MOLECULAR MODELING OF CANNABINOID BINDING TO THE CB1 RECEPTOR: COMPARING CANNABIS SATIVA AND SYNTHETIC CANNABINOIDS

MODELAGEM MOLECULAR DA LIGAÇÃO DE CANABINOIDES AO RECEPTOR CB1: COMPARANDO) O THC E CANABINOIDES SINTÉTICOS

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Introduction:This study conducted a comparative theorical molecular modeling analysis of tetrahydrocannabinol (THC), the primary active compound in *Cannabis sativa*, and synthetic cannabinoids (SCs) reported by the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) from 2008 to 2022 between 2009 and 2022.The objective was to study aims to analyze the interactions of these compounds with the type 1 cannabinoid receptor (CB1), which is responsible for many of the psychoactive effects of cannabis and its synthetic analogues. Using computer simulations, we sought to identify the differences and similarities in binding affinity and molecular conformations, contributing to a better understanding of the clinical and toxicological impacts of synthetic cannabinoids compared to THC. **Methodology**: In this research, we carried out molecular docking simulations to investigate the interactions between THC and the CB1 cannabinoid receptor, as well as synthetic cannabinoids. We selected compounds described between 2008 and 2022, excluding those unavailable on PubChem. We used the crystallized three-dimensional structure of the Cannabinoid Receptor type 1 (CB1), using the code 5TGZ obtained from the Protein Data Bank (PDB). The structural files of the ligands were extracted from PubChem. The simulations were performed using AutoDock 4 software, targeting the active site of CB1 with a 21 Å grid box centered at coordinates (43.60, 27.40, 318.50. **Results**:The molecular docking results indicate that several compounds have a stronger binding affinity for the CB1 receptor compared to THC (control compound), with EG-018, BB-22, JWH-307 and APINACA standing out. EG-018 exhibited the highest binding affinity, highlighting its potential as a highly potent CB1 ligand. Compounds such as APINACA and BB-22 also exhibited high binding efficiency. The constant spread of synthetic cannabinoids poses a significant challenge due to the unpredictability of their side effects. The results of this study suggest that many SCs have a higher binding affinity for CB1 compared to THC, which may result in more intense and unpredictable clinical and toxicological effects. **Conclusion:** A detailed understanding of the molecular interactions of SCs is fundamental to mitigating their risks and developing safer and more effective therapeutic strategies

Keywords: Molecular interactions, Computer simulation, Drugs synthetic, Bioinformatics