

TARGET IDENTIFICATION OF HIV RELATED
GANODERIC ACIDS USING MOLECULAR DOCKING

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ABSTRACT

Four Ganoderic acids (A, B, C1, H) were studied using molecular docking approach. Both reverse molecular docking and molecular docking were combined to elucidate suitable target(s) for these Ganoderic acids. Outcomes from molecular docking were compared and correlated to experimental data. Compound with the best performance in both molecular docking and correlation analysis were further studied by looking at its molecular interaction with potential target. 1HVR (a type of HIV-1 protease) and Ganoderic acid B performed better in cluster analysis of molecular docking compared to other compounds. Similar trend to experimental data obtained from el-Mekkawy and co-workers (el-Mekkawy et al. 1998) were also observed. Molecular interaction study revealed Ganoderic acid B interactions with ILE50 and ILE50' residues. These two residues have been identified as important residues and play important roles in ligand-protein interaction in HIV-1 protease (Lebon and Ledecq 2000). These interactions not only suggested HIV-1 protease in general is a suitable target for ganoderic acid B, they also indicated a huge potential for HIV drug discovery based on this compound.

ABSTRAK

Empat jenis asam Ganoderik (A, B, H, C1) telah dipelajari dengan menggunakan pendekatan docking molekuler. Kedua-dua jenis docking molekuler yaitu docking molekuler berbalik dan docking molekuler digabungkan untuk mengenal pasti target yang sesuai untuk asam-asam Ganoderik ini. Hasil dari docking molekuler dibandingkan dan dikorelasikan dengan data yang didapatkan melalui eksperimen. Senyawa dengan prestasi terbaik di kedua-dua docking molekuler dan analisis korelasi dikaji lebih terperinci dengan melihat interaksi diperingkat molekuler. 1HVR (sejenis HIV-1 protease) dan asam Ganoderik B didapatkan memiliki keputusan analisis kelompok docking molekuler yang lebih baik dibandingkan dengan senyawa yang lain. Trend G juga didapatkan sesuai dengan data eksperimen yang diperoleh dari el-Mekkawy dan rakan kerja (el-Mekkawy et al. 1998). Kajian interaksi molekuler mendedahkan asam Ganoderik B berinteraksi dengan residu ILE50 dan ILE50'. Kedua-dua residu ini telah dikenal pasti sebagai residu penting dan memainkan peranan besar dalam interaksi ligan-protein HIV-1 protease (LebondanLedecq 2000). Interaksi ini tidak hanya mengesahkan HIV-1 protease pada umumnya merupakan target yang sesuai untuk asam Ganoderik B, ia juga menunjukkan potensi yang sangat besar bagi penemuan ubat HIV berdasarkan senyawa ini.

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LIST OF SYMBOLS AND ABBREVIATIONS

G : free binding energy

Å : Angstrom

RMSD : root mean square deviation

IC₅₀ : Half inhibitory concentration

1HVR : A type of HIV-1 Protease

1DIF : A type of HIV-1 Protease