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Computational Chemistry as an Artillery against Viruses

Genetic mutations (the key engine of evolution) can lead to the emergence of unwanted, drug-resistant entities. The radial distribution function (RDF), weighted by the number of valence shell electrons, is introduced as a novel and simple to calculate descriptor. Its potential has been demonstrated by the successful design of the QSAR model relating descriptors with the inhibition constant for a series of wild type HIV-1 protease inhibitor complexes. The new methodology for evaluating the influence of point mutation on the inhibition constant based on RDF will be presented.

Since the 3D structure of the main protease (3CLpro) of the SARS-CoV-2 virus has been determined, it immediately became one of the main targets in various drug repurposing and drug design projects. We combined molecular docking experiments with molecular dynamics simulations to explore the suitability of more than 25 000 molecules of microbial origin from the Natural Product Atlas as potential inhibitors of the 3CL protease. From this analysis, eight molecules with appropriate ADMET properties are suggested as potential inhibitors. These ligands can bind in the catalytic site as well as the groove between domains II and III, where they interact with a series of residues which have an important role in the dimerization and the maturation of the enzyme, suggesting potential therapeutic efficacy.

Finally, a short overview of computational chemistry potential in revealing reaction mechanisms and photophysical processes, determining bioactive molecules from plant extracts and explaining how intermolecular interactions influence phase transitions in liquid crystals will be given.