PHARMACOKINETICS PREDICTION OF INDOL-THIAZOLE COMPOUNDS USING IN SILICO TOOL

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ABSTRACT

Introduction: The discovery of new therapeutic molecules can be optimized by evaluating their *in silico* properties. Pharmacokinetic evaluation represents a prediction of the efficacy and safety of compounds. This validation is important for the early elimination of unsuitable compounds and the optimization of those with greater therapeutic potential. In this context, indole-thiazole derivatives have aroused increasing interest in medicinal chemistry due to their structural versatility and broad biological activity. Thus, the development of drugs from these compounds becomes relevant for therapeutics. **Objective**: To evaluate through *in silico* study the pharmacokinetic properties of new indole-thiazole derivatives, in order to investigate their absorption, distribution, metabolism and excretion (ADME) characteristics, aiming to identify promising molecules for the development of new drugs. **Methodology:** The pharmacokinetic analysis of the ten molecules of the LPSF/TH series, indole-thiazole derivatives, was performed using the SwissADME software (swissadme.ch). Critical parameters such as gastrointestinal permeability, blood-brain barrier (BBB) permeability, plasma protein binding and potential interaction with CYP450 metabolic enzymes were examined. In addition, the evaluation included the drug-likeness profile, considering rules such as Lipinski, Ghose, Veber, Egan, Muegge, and the identification of possible PAINS (Pan-assay interference compounds) compounds, in order to avoid false positives. **Results and Discussion:** The results indicate that all ten molecules of the LPSF/TH series present high gastrointestinal absorption, suggesting their viability for oral administration. In addition, the molecules demonstrated potential to cross the blood-brain barrier (BBB), which makes them promising for acting in the central nervous system (CNS). They were not identified as P-gp substrates, suggesting a greater chance of action in the CNS, since they would not be efficiently expelled by this efflux mechanism. Regarding lipophilicity, log Po/w values ranged from 3.23 to 4.54, suggesting moderate to high lipophilicity, which facilitates passage through cell membranes. In terms of drug-likeness parameters, the molecules complied with the main rules, such as those of Lipinski, Ghose, Veber, Egan and Muegge, and were not identified as potential PAINS (Pan-assay interference compounds), which reduces the risk of false positives in future biological tests. These results suggest that the compounds have favorable pharmacokinetic characteristics, making them promising candidates for the development of new drugs targeting the CNS. **Conclusion:** The series of compounds analyzed demonstrated a favorable predictive pharmacokinetic profile, with good bioavailability and properties indicative of ease in crossing the blood-brain barrier. These results highlight the potential of the compounds for therapeutic use in the central nervous system. However, further studies are needed to further understand the pharmacokinetic characteristics and to validate its potential in future clinical applications.