ABSTRAK

Candida albicans adalah jamur patogen oportunistik yang mampu membentuk biofilm, sehingga meningkatkan resistensi terhadap agen antijamur konvensional dan menimbulkan tantangan klinis dalam pengendalian infeksi. Penelitian ini bertujuan untuk mengeksplorasi potensi metabolit sekunder dari *Streptomyces* spp. sebagai agen antibiofilm terhadap *C. albicans* menggunakan pendekatan multi-omics. Penelitian ini berfokus pada identifikasi target protein kunci yang berkaitan dengan pembentukan biofilm pada *C. albicans*, pemetaan potensi biosintetik strain *Streptomyces*, karakterisasi profil metabolit, evaluasi aktivitas antijamur dan antibiofilm, serta validasi senyawa kandidat terpilih melalui analisis biologis dan komputasi. Penelitian ini mengintegrasikan proteomik *in silico*, analisis jaringan interaksi protein-protein, ontologi gen, analisis jalur KEGG, penambangan genom, karakterisasi morfologi, optimasi media fermentasi, kemometrik berbasis FTIR, metabolomik berbasis LC-HRMS, uji antibiofilm, analisis mikroskopi, penambatan molekuler, prediksi ADME-Tox, serta validasi eksperimental 7,8-dimethylalloxazine. Tiga strain *Streptomyces*, yaitu GMR22, SHP22-7, dan BSE7F, digunakan sebagai objek penelitian. Agglutinin-Like Sequence 3 (ALS3), Transcription Factor 1 (TEC1), dan Filamentous Growth Regulator 27 (FGR27) diprioritaskan sebagai target molekuler utama yang berperan dalam pembentukan biofilm *C. albicans*. Hasil penelitian menunjukkan bahwa GMR22 merupakan strain yang paling potensial, ditandai dengan kapasitas biosintetik yang tinggi, keragaman kluster gen biosintetik, aktivitas antibiofilm yang kuat, serta profil metabolit yang khas. Ekstrak etil asetat GMR22 menunjukkan penghambatan biofilm *C. albicans* yang paling konsisten, khususnya terhadap biofilm matang. Analisis korelasi LC-HRMS dan bioaktivitas mengidentifikasi turunan indol, lumichrome/7,8-dimethylalloxazine, N6-methyladenosine, flavonoid, dan senyawa fenolik sebagai metabolit yang berasosiasi dengan aktivitas antibiofilm. Penambatan molekuler menunjukkan bahwa lumichrome paling berpotensi sebagai senyawa multi-target terhadap ALS3, TEC1, dan FGR27. Validasi eksperimental mengonfirmasi bahwa lumichrome memiliki aktivitas antibiofilm secara langsung yang meningkat di bawah paparan cahaya, sehingga mengindikasikan potensinya sebagai kandidat antibiofilm turunan *Streptomyces*.

Kata kunci: *Streptomyces*, *Candida albicans*, biofilm, metabolomik, lumichrome.

ABSTRACT

Candida albicans is an opportunistic pathogenic fungus capable of forming biofilms, thereby increasing resistance to conventional antifungal agents and posing clinical challenges in infection control. This study aimed to explore the potential of secondary metabolites from *Streptomyces* spp. as antibiofilm agents against *C. albicans* using a multi-omics approach. The study focused on identifying key biofilm-related protein targets in *C. albicans*, mapping the biosynthetic potential of *Streptomyces* strains, characterizing metabolite profiles, evaluating antifungal and antibiofilm activities, and validating selected candidate compounds through biological and computational analyses. The research integrated *in silico* proteomics, protein–protein interaction network analysis, gene ontology, KEGG pathway analysis, genome mining, morphological characterization, fermentation media optimization, FTIR-based chemometrics, LC-HRMS-based metabolomics, antibiofilm assays, microscopy analysis, molecular docking, ADME-Tox prediction, and experimental validation of 7,8-dimethylalloxazine. Three *Streptomyces* strains, namely GMR22, SHP22-7, and BSE7F, were investigated. Agglutinin-Like Sequence 3 (ALS3), Transcription Factor 1 (TEC1), and Filamentous Growth Regulator 27 (FGR27) were prioritized as key molecular targets involved in *C. albicans* biofilm formation. The results showed that GMR22 was the most promising strain, with high biosynthetic capacity, diverse biosynthetic gene clusters, strong antibiofilm activity, and a distinct metabolite profile. The ethyl acetate extract of GMR22 showed the most consistent inhibition of *C. albicans* biofilm, particularly against mature biofilm. LC-HRMS and bioactivity correlation analyses identified indole derivatives, lumichrome/7,8-dimethylalloxazine, N6-methyladenosine, flavonoids, and phenolic compounds as metabolites associated with antibiofilm activity. Molecular docking suggested that lumichrome has the most potential as a multi-target compound against ALS3, TEC1, and FGR27. Experimental validation confirmed that lumichrome exhibited direct antibiofilm activity, which was enhanced under light exposure, indicating its potential as a *Streptomyces*-derived antibiofilm candidate.

Keywords: *Streptomyces*, *Candida albicans*, biofilm, metabolomics, lumichrome.