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PATHANAKARN SOTHIPATCHARASAI : QUANTITATIVE STRUCTURE-ACTIVITY RELATIONSHIPS OF PHTHALIMIDOALKYL DERIVATIVES AS POTENTIAL HIV-1 REVERSE TRANSCRIPTASE INHIBITORS. THESIS ADVISORS : JIRAPORN UNGWITAYATORN, Ph.D., SUPA HANNONGBUA, Dr.rer.nat. 113 P. ISBN 974-663-457-7

The classical and 3-dimensional quantitative structure-activity relationships (classical and 3D-QSAR) were used to investigate the structural requirements for HIV-1 reverse transcriptase inhibitory activity of the non-nucleoside phthalimidoalkyl compounds. The classical QSAR was performed to correlate the physicochemical properties, i.e., electronic, lipophilic, and steric properties with the inhibitory activity of the synthesized compounds using multiple linear regression (MLR) analysis. Comparative molecular field analysis (CoMFA), one of the most widely used 3D-QSAR techniques was carried out to investigate the correlation between the inhibitory activity with both electrostatic and steric fields. A docking study of the bound conformations of the phthalimidoalkyl molecules was performed as well using FlexiDock option.

The best classical QSAR model was obtained with a multiple correlation coefficient of (r) 0.974. This model indicates that the inhibitory activity correlated to the electronic properties, i.e., partial atomic charge at C2, the highest occupied molecular orbital (HOMO), and the dipole moment. This activity also correlated to the steric property, i.e., molecular volume (MV) and the hydrophobic property, log P. The best CoMFA model with cross-validated r^2 (q^2) = 0.646 was obtained by adding the lowest unoccupied molecular orbital (LUMO) energies to the QSAR table. The predictive utility of CoMFA was used to calculate activity of compounds not included in the training set. The calculated (predicted) and experimental inhibitory activities were well correlated. The study of bound conformations of phthalimidoalkyl ligands by FlexiDock agreed positively with the reported pharmacophore model of non-nucleoside inhibitors.