Computational Design of a Novel Disulfide-Bond Based Prodrug IMQ-S-S-IMQ for Breast Cancer Therapy

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Abstract

Disulfide bond-based prodrugs have unique properties like targeted cancer therapy and drug delivery systems and are crucial to the modern drug development process. The drugs also improve pharmacokinetics, antitumor activity, and safety profiles by encouraging prodrugs to self-assemble into stable nanoparticles, increasing drug loading capacity, and lowering reliance on excipients. Here, a disulfide bond-based small molecule was chosen for the treatment of breast cancer management. In this work, Imiquimod is a hydrophobic anticancer drug that has been selected for the designing of disulfide bond-based prodrug. Imiquimod-S-S-Imiquimod (IMQ-S-S-IMQ) was designed and performed for Molecular Docking with the protein. Following this, Binding Free Energy, Molecular Dynamics Simulation, and ADME prediction were carried out. The results revealed that the designed IMQ-S-S-IMQ prodrug has shown a favorable docking score along with a number of molecular interactions, greater binding affinity, stability, and acceptable pharmacological properties compared to the native Imiquimod ligand. Based on the result, it is inferred that the designed IMQ-S-S-IMQ prodrug could be suitable for the development of an anticancer drug against breast cancer. Furthermore, this drug will be useful for experimental validation, including in vitro and in vivo studies.

Keywords: ADME properties, Breast Cancer, Disulfide bond based prodrug, Imiquimod, Molecular Docking, Molecular Dynamics Simulation