



INTISARI

Senyawa antiplasmodium berat molekul rendah yang diisolasi dari bakteri, khususnya *Streptomyces* belum banyak dilaporkan. Penelitian ini bertujuan untuk mengetahui potensi senyawa berat molekul rendah dari *Streptomyces* sp. GMR22 sebagai antiplasmodium. *Genome mining* dilakukan menggunakan antiSMASH 5.1. Isolasi senyawa berat molekul rendah dari kultur vial dan supernatan kultur fermentasi masing-masing dilakukan dengan menggunakan SPME (fiber DVB/CAR/PDMS) dan pelarut organik *n*-heksana:etilasetat (EtOAc) (85:15v/v) dan diidentifikasi menggunakan *gas chromatography-mass spectrometry* (GC-MS). Uji aktivitas antiplasmodium ekstrak *n*-heksana:EtOAc dilakukan secara *in vitro* terhadap *P. falciparum* 3D7. Persentase parasitemia didapatkan melalui pengamatan mikroskopis dan 50% *inhibitory concentration* (IC₅₀) didapatkan melalui analisis probit. Uji konfirmasi antiplasmodium dilakukan dengan analisis *flow cytometry* menggunakan SYBR Green I untuk DNA *Plasmodium* dan antibodi CD235a untuk eritrosit. *Drug-likeness* senyawa berat molekul rendah diselidiki menggunakan SwissADME. *Streptomyces* sp. GMR22 diketahui memiliki 65 *biosynthetic gene clusters* (BGCs), dimana 5 diantaranya merupakan golongan terpena. Empat puluh senyawa berat molekul rendah diidentifikasi dari kultur vial, beberapa merupakan golongan terpena. Ekstrak *n*-heksana:EtOAc diketahui mengandung 21 senyawa berat molekul rendah berasal dari golongan alkohol, hidrokarbon, ester, aromatik/diester, diester, asam lemak, dan triester dimana memiliki aktivitas antiplasmodium potensi sedang (IC₅₀ = 38,61 ± 19,06 µg/mL). Konfirmasi dengan analisis *flow cytometry* menunjukkan bahwa ekstrak pada konsentrasi 50 µg/mL memiliki aktivitas antiplasmodium berdasarkan penurunan intensitas DNA *Plasmodium* yang dibandingkan terhadap kontrol. Hasil skrining *drug-likeness* diperoleh 3 senyawa merupakan *drug-likeness*, yaitu *phenylethyl alcohol*, *ethyl citrate*, dan *di-n-butyl phthalate*. *Streptomyces* sp. GMR22 menghasilkan senyawa berat molekul rendah sebagai antiplasmodium, dan diperlukan penelitian lebih lanjut untuk isolasi, identifikasi, dan uji sitotoksitas senyawa aktif antiplasmodium.

Kata kunci: Senyawa berat molekul rendah, *Streptomyces*, antiplasmodium, antimalaria



ABSTRACT

Low molecular weight (LMW) antiplasmodial compounds isolated from bacteria, particularly *Streptomyces* have not been widely reported. This study aimed to know the potency of the LMW compounds from *Streptomyces* sp. GMR22 as antiplasmodial. Genome mining was carried out using antiSMASH 5.1. Isolation of LMW compounds from the vial culture and the supernatant of fermentation culture was performed using SPME (DVB/CAR/PDMS fiber) and organic solvent of *n*-hexane:ethylacetate (EtOAc) (85:15v/v), respectively, and identified using gas chromatography-mass spectrometry (GC-MS). Antiplasmodial assay of *n*-hexane:EtOAc extract was carried out against *P. falciparum* (3D7). Parasitemia percentage obtained through microscopic observations and 50% inhibitory concentration (IC₅₀) obtained through probit analysis. The antiplasmodial confirmation test was done by flow cytometry analysis using SYBR Green I for *Plasmodium* DNA and anti-human CD235a for erythrocyte. The LMW compounds were investigated using SwissADME for drug-likeness. *Streptomyces* sp. GMR22 possessed 65 biosynthetic gene clusters (BGCs), in which 5 out of 65 were terpene classes. Forty LMW compounds were identified from the vial culture, partially as terpenes. *n*-Hexane:EtOAc extract contained 21 LMW compounds of alcohol, hydrocarbon, ester, aromatic/diester, diester, fatty acid, and triester classes, which possessed moderate antiplasmodial activity (IC₅₀ = 38.61 ± 19.06 µg/mL). The flow cytometry analysis confirmed that the extract at 50 µg/mL exhibited antiplasmodial activity based on a decreased *Plasmodium* DNA intensity as compared to the control group. The result of drug-likeness screening obtained that 3 LMW compounds were drug-likeness, namely phenylethyl alcohol, ethyl citrate, and di-*n*-butyl phthalate. *Streptomyces* sp. GMR22 produced LMW compounds as antiplasmodial, and further study was needed for isolation, identification, and cytotoxicity test of antiplasmodial active compounds.

Keywords: Low molecular weight compounds, *Streptomyces*, antiplasmodial, antimalaria