Computational Predictions in the Design of Affinity-Based Drug Delivery

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Affinity-mediated drug delivery utilizes electrostatic, hydrophobic, or other non-covalent interactions between pharmaceuticals and a delivery system to extend medication release and improve treatment effectiveness. Cyclodextrin polymers, chains of glucose rings, exhibit affinity interaction; however, experimentally testing drug candidates for affinity is time-consuming, making computational predictions a more effective approach. Currently, docking programs provide predictions of affinity, but lack reliability and scalability. Quantitative structure-property relationship models (QSPRs), which analyze statistical relationships between molecular properties, appear a promising alternative. Unfortunately, previously constructed QSPRs are not publicly available, necessitating an openly accessible model. Around 600 experimental affinities between cyclodextrin and guest molecules were cleaned and imported from published research. The software PaDEL-Descriptor calculated over 1000 chemical descriptors for each molecule, which were then analyzed with R to create several QSPRs with different statistical methods. These QSPRs proved highly time efficient, calculating in minutes what docking programs could accomplish in hours. Additionally, on test sets, QSPRs reached R2 values of 0.61-0.71, compared to only 0.18 for docking. The speed, accuracy, and accessibility of these QSPRs improve evaluation of individual drugs and facilitate screening of large datasets for potential candidates in cyclodextrin affinity-mediated delivery systems.

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