THESIS

AUTODOCK AS A TOOL FOR VIRTUAL SCREENING FOR ANTI-INFLUENZA DRUGS

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The high case fatality rate of the present influenza virus epidemics in Asia, Europe and Africa has raised serious concerns about a global flu pandemic, which could become a massive threat to human being if the virus mutates to become human virus. Neuraminidase (NA) inhibitors are currently the only option for treatment or prophylaxis in humans infected with this strain. However, drugs currently on the market often meet with rapidly emerging resistant mutants and only have limited application as inadequate supply of synthetic material. Virtual screening is a method for finding new lead compound that can be used for anti-influenza drugs discovery. The important step before we can use any program as the virtual screening tools is to validate of the method to be applied. In this work we studied the feasibility of using AutoDock and FRED program. We archived a method that showed high correlation between free energy of prediction and experimental data (-log IC_{50}). The result indicated that AutoDock was competent in reproducing the experimentally found binding position and conformation of NIs. When combined AutoDock and FRED program, the results was improved. The compounds on ChemieBase (around 30,000 compounds) and benzoic acid derivatives 47 compounds were screened, five compounds were submitted for neuraminidase inhibition assay. The experimental results showed that these compounds having inhibitory activity neuraminidase with IC_{50} values from 2.19 mM to 4.13 mM. Moreover, one out of the five compounds showed inhibitory activity against three subtypes of influenza viral H5N1, H3N2 and H1N1.

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