ABSTRACT

The increased incidence of fungal infections caused by *Candida albicans* in humans and the development of drug resistance has led to the rise in the search for microorganisms that have the capability of producing bioactive metabolites with antifungal activity. Microorganisms such as *Streptomyces* spp. have been distinguished for their potential to produce antifungal bioactive molecules and genome mining of *Streptomycetes* facilitates rapid discovery of their useful products. The objective of this study was to investigate if the extracts from *Streptomyces* sp. GMR-22 contained secondary metabolites that would inhibit the growth of *C. albicans*; ATCC 10231 and Fluconazole resistant strains (FR) as well as to identify novel secondary metabolites present in *Streptomyces* sp. GMR-22 by a genome mining approach. Gene clusters and chemical structures that encoded for biosynthetic pathways of secondary metabolites in the genome of *Streptomyces* sp. GMR-22 were predicted using the software antiSMASH (4.0). The extraction of *Streptomyces* sp. GMR-22 was carried out using n-hexane and chloroform. The crude extracts obtained from *Streptomyces* sp. GMR- 22 were screened using the TLC method. The MIC values of fluconazole and the *Streptomyces* sp. GMR-22 extracts were determined using the M27-A2 broth dilution method. From this research, it was observed that the minimum inhibitory concentration (MIC) results of n-hexane, chloroform, and water extracts were negative showing no antifungal properties against the tested *C. albicans* ATCC 10231 and the FR strain. TLC results confirmed the presence of secondary metabolites present in the extracts. AntiSMASH 4.0 analysis was able to reveal that the genome of *Streptomyces* sp. GMR-22 contained a total of 150 gene clusters that encoded the biosynthetic pathways of secondary metabolites. PKS was observed to be the major group of the 150 gene clusters, with 3 gene clusters predicted to have antifungal properties; galbonolide A, fengycin, and Bafilomycin B1 (Cluster 11). The 150 gene clusters of secondary metabolites were identified as T1pks, T2pks, nrps, terpenes, lantipeptides, indoles, ectoines, bacteriocins, lassopeptides, and others. This concluded that *Streptomyces* sp. GMR- 22 contained biosynthetic gene clusters with antifungal properties and is a strong potential candidate for secondary bioactive metabolites sources.

Keywords: *Streptomyces* sp. GMR-22, *Candida albicans*, antifungal activity, genome mining, antiSMASH 4.0.

INTISARI

Peningkatan kejadian infeksi jamur yang disebabkan oleh *Candida albicans* pada manusia dan perkembangan resistensi obat telah memicu pencarian mikroorganisme yang memiliki kemampuan memproduksi metabolit bioaktif dengan aktivitas antijamur. Mikroorganisme seperti *Streptomyces* sp. GMR- 22 mengandung metabolit sekunder yang dapat menghambat pertumbuhan *C. albicans*; ATCC 10231 dan strain yang resisten terhadap Fluconazole (FR), juga untuk mengindentifikasi metabolit sekunder baru yang terdapat pada *Streptomyces* sp. GMR- 22 dengan cara penggalian genom. Kelompok gen dan struktur kimia yang mengkode jalur biosintesis metabolit sekunder pada genom *Streptomyces* sp. GMR- 22 diprediksi dengan menggunakan *software* antiSMASH (4.0). Ekstraksi *Streptomyces* sp. GMR- 22 dilakukan menggunakan n-heksana dan kloroform. Ekstrak kasar yang diperoleh dari *Streptomyces* sp. GMR- 22 diskrining dengan metode KLT. Nilai MIC Flukonazole dan ekstrak *Streptomyces sp.* GMR-22 ditentukan dengan metode *broth dilution* M27-A2. Dari penelitian ini diketahui bahwa konsentrasi hambat minimum (MIC) ekstrak n-heksana, kloroform dan air menunjukkan hasil negatif, sehingga tidak ada senyawa antijamur terhadap *C. albicans* ATCC 10231 dan strain FR yang diuji. Hasil KLT mengkonfirmasi adanya metabolit sekunder pada ekstrak. Analisis AntiSMASH 4.0 mampu mengungkapkan bahwa genom *Streptomyces sp.* GMR-22 berisi seluruhnya 150 kelompok gen yang mengkode jalur biosintesis metabolit sekunder. PKS diamati sebagai kelompok utama dari 150 kelompok gen, dengan 3 kelompok gen diperkirakan memiliki sifat anti jamur; galbonolida A, Fengisin dan Bafilomisin B1 (Cluster 11). Kelima kelompok gen metabolit sekunder tersebut diidentifikasi sebagai T1pks, T2pks, nrps, terpen, lantipeptide, indol, *ectoine*, *bacteriocin*, lassopeptide dan lain-lain. Dari penelitian ini disimpulkan bahwa *Streptomyces sp.* GMR- 22 mengandung biosintesis kelompok gen dengan senyawa antijamur dan dan bisa menjadi kandidat potensial kuat untuk sumber metabolisme bioaktif sekunder.

Kata kunci: *Streptomyces sp.* GMR22, *Candida albicans*, aktivitas antijamur, urutan genom, antiSMASH 4.0