Improving Affinity-Based Drug Delivery with Convenient Computational Models

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Delivering pharmaceuticals at the correct dosage to the correct site often proves an obstacle to a drug's effectiveness. Cyclodextrin polymers can localize administration and lengthen the time frame of drug release, improving treatment by exploiting affinity interactions with small drug molecules. Because experimentally testing for affinity to cyclodextrin is resource-intensive, computational models are more practical in searching for candidates. Quantitative structure-activity relationship models (QSARs) have already been created, yet these models either lack verification criteria or are inaccessible to the public. Thus, there is still a need for an open-source, approachable, fully verified model for cyclodextrin. Around 1600 experimental affinities between guest molecules and cyclodextrin were imported and cleaned from published research. The 3D structure files of the guests were run through PaDEL-Descriptor to generate over 1000 chemical descriptors, which were used to build several QSARs with the programming language R. Of the nine QSARs created, six passed verification criteria – including published standards and y-randomization – and were combined into an ensemble, which yielded an R2 of 0.69 for alpha-cyclodextrin and 0.74 for beta-cyclodextrin. To make predicting affinity of guests easier, the ensemble QSARs, a search engine for molecule structure files, and a database of predicted values for common drugs (where the user could explore potential candidates without running the model) were then integrated into a web app using R's "shiny" package. The speed, accuracy, and accessibility of the QSARs streamline the screening of potential candidates for cyclodextrin delivery systems, potentially improving treatment effectiveness in a wide variety of applications.

Awards Won:
Shanghai STEM Cloud Center: STEMCloud Award of $1800 in Engineering Mechanics
American Statistical Association: First Award of $1,500
King Abdulaziz &amp
his Companions Foundation for Giftedness and Creativity: Award of $1500 in Intelligent-Based Solutions in Cyber-security