Penambatan Molekuler Silybin terhadap IKKB dan NIK: Potensi dan Mekanisme Anti Inflamasi pada Jalur Persinyalan Inflamasi Nuclear Factor Kappa Beta (Nf-kb) = Molecular Docking of Silybin against IKKB and NIK: Anti-Inflammatory Potential and Mechanism on Nuclear Factor Kappa Beta (Nf-kb) Inflammatory Signaling Pathway

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Abstrak

Inflamasi memiliki peran penting dalam perkembangan berbagai kondisi patologis, yang dimediasi oleh aktivasi berbagai jalur pensinyalan, termasuk jalur IKK-NF-B. Silybin, senyawa flavonolignan yang ditemukan dalam Milk Tistle (Silybum marianum L) telah digunakan secara tradisional untuk mengobati penyakit hati dan telah dilaporkan memiliki aktivitas anti-inflamasi, antifibrotik, dan imunomodulator. Namun, mekanisme molekuler silybin sebagai agen antiinflamasi potensial terhadap jalur pensinyalan IKKNF- B masih belum jelas. Penelitian ini menggunakan simulasi penambatan molekuler menggunakan Autodock 4.0 untuk menyelidiki interaksi antara Silybin dan NF-B. Hasil penelitian menunjukkan bahwa silybin menunjukkan inhibisi kompetitif-ATP dan memiliki afinitas pengikatan yang tinggi untuk makromolekul IkB kinase beta (IKK) dan NIK (NF-kB-inducing kinase), dengan energi pengikatan -9,73 kkal/mol pada rantai A dan -9,84 kkal/mol pada rantai B IkB kinase beta (IKK) serta -9,34 kkal/mol pada makromolekul NIK (NF-kB-inducing kinase). Konstanta Inhibisi (Ki) ditemukan masingmasing 74,14 nM pada rantai A dan 61,12 nM pada rantai B IkB kinase beta (IKK) serta 141,81 nM mol pada NIK (NF-kB-inducing kinase). Temuan ini menunjukkan bahwa silybin memiliki potensi untuk menghambat jalur pensinyalan IKK-NF-B, sehingga memberikan efek anti-inflamasi. Selain itu, silybin menunjukkan afinitas pengikatan yang lebih tinggi jalur persinyalan kanonikal dibanding jalur perisnyalan alternatif. Studi ini memberikan wawasan tentang mekanisme molekuler silybin sebagai agen antiinflamasi potensial dan aplikasi terapeutiknya dalam terapi penyakit yang berhubungan dengan Inflamasi.
.....Inflammation has a crucial role in the progression of various pathological conditions, mediated by the activation of multiple signaling pathways, including the IKK-NF-B pathway. Silybin, a flavonolignan compound extracted from Milk thistle (Silybum marianum L.) has been traditionally used to treat liver disorders and exhibits pharmacological properties, including anti-inflammatory, antifibrotic, and immunomodulatory activities. However, the molecular mechanisms underlying Silybin's anti-inflammatory potential, particularly its interaction with the IKK-NF-B signaling pathway, remain unclear. This study employed molecular docking simulations using Autodock 4.0 to investigate the interaction between Silybin and NF-B. The results showed that silybin exhibited competitive-ATP inhibition and high binding affinity for IkB kinase beta (IKK) and NIK (NF-kB-inducing kinase) macormolecule, with binding energies of -9.73 kcal/mol on the A chain and -9.84 kcal/mol on the B chain of IkB kinase beta (IKK) and -9.34 kcal/mol on NIK (NF-kB-inducing kinase). Inhibition constants (Ki) were found to be 74.14 nM on chain A and 61.12 nM on chain B of IkB kinase beta (IKK) and 141.81 nM mol on NIK (NF-kB-inducing kinase), respectively. Notably, silybin displays higher binding affinity for the canonical pathway compared to the alternative pathway. These findings suggest that silybin has the potential to inhibit IKKNF- B signaling, leading to anti-inflammatory effects. This study provides valuable insights into the molecular mechanism of silybin as a

potential anti-inflammatory agent and its therapeutic applications in inflammation-related diseases.