Kajian *Molecular Docking* Untuk Prediksi Pemisahan Kromatografi Senyawa Kiral Hidroksiklorokuin

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INTISARI

Prediksi pemisahan senyawa kiral hidroksiklorokuin (HCQ) telah dilakukan berdasarkan pendekatan *molecular docking* menggunakan kolom kiral α-1-acid glycoprotein (AGP) dan cyclobond I 2000 (β-CD). Penelitian diawali dengan optimasi geometri senyawa HCQ menggunakan metode kalkulasi kuantum Semi-empirical (SE), himpunan basis PM6, AM1, dan PM3, serta Ab Initio (AI/HF), dan Density functional theory (DFT/B3LYP) dengan himpunan basis 3-21G, 6-31G, dan 6-311G. Proses *docking* molekul dilakukan dengan aplikasi AutoDock Vina dan PyRx pada *exhaustiveness* 264. *Docking* HCQ dengan AutoDock Vina pada kolom kiral AGP diawali dengan re*docking* dengan koordinat penambatan X= 13.584; Y= 1.47; Z= 18.451 dan ukuran Grid Box 40 x 40 x 40 dengan Grid Spacing 0,375 Å. *Docking* HCQ dengan PyRx menggunakan kordinat penambatan X= 48.7816; Y= 44.5700; Z= 44.4561 dengan ukuran Grid Box maximum. Molekular *docking* AutoDock Vina pada kolom kiral cyclobond I 2000 diawali dengan re*docking* dengan koordinat penambatan X= 57,653; Y= 12,303; Z= 8,842 dengan ukuran Grid Box 40 x 40 x 40 dan Grid Spacing 0,375 Å. Molekular *docking* PyRx memiliki nilai kordinat penambatan X= 68,7849; Y= 23,5078; Z= 20,8568 dengan ukuran Grid Box maximum. Metode DFT dengan basis set 6-311G dianggap paling representatif karena data ^{1}H-NMR hasil perhitungan memiliki nilai PRESS terendah, yaitu 5,0892 dan r^2 paling mendekati satu, 0,9695 jika dibandingkan dengan data ^{1}H-NMR hasil eksperimen. Enantiomer R dan S-HCQ dioptimasi dengan DFT 6-311G, dilanjutkan *molecular docking* pada kolom kiral. Kolom kiral AGP mampu mengikat HCQ dengan kuat dan stereoselektif karena R dan S-HCQ memiliki interaksi berbeda pada kolom kiral AGP. Pada *molecular docking* kiral HCQ pada kolom AGP diperoleh nilai |ΔΔG| antara S dan R-HCQ sebesar 0,32 kkal/mol dengan AutoDock Vina dan 0,36 kkal/mol dengan PyRx, sedangkan pada kolom β-CD diperoleh nilai |ΔΔG| 0,03 kkal/mol dengan AutoDock Vina dan 0,05 kkal/mol dengan PyRx. Hasil kajian *docking* molekul HCQ pada kolom kiral AGP menunjukkan senyawa S-HCQ akan terelusi terlebih dahulu dari R-HCQ pada kolom AGP karena interaksi R-HCQ dengan kolom lebih lemah. Kolom *cyclobond* I 2000 diprediksi kurang sesuai untuk pemisahan senyawa kiral HCQ. β-CD memiliki *cavity* yang besar, sehingga enantiomer HCQ terelusi dengan cepat pada kolom secara bersamaan karena β-CD tidak mampu menahan atau membedakan masing-masing enantiomer HCQ.

Kata kunci: *docking molecular*, hidroksiklorokuin, α1-acid glycoprotein, β-cyclodextrin

Molecular Docking Study for Prediction of Chiral Chromatographic Separation of Hydroxychloroquine Compound

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ABSTRACT

Prediction of chiral chromatographic separation of hydroxychloroquine (HCQ) compound has been carried out based on a molecular docking approach using α-1-acid glycoprotein (AGP) and cyclobond I 2000 (β-CD) chiral columns. The study was initialized with geometrical optimization of HCQ using semi-empirical (SE) density function with the basis sets of PM6, AM1, and PM3, Hartree-Fock (HF), and density functional theory (DFT/B3LYP) with the basis sets of 3-21G, 6-31G, and 6-311G. The molecular docking process was carried out by AutoDock Vina and PyRx applications at exhaustiveness of 264. Molecular docking of HCQ compound on AGP chiral columns using AutoDock Vina was initiated by redocking with anchoring coordinates of X= 13,584; Y= 1.47; Z= 18,451 and grid box size of 40 x 40 x 40 and grid spacing of 0.375. Meanwhile, molecular docking of HCQ using PyRx was done by using docking coordinates of X= 48.7816; Y= 44.5700; Z= 44.4561 and grid box size was set at maximum level. Furthermore, molecular docking of HCQ on β-CD using AutoDock Vina was begun by redocking with anchoring coordinates of X= 57.653; Y= 12,303; Z= 8.842 using the grid box size of 40 x 40 x 40 and grid spacing of 0.375, while that using PyRx was done with docking coordinate value of X= 68.7849; Y= 23.5078; Z= 20.8568 and maximum level of grid box size. Results of the study show that the DFT method with a basis set of 6-311G gives the most accurate results because the calculated ^{1}H-NMR data has the lowest PRESS value (5.0892) and the closest r^2 to unity (0.9695) as compared to the experimental ^{1}H-NMR data. The R and S HCQ enantiomer were optimized by DFT, followed by molecular docking on the chiral column. The AGP chiral column is found to be able to interact with HCQ strongly and stereoselectively because R and S-HCQ have different interaction modes on the AGP chiral column. From molecular docking of HCQ on AGP column, it was obtained that the value of |ΔΔG| between S and R-HCQ is 0.32 kcal/mol using AutoDock Vina and 0.36 kcal/mol using PyRx, while on β-CD column, the value of |ΔΔG| was 0.03 kcal/mol using with AutoDock Vina and 0.05 kcal/mol with PyRx. Result of HCQ docking on the AGP chiral column suggests that S-HCQ will be eluted first from AGP column followed by R-HCQ because its interaction with the coloumn is weaker. In addition, the cyclobond I 2000 column is predicted to be unsuitable for the separation of chiral HCQ compounds. β-CD has a large cavity, so that the S and R-HCQ enantiomer will be eluted quickly and simultaneously on the column because β-CD is unable to retain or discriminate each HCQ enantiomer.

Keywords: docking molecular, hydroxychloroquine, α-1-acid glycoprotein, β-cyclodextrin