hes. This variety of sources can produce inconsistency in the data, defined as diverging activity results for the same compound against the same target. Because such inconsistency can reduce the accuracy of predictive models built from these data, we are addressing the two questions (i) how best to use data from publicly and commercially accessible databases to create accurate and predictive QSAR models; (ii) how the data from different sources (including databases as well as the scientific publications) might be mixed and matched.

Earlier we have investigated the suitability of commercially and publicly available databases to QSAR modeling of antiviral activity (HIV-1 reverse transcriptase (RT) inhibition). We presented several methods for the creation of modeling (i.e., training and test) sets from two, either commercially or freely available, databases: Thomson Reuters Integrity and ChEMBL. We found that the performances of QSAR models obtained using these different modeling set compilation methods differ significantly from each other. The best results were obtained using training sets compiled for compounds tested using only one method and material (i.e., a spec ific type of biological assay performed using specific biological material). Compound sets aggregated by target only typically yielded poorly predictive models. We discussed the possibility of «mix-and-matching» assay data across aggregating databases such as ChEMBL and Integrity and their current severe limitations for this purpose. One of them is the general lack of complete and semantic/computer-parsable descriptions of assay methodology carried by the databases of these two investigated biologically active compounds that would allow one to determine mix-and-matchability of result sets at the assay level.

Currently we develop an approach to estimate the similarity of the experimental protocols using the descriptions extracted from the scientific publications based on the text-mining. We believe, such an approach allows to create homogenous data sets for the creation of the accurate and predictive (Q)SAR models of RT inhibition, which can be further used for the design of the new HIV-1 antiretroviral chemicals and drugs.

Novel nonnucleoside inhibitors of HIV-1 reverse transcriptase inhibitors based on substituted pyrimidines

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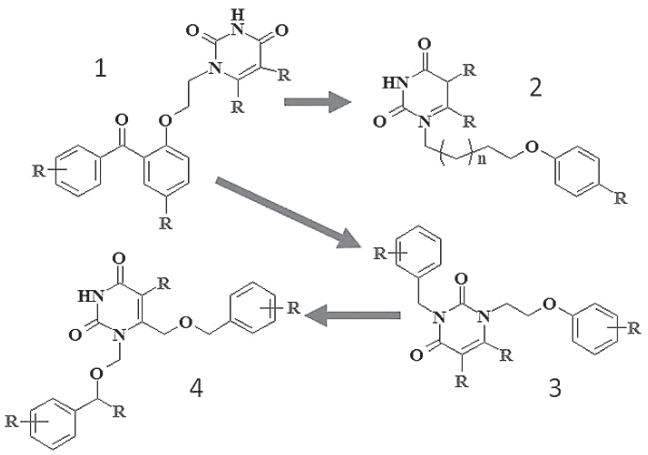
To this moment, the fact that more than 30 anti-HIV drugs were approved by FDA leads to the personification of HAART for each patient. However drug resistance is still a huge problem due to HIV high variability. Some combinations of drug-resistant mutations can make a whole class of anti-HIV drugs completely ineffective and this stimulates a search for new antiretroviral compounds. NNRTIs are a prime example of a struggle between scientific society versus drug resistance. Discovery of the second generation of NNRTIs (ETV, RPV) made possible to efficiently inhibit viral replication in case of patients with a full resistance to NVP, DLV and EFV that are usually used in the first line of HAART drug combinations.

This study was focused on a development of highly effective NNRTIs based on substituted pyrimidines. Rational drug design allows to find some new classes of compounds with high antiretroviral activity and genetic barrier to drug resistance. New highly active compounds with a benzophenone moiety (1) were obtained using the molecular hybridization paradigm. Rational drug design based on a structure-activity relationship improved IC_{50} against a wild type reverse transcriptase (WT RT) of HIV to submicromolar values (the best was 86 nM) and a study of the inhibitory activity of compounds highly active against WT RT on a panel of drug-resistant mutants of RT led to identification of lead compounds with high genetic barrier against drug resistance. Along with the development of these compounds during this study some more classes of pyrimidine-based NNRTIs were found. Compounds with IC_{50}<1μM were identified within classes of N1 (**2**), N1-N3 (**3**) and N1-C6 (**4**) substituted pyrimidines.



The search of informative biomarkers for early immunological diagnosis of tuberculosis in patients with HIV Infection.

HIV is a major cause of dilated cardiomyopathy

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Human immunodeficiency virus (HIV) disease is recognized as an important cause of dilated cardiomyopathy also