Studi in silico senyawa analog suberoyl anilide hydroxamic acid (SAHA) berbasis organotitanium sebagai inhibitor potensial histone deacetylase (HDAC) kelas II homo sapiens = In silico study of organotitanium based (SAHA) analogues as potent homo sapiens class II histone deacetylase inhibitors

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Abstrak

[ABSTRAK
Kanker serviks adalah penyakit atau ketidaknormalan epigenetik yang disebabkan oleh Human papillomavirus (HPV). Ketidaknormalan epigenetik yang dimaksudkan dan berkaitan dengan penyakit ini adalah ketidaknormalan histon deasetilase (HDAC). Kemoterapi merupakan tindakan pengobatan yang bertujuan untuk memperpanjang umur dan memperbaiki kualitas hidup. Inhibitor HDAC merupakan agen terapi yang paling menjanjikan. Oleh karena itu, pengembangan HDAC menjadi area penelitian yang menarik. Pada penelitian ini, SAHA dimodifikasi dengan menggunakan senyawa berbasis organotitanium. Pada penelitian ini, sebanyak ± 1900 senyawa (ligan) telah dirancang dan ditapis melalui simulasi molecular docking. Ligan yang memiliki nilai Gbinding terendah dari molecular docking, dianalisis karakter farmakologinya dengan menggunakan beberapa perangkat lunak (software). Beberapa proses tapisan tersebut menghasilkan satu ligan terbaik, yaitu Ti2vm5-4s1r5. Ligan terbaik tersebut kemudian dianalisis melalui simulasi dinamika molekul untuk melihat kestabilannya membentuk kompleks dengan enzim. Kurva RMSD dari simulasi dinamika molekul, menunjukkan bahwa Ti2vm5-4s1r5 stabil dalam kompleks enzim. Berdasarkan hasil tersebut, maka Ti2vm5-4s1r5 dapat menjadi inhibitor HDAC kelas II Homo sapiens yang potensial.
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ABSTRACT
Cervical cancer is an epigenetic disease or abnormality caused by Human papillomavirus (HPV). Abnormal expression of histone deacetylases (HDACs) has been linked with it. To date, chemotherapy is a palliative treatment aimed at prolonging survival and improving quality of life. HDAC inhibitor is the most promising chemotherapy agent. Therefore, the development of HDAC inhibitors has become an interesting research area. In this research, SAHA was modified by utilizing organotitanium-based compounds. Approximately 1900 compounds has been designed and all of them were screened according to Gbinding result from molecular docking simulation. The pharmacological characters of potential ligands with the lowest Gbinding were then analyzed using several softwares. This multistep screening process generated one best ligand, Ti2vm5-4s1r5, which was further studied by means of molecular dynamics simulation. The analyses of molecular dynamics simulation revealed that Ti2vm5-4s1r5 stable in complex with each enzyme. So, Ti2vm5-4s1r5 can be potent inhibitor of histone deacetylase class II Homo sapiens.;Cervical cancer is an epigenetic disease or abnormality caused by Human papillomavirus (HPV). Abnormal expression of histone deacetylases (HDACs) has been linked with it. To date, chemotherapy is a palliative treatment aimed at prolonging survival and improving quality of life. HDAC inhibitor is the most promising chemotherapy agent. Therefore, the development of HDAC inhibitors has become an interesting research area. In this

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