ANALYSIS OF NNRTI AND NRTI STRUCTURES AND CORRELATIONS WITH BINDING AFFINITY CONSTANTS

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Our recently published work with low toxicity *s*-triazine derivates [1], motivated to look more into other published Human Immunodeficiency Virus (HIV-1) reverse transcriptase (RT) structures of inhibitors with data available for binding affinity constants. The purpose of current work was to understand how our compounds are positioned on the structural landscape of different families of inhibitors and derive QSAR models for describing and estimating binding affinity constants.

Publicly available Human immunodeficiency virus (HIV-1) reverse transcriptase inhibitors were extracted from the ChEMBL database (version 18), carefully curated and grouped into nucleoside analogue reverse-transcriptase inhibitors (NRTIs) and non-nucleoside analogue reverse-transcriptase inhibitors (NNRTIs), by verifying original literature. This curated diverse data set was analysed using a hierarchical classification of common core structures that resulted in patterns of known and virtual scaffolds. Then data sets consisting of NNRTIs and NRTIs were modelled with best multi-linear regression approach.

Hierarchical classification analysis divided NRTIs into four different scaffold trees based on parent types: uracil, pyrimidine, pyrimidione, imidazole and NNRTIs into ten different scaffold trees: oxazepanone, piperazinone, pyrazine, oxazinanone, diazinanone, pyridine, pyrrole, diazepanone, thiazole and triazine. The recently published *s*-triazine derivates positioned as a separate tree on the landscape of already known families of inhibitors. Derived QSAR models for NRTI and NNRTI sub sets, allowed to discuss which structural parameters and how they influence binding affinity of the molecules of interest.

References

1. B.Viira, A. Selytina, AT. García-Sosa, M. Karonen, J. Sinkkonen, A. Merits, U. Maran, 2016, *Bioorg. Med. Chem.*, 24:2519-29.

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