Chemical descriptors and pancreatic lipase (1LPB) inhibition by natural products: A DFT investigation and molecular docking prediction against obesity

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Code CCP13

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Introduction & Objectives: Commonly, the natural products are of great importance due to their biological activities. There is a growing significance in developing drugs by using natural products; suggesting an immense possibility of new routes for therapeutic candidates,[1–2] which possess vast chemical diversity and giving rise to great potential to discover different types of bioactive compounds.[3] Biologically active natural products should offer selective ligands for targets in relationship with different diseases.[7] The docking studies were performed to analyze the binding affinities and the mode of interactions of the human pancreatic lipase enzyme 1LPB with the nine natural products as ligands which will be compared to previous works of synthesized compounds.

Methodology (Material and methods): Density functional theory (DFT) calculations were carried out on the studied molecules in water using the Amsterdam Density Functional (ADF) program. All geometries were optimized at the hybrid-type B3LYP functional. Representation of the molecular orbitals and molecular structures was done using ADF-GUI. The docking analyses of the candidate ligands Eug **1**, Ging **2**, AA **3**, Oleu **4**, Pip **5,** Hesp **6**, Quer **7**, Lute **8** and Cur **9** with human pancreatic lipase protein (1LPB) were carried out using the AutoGrid and AutoDock programs (version 4.2.6) implemented in AutoDockTools (ADT 1.5.6) software.The 1LPB protein was cleaned by removing all water molecules, ligands, and ions using UCSF Chimera (ver 1.10.2). The docked receptor and ligand interactions were visualized using CHIMERA (UCSF) BIOVIA Discovery studio visualizer (version 1.10.2).

Results and Discussion:

The biological activity predictions are based on the global and local chemical descriptors, namely, HOMO-LUMO gaps. The frontier orbitals offer a deeper insight concerning the electron-donor acceptor capabilities, whereas, the local descriptors resulting from Fukui functions put emphasis on the active sites of different candidate ligands.

Conclusion: The molecular docking was performed in order to compare and identify the inhibition activity of the natural candidate ligands against pancreatic lipase which were compared to that of synthesized ones.

Keywords: Binding free energy, chemical descriptors, Fukui functions, molecular docking,

Références bibliographiques

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