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Docking studies of the Cannabinoids derivatives in O- GlcNAc Transferase (OGT) as anti-cancer candidates

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Highlights

Molecular docking is a method that analyzes the conformation and orientation of molecules into the binding site of a macromolecular target. Poses that could be taken are generated by search algorithms and ranked by scoring functions. Some well-known examples of software developed over the past few decades are AutoDock, AutoDock Vina, DockThor, GOLD, FlexX, and Molegro Virtual Docker. In this study we aim to use GOLD software in order to generate distance restraints, which greatly increase protein-small molecule docking accuracy. The visualization is very important to assess cannabinoids binding site, specificity and affinity on OGT protein.

Resumo/Abstract

O-GlcNAc Transferase (OGT) is an enzyme that transfers N-acetylglucosamine from UDP to serines and threonines in cytoplasmic, nuclear, and mitochondrial proteins. Most human malignancies exhibit increased OGT expression, and OGT inhibition reduces cancer cell proliferation. Several chemical classes were tested as OGT inhibitors. Around of that, cannabinoid derivative THC demonstrated a potent inhibitory activity against this target.

Cannabinoids have been shown to be beneficial in the treatment of several diseases. High-thickness tetrahydrocannabinol (THC) may be useful for reducing chemotherapeutic drug resistance. Treatment with CBD has been demonstrated to promote apoptosis and autophagy in various cancer cells. One of the most prevalent diseases in the world and a leading cause of mortality globally is cancer. Over the past 50 years, more innovative treatments and targets have been created, yet the incidence of cancer fatalities has continued to climb.

For a better understanding the cannabinoids derivatives interactions with OGT structure, were performed docking studies between with crystal structure (4GZ3) and cannabinoids derivatives THC and CBD.

The docking results showed that CBD and THC exhibit the same interactions as the co-crystalized ligand where the same residues are involved: Histidine at 498, Leucine at 653 and Histidine at 920. CBD has RMSD of 0.17 and a score of 8.44. THC has an RMSD of 0.24 and a score of 8.18. The interactions are mostly H-bonds and Van der Waals forces. The pharmacophoric features were determined including HB donors, HB acceptors and hydrophobic features. Future work will be focused to select new cannabinoids derivatives with OGT inhibitory activity.

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