Simulasi dinamika molekuler beberapa senyawa terpilih dari pangkalan data herbal Indonesia hasil penambatan molekuler terhadap enzim DNA metiltransferase (DNMT) = Molecular dynamic simulations of several selected compounds from herbal database Indonesia results of molecular docking against DNA methyltransferase (DNMT) enzyme

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Abstrak

Kanker merupakan penyebab kematian utama di seluruh dunia. Salah satu faktor terjadinya kanker adalah modifikasi epigenetik yang abnormal (hipermetilasi). Hipermetilasi yang terjadi pada gen diyakini bahwa yang berperan besar dalam proses karsinogenesis adalah enzim DNA metiltransferase (DNMT). Penelitian-penelitian yang dilakukan saat ini untuk menemukan senyawa inhibitor DNMT dari bahan alam. Salah satu metode yang mendukung untuk analisis ini adalah metode in silico. Dalam penelitian ini, diteliti beberapa senyawa pilihan dari basis data herbal Indonesia hasil penapisan virtual terhadap aktivitasnya sebagai inhibitor DNMT. Hasil penambatan molekuler senyawa Cassiamin C, Procyanidin B2, Ent-epicatechin-4alpha-8-ent-epicatechin, Epicatechin-4beta-8-epicatechin-3-O-gallate, Neorhusflavanone, 3-O-galloylepigallocatechin-4beta-6-epicatechin-3-O-gallate, Withanolide, 3-O-galloylepigallocatechin-4beta-6-epigallocatechin-3-O-gallate, Cyanidin-3-6"-caffeylsophoroside-5-glucoside, Epifriedelinol, Gallo-catechin-4alpha-8-epicatechin, Scutellarein-7-glucosyl-1-4-rhamnoside, Epigallo-catechin-3-gallate (EGCG) (kontrol positif), dan sinefungin (kokristal) didapatkan nilai ΔG secara berturut-turut, -9.34, -10.95, -7.95, -11.01, -8.78, -8.87, -11.49, -7.98, -5.92, -8.92, -9.17, -8.76, -9.70, dan -9.11 kkal/mol. Senyawa cassiamin C, procyanidin B2, epicatechin-4beta-8-epicatechin-3-O-gallate, withanolide, dan gallocatechin-4alpha-8-epicatechin memiliki ΔG lebih rendah dari senyawa sinefungin (kokristal) dan EGCG (kontrol positif). Sehingga, tahap selanjutnya akan dilakukan simulasi dinamika molekuler terhadap tujuh ligan tersebut. Hasil simulasi dinamika molekuler menunjukkan aktivitas terbaik secara keseluruhan yaitu pada senyawa procyanidin B2, epicatechin-4beta-8-epicatechin-3-O-gallate, dan gallocatechin-4alpha-8-epicatechin. Residu asam amino yang penting bagi aktivitas inhibitor DNMT1 adalah Phe1145, Glu1168, Met1169, Cys1191, Glu1266, Ala1579, dan Val1580.

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Cancer is the leading cause of death worldwide. Factors of cancer is an abnormal epigenetic modifications (hypermethylation). Hypermethylation that occur in genes believed that played a major role in process of carcinogenesis is DNA methyltransferase (DNMT) enzyme. Recent studies is conducted to find DNMT inhibitor compounds from natural materials. Method that support for this analysis is in silico studies. In this study, several selected compounds from herbal database Indonesia results of virtual screening will be studying for the activity as an inhibitor DNMT. Results molecular docking of Cassiamin C, Procyanidin B2, Epicatechin-4alphaent-8-ent-epicatechin, Epicatechin-4beta-8-epicatechin-3-O-gallate, Neorhusflavanone, 3-O-galloylepigallocatechin-4beta-6-epicatechin-3-O-gallate, Withanolide, 3-O-galloylepigallocatechin-4beta-6-epigallocatechin-3-O-gallate, Cyanidin-3-6"-caffeylsophoroside-5-glucoside, Epifriedelinol, Gallocatechin-4alpha-8-epicatechin, Scutellarein-7-glucosyl-1-4-rhamnoside, Epigallocatechin-3-gallate (EGCG) (positive control), and Sinefungin (co-crystal) compounds, ΔG values obtained -9.34, -10.95,

-7.95, -11.01, -8.78, -8.87, -11.49, -7.98, -5.92, -8.92, -9.17, -8.76, -9.70, and -9.11 kcal/mol, respectively. Cassiamin C, Procyanidin B2, Epicatechin-4beta-8-epicatechin-3-O-gallate, Withanolide, and Gallocatechin-4alpha-8-epicatechin compounds had lower ΔG than Sinefungin (co-crystal) and EGCG (positive control) compounds. Therefore, molecular dynamic simulation of seven selected compounds will be performed. The results of molecular dynamic simulation shows the best overall activity is Procyanidin B2, Epicatechin-4beta-8-epicatechin-3-O-gallate, and Gallocatechin-4alpha-8-epi-catechin compounds. Amino acid residues which are important for the activity of DNMT1 inhibitor is Phe1145, Glu1168, Met1169, Cys1191, Glu1266, Ala1579, and Val1580.