A Computational Study of Cyp26A1 Enzyme as a Potential Target for Therapeutic Applications

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Abstract

CYP26A1 is the principle all-trans retinoic acid (ATRA) metabolizing enzyme. inhibiting CYP26A1, is proven to be beneficial in Wound healing, Psoriasis, Osteoarthritis, and cancer. Designing novel inhibitors necessitates the knowledge of CYP26A1 binding interactions but a crystal structure of CYP26A1 is yet to be resolved thus a homology model of CYP26A1 based on CYP120A1 (34% identity) was built utilizing Molecular Operating Environment (MOE), Swiss model, and Galaxy model refine, the model had an RMSD of 0.8 Å with the template. The model was validated by docking ATRA and known inhibitors. Binding energies ranged between −8.0 and −12 kcal/mol. ATRA's C-4 was the closest to the heme's iron in agreement with experimental data. A pharmacophore hypothesis was built and used to screen 2083 Food and drug administration (FDA) drugs. The 50 drugs that passed the screen including Bexarotene and Adapalene were docked in the model, and three FDA drugs Ivacaftor, Fenofibric

Acid, and Omeprazole were found as potential inhibitors of CYP26A1. The three drugs can be in-vitro tested to evaluate their inhibition potency of CYP26A1, also the homology model and pharmacophore hypothesis built in this study can be used to screen large databases to find novel potent and selective inhibitors of CYP26A1.

Keywords: Comparative modeling, CYP26A1 enzyme, Molecular docking, Retinoic acid metabolism blocking agents (RAMBAs)