USE OF MOLECULAR DOCKING STUDIES TO COMPREHEND THE NOX INHIBITION AND TO DESIGN NEW COMPOUNDS APOCYNIN DERIVATIVES

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NADPH oxidase (NOX) is a multienzyme complex that generates some reactivity oxygen species (ROS), as superoxide anion, and it is involved in diabetes, inflammatory and vascular diseases, such as atherosclerosis and hypertension. Apocynin (1-(4-hydroxy-3-methoxyphe-nyl) ethanone) is a NOX inhibitor, which acts by blocking NOX assembly (between p47phox and p22phox). New apocynin derivatives may be a potential inhibitor of NOX with a potential use as therapeutic agent to treat diseases associated with the NOX enzyme. Molecular docking studies are computational procedures used as a key process to understanding the molecular interactions between ligands and the amino acid residues of active site of enzyme. In this study, we performed docking of apocynin and two derivatives on p47phox aiming to understand the ligand-enzyme interactions and to design new bioactive agents. Apocynin and derivatives structures, diapocynin and chalcone, were design in Spartan 08’ for Windows software and submitted to geometry optimizations using DFT/B3LYP 6.31G* method. The optimized chemical structures were submitted to docking analysis. The structure of enzyme p47phox (autoinhibited form) was downloaded from Protein Data Bank (code PDB 1NG2). The p47phox were prepared using the Autodock Tools (v.1.5.6).The blind docking was performed using SwissDock website and this software was used to determine the principal ligand-enzyme sites of interaction. DockThor website was used to perform rigid molecular docking of compounds and p47phox, and also to complement the results obtained with SwissDock. The results allowed identifying two interaction locals in 1NG2 structure, the SH3B and SH3A. DockThor results showed that apocynin and chalcone are binding in the same amino acid residues (ARG 140, PRO 144), and a different position of diapocynin. Therefore, chalcone is able to fit into the active site of 1NG2, having similar binding as apocynin and it could be studied as a potential p47phox inhibitor.

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