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Computational investigation of the effect of natural derivatives of Curcumin as anti-Asthma drugs

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Asthma, a chronic respiratory disease, necessitates long-term control medications to manage symptoms and maintain stable control. However, the search for novel therapeutics with improved efficacy and reduced side effects remains ongoing. This computational study focused on exploring the potential of curcumin derivatives as long-term control medications for asthma. Key molecular targets implicated in asthma pathogenesis, Interleukin-4, Interleukin-13, Nuclear factor kappa B (NF-κB), Tumor necrosis factor-alpha (TNF-α), Signal transducer and activator of transcription 6 (STAT6), Phosphoinositide 3-kinase (PI3K), Transforming growth factor-beta (TGF-β), Peroxisome proliferator-activated receptor gamma (PPAR-γ) and Cyclooxygenase-2 (COX-2), were selected for investigation. A library of Curcumin derivatives was designed, and molecular docking experiments were conducted using Auto Dock 4.2 to predict the binding affinity and binding modes of the derivatives with the selected asthma targets. Montelukast was used as the reference drug, which is a medication commonly used in the long-term control of asthma and the management of seasonal allergies. The results of the molecular docking revealed strong binding affinities of several curcumin derivatives towards the targeted asthma proteins: Nitro-curcumin, Cyclo-curcumin, and Desmethoxycurcumin (DMC). The docking scores and interaction profiles provided insights into the potential mechanisms of action of the curcumin derivatives as long-term control medications. Additionally, analysis of the binding modes offered understanding regarding the key interactions driving the binding process. Molecular dynamics (MD) simulations were performed to investigate the stability and dynamic behaviour of the selected curcumin derivatives in complex with the asthma targets. These simulations enabled the observation of conformational changes, flexibility, and stability of the curcumin derivatives within the binding pockets of the asthma targets over extended time scales. Evaluation of stability was conducted using parameters such as root mean square deviation (RMSD) and root mean square fluctuation (RMSF). The information gained from MD simulations complemented the docking results, offering a comprehensive understanding of the binding modes and stability of the curcumin derivatives. Calculating binding free energies using advanced scoring functions provided by Auto Dock allowed the estimation of binding affinities, aiding in understanding the relative potency and selectivity of the derivatives towards the asthma targets. In conclusion, this computational study demonstrated the potential of curcumin derivatives as long-term control medications for asthma. This computational investigation has allowed for further experimental investigations and optimization of curcumin derivatives as effective long-term control medications for asthma.

Keywords: Asthma, Computational chemistry, Curcumin derivatives, Molecular docking, Molecular dynamics