STUDI *IN SILICO* SENYAWA AKTIF TANAMAN SILYMARIN (*Silybum marianum L.*) TERHADAP INHIBITOR RESEPTOR CDK 6 (*Cyclin-dependent kinase* 6) SEBAGAI ANTI KANKER PAYUDARA

ABSTRAK

Menurut Menurut Organisasi Kesehatan Dunia (WHO), kanker adalah penyebab kematian paling umum di seluruh dunia dan kasusnya terus meningkat. Pada tahun 2022, jumlah kasus baru kanker mencapai 19,9 juta jiwa dan jumlah kematian akibat kanker mencapai 9,4 juta jiwa. *Silybum marianum* L. Juga dikenal (milk thistle) mengandung senyawa aktif seperti silymarin, apigenin, kaempferol, luteolin, dan quercetin yang berpotensi berfungsi sebagai antikanker. Penelitian ini menganalisis potensi senyawa aktif *S. marianum* sebagai inhibitor CDK6 (Cyclin-Dependent Kinase 6) melalui pendekatan *in silico*. Metode meliputi *molecular docking* menggunakan *Protein Data Bank* dan BIOVIA Discovery Studio terhadap reseptor CDK6 (PDB: 3NUP, 3NUX, 2EUF, 4EZ5, 8I0M, 5L2I, 5L2S, 4TTH). Hasil menunjukkan doxorubicin (senywa pembanding obat) memiliki afinitas tertinggi (-7,36 kcal/mol), diikuti apigenin (-6,29 kcal/mol), luteolin (-6,33 kcal/mol), quercetin (-6,19 kcal/mol), dan kaempferol (-6,03 kcal/mol).

Analisis statistik (ANOVA) menunjukkan perbedaan signifikan antara doxorubicin dengan flavonoid ($p < 0,05$). Analisis interaksi molekuler mengungkap flavonoid berikatan dengan residu kritis CDK6 (VAL141, LEU166, ASP163) melalui ikatan hidrogen dan hidrofobik. Apigenin menunjukkan afinitas lebih tinggi daripada doxorubicin pada reseptor 5L2I (-7,5 kcal/mol dan -7,0 kcal/mol), mengindikasikan potensinya sebagai inhibitor alami CDK 6. Penelitian lanjutan (in vitro/in vivo) diperlukan untuk membuktikan keamanan dan efektivitasnya sebagai kandidat pengobatan antikanker payudara.

Kata kunci: *Silybum marianum*, kanker payudara, CDK6, *molecular docking*, flavonoid.

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ABSTRACT

According to the WHO, Globally, cancer is the biggest cause of mortality, and the number of cases is rising. The quantity of new cases of cancer cases in the world reached 19.9 million people and cancer deaths in 2022 reached 9.4 million people. *Silybum marianum* L. (milk thistle) contains bioactive compounds such as silymarin, apigenin, kaempferol, luteolin, and quercetin with potential anticancer properties. This study aimed to analyze the potential of *S. marianum* compounds as CDK6 (*Cyclin-Dependent Kinase 6*) inhibitors by using in silico methods. *Protein Data Bank* was utilized to achieve molecular docking and BIOVIA Discovery Studio on CDK6 receptors (PDB: 3NUP, 3NUX, 2EUF, 4EZ5, 8I0M, 5L2I, 5L2S, 4TTH). Results showed doxorubicin (control) had the highest binding affinity (-7.36 kcal/mol), followed by apigenin (-6.29 kcal/mol), luteolin (-6.33 kcal/mol), quercetin (-6.19 kcal/mol), and kaempferol (-6.03 kcal/mol).

Statistical analysis (ANOVA) revealed significant differences between doxorubicin and flavonoids ($p < 0.05$ Molecular interaction analysis revealed flavonoids bound to critical residues of CDK6 (VAL141, LEU166, ASP163) via hydrogen and hydrophobic bonding. Apigenin exhibits a higher affinity than doxorubicin at 5L2I receptors (-7.5 kcal/mol and -7.0 kcal/mol), indicating its potential as a natural inhibitor of CDK6. Further research (in vitro/in vivo) is needed to confirm its safety and efficacy as a breast cancer anticancer contender.

FKeywords: *Silybum marianum*, breast cancer, CDK6, molecular docking, flavonoids.