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Computational assessment of novel derivatives of Epigallocatechin gallate as potential anti-Tuberculosis agents

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Tuberculosis (TB) is a highly contagious bacterial infection caused by *Mycobacterium tuberculosis*. This research focuses on the computational assessment of novel derivatives of Epigallocatechin Gallate (EGCG) as potential anti-TB agents. Through the utilization of molecular docking studies using AutoDock 4.2 and molecular dynamics (MD) simulations employing GROMACS, this study aims to explore the therapeutic potential of these EGCG derivatives. Specific molecular targets associated with TB, including Pantothenate kinase, UDP-N-acetylmuramoyl-l-alanyl-d-glutamate-2,6-diaminopimelate ligase, 3-oxoacy-(Acyl-carrier-protien) reductase, Decaprenylphosphoryl-β-D-ribose oxidase, Dihydrofolate reductase, Enoyl-[acyl-carrier-protein] reductase (NADH) were selected for investigation. Bedaquiline, an approved tuberculosis medication, was utilized as a benchmark molecule for validation purposes. By conducting molecular docking studies, strong binding affinities were observed between certain EGCG derivatives and the targeted tuberculosis proteins. To gain insights into the stability, dynamic behaviour, and conformational changes, MD simulations were performed using GROMACS, which allowed for extended-time observations of the EGCG derivatives within the binding pockets of the TB targets. Evaluation of stability parameters, such as root mean square deviation (RMSD) and root mean square fluctuation (RMSF) complemented the docking results, providing a comprehensive understanding of the binding modes and stability of the EGCG derivatives. Furthermore, the calculation of binding free energies using advanced scoring functions from AutoDock facilitated the estimation of binding affinities, thus aiding in the assessment of relative potency and selectivity of the derivatives towards the TB targets. The reference drug Bedaquiline, known for its effectiveness against TB, was also included in the comparative analysis. In conclusion, this computational study highlights the promising potential of EGCG derivatives as long-term control medications for TB. The integration of molecular docking, MD simulations, binding free energy calculations, and interaction studies provided valuable insights into the binding affinity, stability, selectivity, and delivery optimization of these derivatives. These findings significantly contribute to the field of computational drug discovery and pave the way for future experimental investigations and optimization of EGCG derivatives as highly effective long-term control medications for tuberculosis.

Keywords: Molecular Docking, EGCG, Derivatives, Tuberculosis, Molecular Dynamics