In Silico Screening of Novel Phytochemicals as Modulators of Cytochrome P450 3A4 in Cancer Therapy

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Abstract

1. One of the primary goals in the treatment of cancer is the development of novel therapies with greater sensitivity and reduced resistance. In this context, CYP3A, a key enzyme of drug metabolism is recognised as an attractive drug target to improve efficacy of cancer therapeutic regimens. This work aimed to identify new phytochemical CYP3A4 modulators by employing an *in silico* approach.
2. A comprehensive screening of diverse phytochemical repositories was conducted using molecular docking and pharmacokinetic analysis to evaluate their potential as CYP3A4 modulators. Additionally, Desmond software with the OPLS-2005 force field was used to perform molecular dynamics simulations.
3. The identified subset of potential modulators include Ajmalicine, Velbanamine, Cathenamine, Perivine, Triptolide, and Triptonide with respective binding energies of -9.9 kcal/mol, -10 kcal/mol, -9.8 kcal/mol, -10 kcal/mol, -9.8 kcal/mol, and -10.4 kcal/mol. Among these, Ajmalicine and Velbanamine demonstrated great potential because of their stable binding with CYP3A4, mostly via van der Waals and Coulombic interactions.
4. These identified CYP3A4 modulators may improve drug efficacy and reduce drug resistance. These results collectively offer a firm foundation for subsequent preclinical research and experimental verification in the context of cancer treatment.

Keywords: Cancer therapy, CYP3A4, drug resistance, phytochemical, molecular docking, Molecular Dynamics (MD)