Pemanfaatan senyawa flavonoid sebagai inhibitor tirosin kinase pada kanker payudara berbasis fragment-based drug design dan molecular docking = Utilization of flavonoid compounds as tyrosine kinase inhibitor in breast cancer using fragment-based drug design and molecular docking

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Abstrak

Kanker payudara merupakan salah satu penyebab utama kematian pada wanita di seluruh dunia. Protein HER2 tirosin kinase merupakan salah satu penyebab kanker payudara, yaitu sebesar 30% dari keseluruhan jumlah kasus kanker payudara. Protein HER2 tirosin kinase berperan penting dalam reaksi dimerisasi yang menyebabkan terjadinya autofosforilasi residu tirosin pada domain sitoplasma. Mekanisme ini dapat memicu pertumbuhan sel kanker. Penghambatan aktivitas protein HER2 dapat menjadi alternatif pengobatan kanker payudara. Dalam penelitian ini digunakan senyawa bahan alam flavonoid sebagai basis data dalam perancangan obat kanker payudara secara in silico. Pada perancangan obat secara in silico, dilakukan beberapa tahapan antara lain, preparasi protein, preparasi flavonoid, preparasi standar, simulasi penambatan molekul, pertumbuhan fragmen, serta studi farmakologi kandidat obat. Proses preparasi dan simulasi penambatan molekul dilakukan dengan menggunakan perangkat lunak MOE 2014.09. Tahapan pertumbuhan fragmen dilakukan dengan perangkat lunak Osiris DataWarrior. Studi farmakologi kandidat obat dilakukan dengan perangkat lunak pkCSM, SwissADME, dan AdmetSar. Penelitian ini diharapkan dapat menemukan kandidat ligan penghambat aktivitas protein HER2.

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Breast cancer is one of the main women death cause around the world. HER2 tyrosine kinase protein is one of the causes of breast cancer, which is 30% of the total number of breast cancer cases. The HER2 tyrosine kinase protein plays an important role in the dimerization reaction which causes the autophosphorylation of tyrosine residues in the cytoplasmic domain. This mechanism can trigger the growth of cancer cells. The inhibition of HER2 protein activity can be an alternative treatment for breast cancer. In this study, natural flavonoid compounds were used as a database in designing breast cancer drugs. In drug design using in silico method, several steps were carried out, such as protein preparation, flavonoid preparation, standard preparation, molecular docking simulation, fragment growing process, and pharmacological studies of drug candidates. The preparation and molecular docking simulation process were conducted using MOE 2014.09 software. Fragment growing process were conducted with Osiris DataWarrior software. Pharmacological studies of candidate drugs were carried out with pkCSM, SwissADME, and AdmetSar software. This study is expected to find inhibitor candidates to inhibit the HER2 protein activity.