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Computational thermodynamics of Spilanthol as a COX-2 inhibitor: Docking, dynamics, and binding energy analysis

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Spilanthol, a bioactive compound from *Acmella oleracea*, has been evaluated for its potential as a COX-2 inhibitor through computational methods. The study utilizes Lipinski's rule of 5, Molinspiration scoring, molecular docking, MM-GBSA/MM-PBSA calculations, and molecular dynamics simulations to assess Spilanthol's drug-likeness, binding affinity, and interaction stability with COX-2. Spilanthol meets several criteria of the Lipinski rule, indicating favorable drug-like properties. The Molinspiration analysis reveals that Spilanthol has significant enzyme inhibition potential, though it is less effective against other targets such as GPCRs and kinases. Molecular docking results demonstrate a strong binding affinity with COX-2, evidenced by a binding energy of –7.50 kcal/mol and an inhibition constant of 3.21 μM. MM-GBSA/MM-PBSA calculations further support these findings with negative binding energies, indicating stable interactions. Molecular dynamics simulations highlight significant conformational changes in COX-2 upon Spilanthol binding, as reflected by alterations in RMSF values. These results suggest that Spilanthol effectively binds to and inhibits COX-2, offering it as a potential natural anti-inflammatory agent. The compound's interaction profile and stability within the COX-2 active site emphasizes its promise for development as an alternative to synthetic COX-2 inhibitors, and which may be offered as an alternative to synthetic COX-2 inhibitors, though further experimental validation is needed.

Keywords: Spilanthol, COX-2, Molecular docking, MM-GBSA, Molecular dynamics, Lipinski rule