Penggunaan senyawa boron untuk Modifikasi senyawa suberoyl anilide Hydroxamic acid (saha) sebagai inhibitor Histone deacetylase (hdac) kelas ii Homo sapiens = The Use of boron compound to modify Suberoyl anilide hydroxamic acid (saha) As homo sapiens histone deacetylase (hdac) Class ii inhibitor

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Abstrak

Histon deasetilase (HDAC) memiliki fungsi kritis dalam meregulasi ekspresi gen. Penelitian terkini mengungkapkan bahwa HDAC juga memiliki peranan penting dalam karsinogenesis. Oleh karenanya, penghambatan HDAC telah berkembang menjadi area riset antikanker yang menarik yang menargetkan proses-proses biologis seperti siklus sel, apoptosis, dan diferensiasi sel.
Dalam penelitian ini suatu inhibitor HDAC yang telah tersedia secara komersial, Suberoyl Anilide Hydroxamic Acid (SAHA), dimodifikasi untuk meningkatkan efikasi dan mengurangi efek samping senyawa tersebut. Bagian hydrophobic cap dan zincbinding group dari senyawa ini disubstitusi dengan senyawa berbasis boron, sedangkan daerah linker disubstitusi dengan p-aminobenzoic acid. Simulasi molecular docking terhadap SAHA dan senyawa turunannya dilakukan untuk mendapatkan ligan potensial yang memiliki nilai Gbinding terendah.
Analisis docking menghasilkan 8 ligan dengan Gbinding yang jauh lebih negatif dibandingkan standar, SAHA dan TSA, yaitu Nova2(9058064-6), Nova2(95752-88-8), Nova2(88765-82-6), Nova2(unique10), Nova2(16876-27-0), Nova2(513246-99-6), Nova2(unique80), dan Nova2(279262-23-6). Kedelapan ligan tersebut dianalisis berdasarkan sifat QSAR (quantitative structure-activity relationship), farmakologis, dan ADME-Tox (absorption, distribution, metabolism, excretion and toxicity) yang dimiliki untuk mendapatkan inhibitor potensial HDAC kelas II Homo sapiens. Proses penapisan bertahap ini menghasilkan 1 ligan terbaik, yaitu Nova2(513246-99-6), yang kemudian dipelajari lebih lanjut melalui simulasi molecular dynamics.
<hr><i>Histone deacetylase (HDAC) plays critical functions in the regulation of gene expression. Recent studies revelead that HDAC also has important role in carcinogenesis. The inhibition of HDAC has emerged as a new interesting area of anticancer research that targets the biological processes including cell cycle, apoptosis and differentiation.
In this research, a commercially available inhibitor of HDAC known as Suberoyl Anilide Hydroxamic Acid (SAHA) were modified in order to improve its efficacy and reduce its side effects. The hydrophobic cap and zinc-binding group of this compound were substituted by boron-based compounds, while its linker region was modified by p-aminobenzoic acid. Molecular docking simulation was conducted on SAHA and its derivatives to obtain potential ligands with the lowest Gbinding.
Docking analysis revealed 8 potential ligands with far more negative Gbinding than standards, SAHA and TSA, they are Nova2(9058064-6), Nova2(95752-88-8), Nova2(88765-82-6), Nova2(unique10), Nova2(16876-27-0), Nova2(513246-99-6), Nova2(unique80), and Nova2(279262-23-6). All of these ligands were analyzed according to their QSAR (quantitative structure-activity relationship), pharmacological analysis and ADME-Tox (absorption, distribution, metabolism, excretion and toxicity) to obtain potential

inhibitor of HDAC class II Homo sapiens. This multistep screening process generated one best ligand, Nova2(513246-99-6), whis was further studied by means of molecular dynamics simulation.</i>