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Editorial

Recent Advances in Multi-Task QSAR Modeling for Drug Design

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Computer-aided drug design may provide a massive scope to reduce the overall duration as well as the expenditure associated with drug discovery.[1-2] Although the concept of Quantitative Structure Activity Relationship (QSAR) is almost fifty years old, it is still considered as a very useful method for finding novel therapeutic agents. In the last decade, the field of QSAR has witnessed great advances in terms of techniques, ideas and approaches.[3] Multi-task QSAR is one such approach that has a huge opportunity to contribute in the discovery of novel therapeutic agents.[4] Classical QSAR techniques focus on the classical idea that one drug is aimed to act on one target. However, due to the highly complex and multi-factorial nature of some diseases like cancer, microbial infections, neurodegenerative and metabolic disorders, the classical idea of drug development frequently produces less satisfying effects. The effect of the inhibition of one specific target is compensated by different back-up or fail-safe mechanisms.[5,6] Polypharmacology focuses on the concept of simultaneous inhibition of multiple targets by single therapeutic agents. Contrary to single target drugs that bind with a specific target with high affinity, multi-target agents are low affinity binders. Therefore, management of therapy is easier for the multi-target agents.[5,7] Multi-task QSAR techniques are able to incorporate the ideas of polypharmacology. While conventional QSAR techniques are based on the datasets of compounds with a single target and same or similar assay conditions, multi-task QSAR can consider data on multiple targets and various assay conditions at a time.[8,9] In addition, multi-task QSAR techniques are also useful to address the problems of fewer data-points. QSAR is a statistical technique and a higher amount of data-points generates more reliable models. However, for several diseases the availability of a data is less and developed models on the available data may not be able to provide detailed insight into structural requirements of the molecules for higher potency. As multi-task QSAR models may be developed on the data collected from different assay conditions, more information may be retrieved for the explanation of structural patterns.[6,9] Therefore, multi-task QSAR has emerged as one of the most essential tools in the last few years and various groups of researchers participated in the development of multi-task QSAR models.[10] Though conventional 2D QSAR techniques have found several alternatives such as 3D QSAR, pharmacophore mapping as well as molecular docking, 2D-QSAR is unique in handling problems of multi-task modeling. Multi-task QSAR has been utilized for the developing models for anti-cancer,[11,12] anti-bacterial[13-17] and neuroprotective agents.[18-20] In addition, reports on multi-target modeling on kinase[6] and ubiquitine-proteosome pathways[21] are also found. Furthermore, multi-task agents are also useful for understanding structural patterns required for toxicities of nanoparticles, environmental pollutants etc.[4,22,23]

Although development of multi-task QSAR model is quite similar to conventional modeling as far as descriptor calculation and model generation are concerned, the construction and management of a dataset is quite different. In most of the cases, classification models are generated with the data by suitable machine learning tools such as Linear Discriminant Analyses (LDA), Artificial Neural Network (ANN), Support Vector Machine (SVM) etc.[4] Generally, a specific cut-off value for each system is fixed by the user to classify the data into 'sensitive, and 'non-sensitive'. Sometimes special statistical treatments, like averaging the descriptor values for specific system[11,12] and calculation of moving average,[18,21] are required for handling the complicated data. Some attempts were taken to develop regression based multi-target models.[6,13] However, there still is a debate about the actual effectiveness of multi-target QSAR modeling as the size of a data set is sometimes so increased that the model may not be properly validated by conventional approaches. Moreover, there are concerns over applicability domain of the multi-task models.[4] Nevertheless, multi-task QSAR models may provide opportunity to widen the area of QSAR studies as well as to contribute to the investigation of different emerging areas such as nanotoxicity, polypharmacology, drug repositioning, environmental safety management etc.

Conflict of Interest

The authors report no conflicts of interest.

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