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PAKORN AMORNLERTVIT : HIV-1 REVERSE TRANSCRIPTASE INHIBITORS: SYNTHESIS OF BENZIMIDAZOLE DERIVATIVES AND COMPARATIVE MOLECULAR FIELD ANALYSIS OF PHTHALIMIDE DERIVATIVES. THESIS ADVISORS : JIRAPORN UNGWITAYATORN, Ph.D. LEENA LEELASVATANAKIJ, Ph.D. 107 p. ISBN 974-663-138-1

HIV-1 reverse transcriptase (RT) is an important target for acquired immunodeficiency syndrome (AIDS) drug therapy. This enzyme is inhibited by various nucleoside and non-nucleoside analogues. Non-nucleoside HIV-1 RT inhibitors comprise a structurally diverse class of molecules that exhibit noncompetitive inhibition and bind to a unique site of HIV-1 RT. This results in high specificity of non-nucleoside analogues for HIV-1 RT over other cellular DNA polymerases.

A new series of non-nucleoside inhibitors, benzimidazole derivatives, was synthesized in this study. These derivatives consist of benzimidazole nucleus linking to a pyridine ring via alkylamine group. The synthesized compounds will be evaluated later for their inhibitory activity.

Comparative Molecular Field Analysis (CoMFA) relationships, one of the 3-dimensional quantitative structure activity relationship (3D-QSAR) techniques, was performed using the previously synthesized phthalimide derivatives as the training set. CoMFA correlates the steric and electrostatic fields of the compound in the training set with their enzyme inhibitory activity. The best CoMFA model was obtained with cross-validated correlation coefficient (Q^2) 0.580. This CoMFA model was used to design new analogues in phthalimide series with good inhibitory activity.

For further investigation, more physicochemical parameters and more synthesized compounds should be added in the training set in order to obtain better statistical results.