Studi senyawa fenolik yang berpotensi sebagai anti candida kursei resistensi terhadap flukonazol dengan pendekatan farmakofor model = Study of phenolic compounds that have potential as Anti-Candida kursei resistance to flukonazol using a pharmacophore model approach

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Abstrak

Kandidiasis merupakan suatu penyakit kulit yang diakibatkan oleh Candida krusei yang telah resisten terhadap antijamur Flukonazol. Resistensi disebabkan gen penanda: ERG11, FKS1, ABC1 dan ABC2 yang meningkatkan aktivitas membran transporter. Maka diperlukan pencarian kandidat antijamur yang dapat menggantikan Flukonazol, dimulai dengan memanfaatkan senyawa fenolik yang terdapat pada tanaman herbal. Penelitian ini dilakukan untuk mencari kandidat antijamur Candida krusei dari golongan senyawa fenolik melalui perspektif studi In Silico dengan protein target Enzim lanosterol 14 -demetilase dengan kode PDB 5V5Z. Aplikasi LiganScout digunakan untuk Virtual Screening, ditemukan beberapa senyawa fenolik, diambil tiga senyawa yaitu Eugenol, Kuersetin, dan Asam Galat. Dilanjutkan dengan penambatan molekular menggunakan Aplikasi Molegro 2011. Hasil penambatan molekular senyawa ligan natif, Flukonazol, dan ketiga senyawa fenolik terhadap Enzim lanosterol 14-demetilase wild type menunjukkan rerank score berturut-turut: -154.433; -98.3027; -97.4626; -66.4573 dan -65.2084, sedangkan rerank score mutan: -31.0348; -99.4858; -92.1078; -63.9848; dan -62.6408. Ketiga senyawa fenolik menunjukkan potensi antijamur karena rerank score lebih baik dari ligan natif, meski tidak lebih baik dari rerank score Flukonazole. Dilakukan uji aktivitas Antijamur ketiga senyawa fenolik dan Flukonazol, didapatkan nilai uji hambat berturut-turut 3,33; 1,25; 0,63 dan 0 mm. Hal ini menunjukkan ketiga senyawa fenolik berpotensi sebagai Antijamur menggantikan Flukonazol di masa depan.

.....Candidiasis is a dermatological condition caused by the fungus Candida krusei, which exhibits resistance to the antifungal medication Fluconazole. The presence of marker genes, namely ERG11, FKS1, ABC1, and ABC2, leads to resistance via enhancing the function of membrane transporters. It is imperative to seek other antifungal options to replace Fluconazole. This can be achieved by harnessing the potential of phenolic chemicals derived from herbal plants. The purpose of this study was to identify potential antifungal agents for Candida krusei from the phenolic chemical category using In Silico experiments, focusing on the lanosterol 14 -demethylase enzyme with the PDB code 5V5Z. The LiganScout software was employed for Virtual Screening, resulting in the identification of many phenolic compounds. Three specific compounds were selected, namely Eugenol, Kuersetin, and Gallic Acid. Subsequently, molecular docking was performed utilizing the Molegro 2011 Application. The molecular docking results of the natif ligan compound, Fluconazole, and the three phenolic compounds against the wild type lanosterol 14-demethylase enzyme yielded rerank scores of -154.433, -98.3027, -97.4626, -66.4573, and -65.2084 respectively. The mutant rerank scores were -31.0348, -99.4858, -92.1078, -63.9848, and -62.6408. The three phenolic compounds exhibited antifungal efficacy as their rerank score surpassed that of the natural ligan, while it did not surpass the rerank score of Fluconazole. The antifungal activity of the three phenolic compounds and Fluconazole was individually examined using an inhibition test. The corresponding inhibition test values were 3.33 mm, 1.25 mm, 0.63 mm, and 0 mm, respectively. These findings demonstrate that the three

phenolic compounds possess the capacity to function as antifungal agents, potentially replacing Fluconazole in the future.