modes. The stability and dynamic behaviour of the chosen curcumin derivatives in complex with the TB targets were examined using MD simulations. These simulations allowed for the long-term study of conformational changes, flexibility, and stability of the derivatives of curcumin within the binding pockets of TB targets. Understanding the dynamic behaviour and interactions of the curcumin derivatives with TB targets was made possible by MD simulations. Root mean square deviation (RMSD) and root mean square fluctuation (RMSF) are two metrics used to assess stability. The results of the docking were supplemented by information from the MD simulations, providing a thorough insight into the binding modes and stability of the curcumin derivatives. By estimating binding affinities through the use of Auto Dock's advanced scoring methods, it was possible to calculate binding free energies and it revealed that all derivatives except one have good binding affinities with the studied proteins. It helped to reveal that the studied natural derivatives clarify the relative potency and selectivity of the derivatives for the tuberculosis targets. In conclusion, the computational findings of this study suggest that natural derivatives of curcumin hold promise as anti-TB drugs. These findings provide a basis for further experimental investigations and optimization of the identified curcumin derivatives as potential candidates for the development of novel anti-TB drugs.

Keywords: Tuberculosis, Curcumin, Derivatives, Molecular docking, Molecular dynamics simulation