

Uji aktivitas senyawa stilbenoid sebagai inhibitor neuraminidase virus influenza A subtype H5N1 secara in silico = In silico screening of stilbenoid compounds as inhibitor of neuraminidase influenza a virus subtype a

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Abstrak

Avian Influenza diakibatkan oleh virus influenza A subtype H5N1 yang dapat mengalami mutasi sehingga antigennya, neuraminidase dan haemagglutinin, dapat beradaptasi dan menjadi lebih patogen dari sebelumnya serta resisten terhadap obat-obatan yang ada. Oleh karena itu dibutuhkan suatu obat baru yang dapat digunakan secara umum, yaitu jenis inhibitor neuraminidase. Pada penelitian ini 300 senyawa stilbenoid diujicobakan terhadap neuraminidase H5N1 strain Indonesia secara in silico. 61 ligan senyawa stilbenoid memiliki energi ikatan lebih rendah dibandingkan standar oseltamivir karboksilat dan zanamivir. 30 ligan terbaik diuji sifat fisika dan kimianya, sebagian ligan tidak memenuhi Lipinski's rule of five. Terdapat 2 (dua) senyawa beresiko genotoksik dan karsinogenik berdasarkan hasil uji toksikologi. Terdapat 11 ligan yang memiliki drug score cukup baik. Berdasarkan uji farmakologi dan efek kesehatan, diperoleh 2 (dua) ligan yang berpotensi baik. Ligan terbaik dipilih berdasarkan efek negatif terhadap kesehatan yang lebih sedikit adalah gnetumontanin A dari spesies *Gnetum montanum*. Kestabilan kompleks dengan ligan terbaik diuji kestabilannya dengan keberadaan pelarut menggunakan simulasi dinamika molekul. Berdasarkan hasil RMSD dinamika molekul pada suhu 310 dan 312 K kompleks enzim-ligan memiliki kestabilan yang baik. Penelitian ini diharapkan dapat menghasilkan kandidat inhibitor neuraminidase yang lebih potensial.

.....Avian Influenza is a respiratory disease caused by influenza A virus subtype H5N1 which can undergo mutation in its antigens, neuraminidase and haemagglutinin, and build a much more pathogenic virus. The mutation leads to resistance towards standard drugs. Therefore, a new drug that can be used in general which is the types of neuraminidase inhibitors is an urgent need. In this research, 300 stilbenoid compounds were tested to neuraminidase H5N1 Indonesia strain by using in silico method. According to the result of molecular docking, 61 ligands have binding energy lower than standard oseltamivir acid and zanamivir. 30 ligands were tested toward its physical chemistry properties, half of those ligands could not fulfil Lipinski's rule of five. Virtual toxicity test were done and only 2 ligand is potent to be genotoxic carcinogenic. Only 11 ligands have good drug scores, and only 2 of them are potential to be developed as new oral-drugs based on pharmacology and health effect test. The best ligand selected by lower negative health effect is gnetumontanin A which can be isolated from plant species *Gnetum montanum*. Stability of enzyme-best ligand complex with the addition of solvent were tested in molecular dynamic simulation. RMSD curve of dynamic simulation shows that the complex is stable while conducted in 310 and 312 K.