1st INTERNATIONAL SYMPOSIUM of DOHaD and Pandemic: LESSONS FROM COVID-19
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1º SIMPÓSIO INTERNACIONAL de DOHaD e Pandemia: LIÇÕES DO COVID-19
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IDENTIFICATION OF GLUCAGON-LIKE PEPTIDE-1 RECEPTOR LIGANDS AND THEIR IMPACTS IN THE TREATMENT OF TYPE 2 DIABETES

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Diabetes mellitus is a chronic disease responsible for one of the world's most common public health problems. Its prevalence, comorbidities, and medical costs assume a dramatic scale and an efficient response to these projections is the intensified search for new agents and approaches. Therefore, for the development of potential glucagon-like peptide-1 receptor (GLP-1R) agonists, a virtual screening technique based on molecular docking using the crystallographic structure of human GLP-1R as a target was employed in two product libraries natural, Zinc15 and Sigma-Aldrich. The structure of the protein (PDB id 6X1A) bound to Pfizer compound PF-06882961 was modeled by homology. The best-presented model was inserted into a lipid bilayer and subjected to structure minimization, redocking, virtual screening, and molecular dynamics simulations. After simulations, 39 molecules were selected and analyzed by predicting bioactivity and pharmacokinetics resulting in 4 ligands (Zinc1901002, Zinc1901002m, 336188752 e 336185530). The ligands were inserted into the 6X1A crystallographic structure to analyze the conformational changes and the stability of protein-ligand interactions through molecular dynamics simulations for 50 ns. We observed that the ligands coupled to GLP-1R remained stable without conformational changes throughout the simulation, indicating that the selected ligands can act as potential GLP-1R agonists.

Keywords: Type 2 Diabetes Mellitus, Glp-1r, Virtual Screening

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