Pharmacokinetics and drug-likeness of antidiabetic flavonoids: Molecular docking and DFT study

Abstract

The pharmaceutical industry became interested in computer-aided toxicity and pharmacokinetic prediction studies as a substitute method of predicting possible medication candidates. SwissADME, Pro Tox II, vNN, and ADMETlab web tools were used in this investigation to analyze the in-silico pharmacokinetic properties (ADME), drug-likeness, and toxicity pro-files of sixteen antidiabetic flavonoids with optimal bidentate chelating sites for metal ion coordination. Quantum chemical descriptors of the substances were also computed using density functional theory (DFT) calculations. Additionally, investigations using molecular docking against human alpha amylase were carried out. The outcomes were contrasted with those of the control medications, acarbose and metformin. With the exception of myricetin, all flavonoids were found to follow Lipinski's rule of five regarding their drug-like molecular nature, according to the results of the drug-likeness prediction. Chrysin, wogonin, genistein, baicalein, and apigenin demonstrated the best absorption profile pharmacokinetically, with an HIA value of approximately 30%, in contrast to the other flavonoids. It was projected that quercetin, ellagic acid, eriodyctiol, butein, baicalein, and fisetin would exhibit carcinogenicity. All of the flavonoid derivatives taken into consideration in this work are expected to be good candidates for CYP3A probes, with the exception of eriodyctiol, which has a P-glycoprotein (p-gp) interaction. According to the toxicological endpoints prediction analysis, the median lethal dosage (LD50) values vary from 159 to 3919 mg/Kg, with butein being the only immunotoxin and baicalein and quercetin being mutagenic. The results of molecular docking studies indicated that the important amino acids Asp 197, Glu 233, Asp 197, Glu 233, Trp 59, Tyr 62, His 101, Leu 162, Arg 195, His 299, and Leu 165 had a significant interaction (-7.5 to -8.3 kcal/mol) with the studied molecules in the binding pocket of the α-amylase protein compared to the control metformin. In comparison to metformin (78.3%), chysin was expected to be a ligand with high absorption and lipophilicity, with an absorption of 84.6%. Furthermore, it was anticipated from molecular docking profiles, drug-likeness, ADMET, quantum chemistry, and drug-likeness that chrysin is a promising bidentate ligand.