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Chemometric study of antiretroviral activities of HEPT derivatives using Multiple Linear Regression

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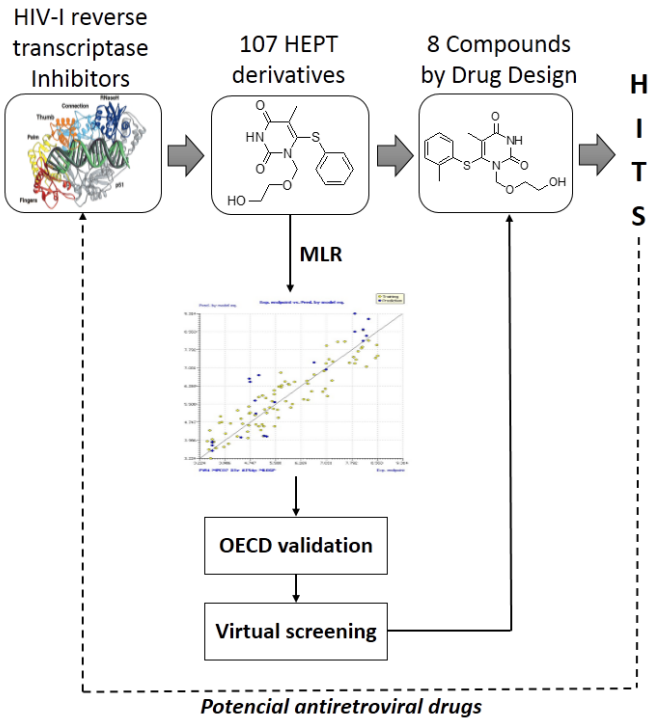
Graphical Abstract



Abstract

Reverse transcriptase is an enzyme whose function is to synthesize double-stranded DNA using the single-stranded RNA of HIV as the template. Antiretroviral drugs are effective against HIV infection because they reduce virus replication and slow the progression of the disease, even though it does not mean a definitive cure. In addition, existing drugs present a large number of adverse reactions, so the search for new antiretroviral drugs continues to be a major challenge today. In this study, a series of 107 experimentally tested 1-[(2-hydroxyethoxy)methyl]-6-(phenylthio) thymine (HEPT) derivatives were used against HIV-I reverse transcriptase to model antiretroviral activity using molecular descriptors of DRAGON. Subsequently, a mathematical model of Multiple Linear Regression, implemented in the QSARINS software, was developed by common least squares and genetic algorithm for the variables

	selection, with a good performance of its parameters. The model is extensively validated in accordance with OECD regulations so that its robustness (R^2=0.84), stability (Q^2_{LOO}=0.81; Q^2_{LMO}=0.80), low correlation of the descriptors (K_{XX}=0.58) and good predictive power (R^2_{EXT}=0.85). In addition, it was found that the fit of the model is not a product of a random correlation ($R^2_{Y\text{-}scr}$=0.06; $Q^2_{Y\text{-}scr}$=-0.09), so it was used to predict the antiretroviral activity of eight compounds obtained by rational drug design.

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