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WEERASAK SAMEE SYNTHESIS AND EVALUATION OF CHROMONE DERIVATIVES AS POTENTIAL HIV-1 PROTEASE INHIBITORS. THESIS ADVISORS : JIRAPORN UNGWITAYATORN, Ph.D., CHANPEN WIWAT, Ph.D. 111 P. ISBN 974-662-781-3

Human immunodeficiency virus type-1 (HIV-1) protease (PR) has been identified as a significant target enzyme for acquired immunodeficiency syndrome (AIDS) drugs research. Inhibition of this enzyme leads to production of immature non-infectious viral progeny, and hence prevention of further rounds of infection. Peptide derived compounds are of limited utility as potential therapeutic agents due to low oral bioavailability and difficult synthesis due to the high molecular weight. Recent advances have resulted in HIV-1 PR inhibitors with reduced peptidic characters that are more orally available.

Our research group has designed and synthesized a new class of non-peptidic analogs in chromone derivatives. The chemical structures consist of 7-hydroxy, 8-hydroxy or 7,8-dihydroxy benzopyran-4-one nucleus with substituents at position 2 and 3, i.e., methyl, phenyl or benzyl. Nine compounds were tested for HIV-1 PR inhibitory activity *in vitro* using spectrophotometric assay. The inhibitory activity evaluation was carried out at concentration 20 μg/ml of synthesized compounds. Compound 8, 7,8-dihydroxy-2-phenyl chromone, was the most active compound in this series showing 94% inhibition and compound 2, 8-hydroxy-2-phenyl chromone, was the least active with 7% inhibition. The other compounds showed inhibitory activity in the range of 33% to 87% inhibition. The first four most potent compounds, 7,8-dihydroxy-2-phenyl chromone (8), 7-hydroxy-3-methyl-2-phenyl chromone (11), 7-hydroxy-2-benzyl-3-methyl chromone (12) and 7-hydroxy-2-benzyl chromone (6), possessed IC_{50} values of 4.06 μM, 11.08 μM, 18.08 μM, and 22.56 μM respectively