Modifikasi (1R,2R,3R,5S)‐(‐)‐Isopinocampheylamine sebagai inhibitor M2 proton channel pada virus influenza a subtipe H1N1 secara in silico

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Abstrak

Pada tahun 2009, flu babi kembali menyerang berbagai negara di dunia. Organisasi Kesehatan Dunia (WHO) menetapkan wabah virus influenza A H1N1 sebagai pandemi global pada 11 Juni 2009. Setidaknya ada sekitar 18.449 orang di seluruh dunia yang meninggal akibat serangan virus ini. Kemudian pada tanggal 10 Agustus 2010 Badan Kesehatan Dunia (WHO) secara resmi mengumumkan pandemi flu babi di dunia telah berakhir dan berganti menjadi fase post pandemic Fase post pandemic ini fase paling tepat untuk menemukan antiviral yang dapat mengatasi infeksi virus ini. Salah satu antiviral yang telah ada yaitu amantadine dan rimantadine dilaporkan telah mengalami resistansi. Oleh karena itu perlu ditemukan antiviral baru untuk menggantikan amantadine dan rimantadine sebagai inhibitor protein M2 channel virus influenza A H1N1. Belakangan dilaporkan bahwa senyawa (1R,2R,3R,5S)-(-)-isopinocampheylamine memiliki kemampuan untuk menginhibisi protein M2 channel virus influenza A H1N1.
Pada penelitian ini akan dilakukan modifikasi (1R,2R,3R,5S)-(-)-isopinocampheylamine secara in silico untuk mendapatkan inhibitor yang lebih baik. Terhadap protein M2 channel, dilakukan docking dengan tiga inhibitor standar dan 52 inhibitor modifikasi, serta dilakukan drug scan terhadap modifikasi inhibitor. Hasil docking didapatkan 3 inhibitor modifikasi terbaik yang mempunyai afinitas ikatan dan potensi inhibisi yang lebih baik dibanding ligan standar. Berdasarkan analisa drug scan, inhibitor modifikasi mempunyai sifat farmakologi yang baik, ditunjukkan oleh nilai drug likeness, drug score, bioavailabilitas oral, dan toksisitas.
.....In 2009, swine flu attacked various countries in the world. World Organization (WHO) set a pandemic of influenza A H1N1 virus as a global pandemic on June 11, 2009. At least there are approximately 18,449 people worldwide who die from this virus attack. Then on August 10, 2010 World Health Organization (WHO) officially announced the swine flu pandemic in the world has ended and changed into post-pandemic phase. Post-pandemic phase is the most appropriate phase to find antiviral that can overcome the infection with this virus. One of the existing antivirals amantadine and rimantadine are reported to have experienced resistance. Therefore it is necessary to find new antiviral to replace amantadine and rimantadine as the M2 channel protein inhibitor of influenza A H1N1 virus. Later it was reported that compound (1R, 2R, 3R, 5S)-(-)- isopinocampheylamine have the ability to inhibit channel M2 protein of influenza A H1N1 virus.
This research will be modified (1R, 2R, 3R, 5S)-(-)-isopinocampheylamine in silico to obtain better inhibitors. Against the M2 protein channel, performed three inhibitor docking with standard and 52 inhibitors modifications, and also done a drug scan for modifications inhibitor. Docking results obtained three best binding affinity of modifications inhibitor and its potency of inhibition is much better than standard ligands. Based on drug analysis scan, the inhibitor of modification has a good pharmacological properties, indicated by the value of drug-likeness, drug score, oral bioavailability, and toxicity.