

Title: In silico analysis of potential inhibitors for breast cancer targeting 17 β -hydroxysteroid dehydrogenase type 1 (17 β -HSD1) catalyses

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Abstract: Breast cancer (BC) is still one of the major issues in world health, especially for women, which necessitates innovative therapeutic strategies. In this study, we investigated the efficacy of retinoic acid derivatives as inhibitors of 17 β -hydroxysteroid dehydrogenase type 1 (17 β -HSD1), which plays a crucial role in the biosynthesis and metabolism of oestrogen and thereby influences the progression of BC and, the main objective of this investigation is to identify the possible drug candidate against BC through computational drug design approach including PASS prediction, molecular docking, ADMET profiling, molecular dynamics simulations (MD) and density functional theory (DFT) calculations. The result has reported that total eight derivatives with high binding affinity and promising pharmacokinetic properties among 115 derivatives. In particular, ligands 04 and 07 exhibited a higher binding affinity with values of -9.9 kcal/mol and -9.1 kcal/mol, respectively, than the standard drug epirubicin hydrochloride, which had a binding affinity of -8.2 kcal/mol. The stability of the ligand-protein complexes was further confirmed by MD simulations over a 100-ns trajectory, which included assessments of hydrogen bonds, root mean square deviation (RMSD), root mean square Fluctuation (RMSF), dynamic cross-correlation matrix (DCCM) and principal component analysis. The study emphasizes the need for experimental validation to confirm the therapeutic utility of these compounds. This study enhances the computational search for new BC drugs and establishes a solid foundation for subsequent experimental and clinical research.

Keywords: DFT calculation; Breast cancer; In silico studies; Molecular docking; Molecular dynamics simulation; Pass prediction; Retinoic acid.

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