Ratsupa Thammaporn 2009: Kinetic Study of HIV-1 Reverse Transcriptase Complexed with Novel Inhibitors Based on Fluorometric Measurement and Molecular Docking Calculations. Master of Science (Chemistry), Major Field: Chemistry, Department of Chemistry. Thesis Advisor: Associate Professor Supa Hannongbua, Dr.rer.nat.
79 pages.

Currently, HIV infection is an important problem in the worldwide. The rate of infected patients is very high and increase every year. The mutation of HIV-1 reverse transcriptase (HIV-1 RT) reduces the efficient inhibition of anti-AIDS drugs. Accordingly, novel inhibitors are developed to inhibit HIV-1 RT. The objective of this work is to develop biological testing of novel HIV-1 RT inhibitor by using fluorometric measurement. Expression and purification of the wild-type HIV-1 RT were produced from the recombinant bacteria. The yield of HIV-1 RT in culture 1 liter was 14.06 mg. The efficiency of the purified HIV-1 RT was comparable to the commercial HIV-1 RT. The inhibition of nevirapine and dipyridodiazepinone derivatives on the enzymatic activity of the wild-type HIV-1 RT was investigated using a fluorometric measurement. From screening with 1 μM dipyridodiazepinone derivatives, inhibition of HIV-1 RT activity with compounds namely, NA14, NA15, NA16, NA17 and 68NV was found to be higher efficiency than nevirapine. The IC_{50} value of nevirapine was 15.67 μM which is layed in the range of reported by the other groups. Therefore, the fluorometric method can be successfully applied for inhibiting studies of HIV-1 RT activity. In addition, the dipyridodiazepinone derivatives, NA14 and NA15 were shown the best inhibiting efficiency for the wild-type HIV-1 RT among other derivatives with IC_{50} values of 0.2138 and 0.5199 μM, respectively. Furthermore, the molecular docking was used to study the orientations of inhibitors in HIV-1 RT binding pocket by using GOLD program with GoldScore and ChemScore fitness functions. The results indicate that the ChemScore fitness function is suitable to consider the docked orientations. The thiophenyl side chains of NA14 and NA15 interact with residues such as Lys103, Val106, Phe227, Leu234, His235, Pro236 and Tyr318. The present of methyl group at R_1 position interact with Trp229. Moreover, the methoxy group at the thiophenyl side chain of NA15 generated H-bonding with backbone of residue Val106 with 2.86 Å.

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