STUDI PENAMBATAN MOLEKUL, SINTESIS, DAN UJI BIOAKTIVITAS ANTIPLASMODIUM SENYAWA POLISIKLIK γ-LAKTAM

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INTISARI

Telah dilakukan studi tentang potensi senyawa polisiklik γ-laktam sebagai kandidat antiplasmodium. Penelitian diawali dengan penambatan molekul tiga senyawa polisiklik γ-laktam **A**, **B**, dan **C** terhadap protein *Plasmodium falciparum dihydrofolate reductase enzyme* (*PfDHFR*), *Plasmodium falciparum Enoyl-Acyl-Carrier Reduktase Gene* (*PfENR*), dan *Plasmodium falciparum Heat shock protein* 90 (*PfHsp90*). Penambatan molekul dilakukan menggunakan *software* AutoDockTools untuk mengetahui nilai energi ikatan dan interaksi yang terbentuk antara senyawa turunan polisiklik γ-laktam dengan sisi aktif protein. Selanjutnya, senyawa polisiklik γ-laktam disintesis dengan bahan dasar anhidrida ftalat dan aminopropanol melalui reaksi kondensasi, reduksi, dan siklisasi intramolekul. Produk reaksi dielusidasi dengan spektrometer ^{1}H-NMR, ^{13}C-NMR, GC-MS, dan FTIR. Senyawa polisiklik γ-laktam hasil sintesis diuji bioaktivitasnya sebagai senyawa antiplasmodium secara *in vitro* terhadap *Plasmodium falciparum* galur 3D7.

Nilai energi ikatan hasil penambatan molekul senyawa polisiklik γ-laktam **A**, **B**, dan **C** terhadap protein PfDHFR adalah sebesar -4,24; -6,07; dan -5,71 kkal/mol, terhadap protein PfENR adalah sebesar -5,51; -7,47; dan -5,99 kkal/mol dan terhadap protein PfHsp90 adalah sebesar -4,68; -6,33; dan -5,26 kkal/mol. Berdasarkan hasil penambatan molekul polisiklik γ-laktam **B** dilanjutkan untuk disintesis dan diuji bioaktivitas antiplasmodium. Senyawa polisiklik γ-laktam **B** berhasil disintesis dengan tiga tahap reaksi dan diperoleh persen hasil berturut-turut adalah 97, 80, dan 86%. Hasil uji bioaktivitas antiplasmodium secara *in vitro* menunjukan senyawa polisiklik γ-laktam **B** memiliki nilai IC_{50} sebesar 97,726 µg/mL dan dikategorikan bioaktivitas kurang aktif terhadap *Plasmodium falciparum* galur 3D7.

Kata Kunci : Penambatan molekul, *Plasmodium falciparum* galur 3D7, Polisiklik laktam, Uji antiplasmodium.

STUDY OF MOLECULAR DOCKING, SYNTHESIS, AND TESTS OF BIOACTIVITY INHIBITION OF ANTIPLASMODIAL POLYCYCLYC γ-LACTAM COMPOUNDS

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ABSTRACT

Studies on potential of polycyclic γ-lactam compounds as antiplasmodial candidates have been conducted. The investigation began with the calculation of binding energy of three polycyclic γ-lactam compounds of A, B, and C towards *Plasmodium falciparum dihydrofolate reductase enzyme* (*PfDHFR*), *Plasmodium falciparum Enoyl-Acyl-Carrier Reductase Gene* (*PfENR*) proteins, and *Plasmodium falciparum Heat shock protein 90* (*PfHsp90*). The molecular docking study was carried out using AutoDockTools software to determine the binding energy and interactions formed between polycyclic γ-lactam derivative and the protein active site. Furthermore, polycyclic γ-lactam compounds were synthesized from the precursors of phthalic anhydride and aminopropanol through condensation, reduction, and intramolecular cyclization reactions. The reaction products were elucidated with ^{1}H-NMR, ^{13}C-NMR, GC-MS, and FTIR spectrometers. The synthesized polycyclic γ-lactam was subjected to antiplasmodium assay against *Plasmodium falciparum* strain 3D7 by in vitro.

The binding energy of the molecular docking of polycyclic γ-lactam compounds A, B, and C to *PfDHFR* protein are -4.24; -6.07; and -5.71 kcal/mol, the *PfENR* protein are -5.51; -7.47; and -5.99 kcal/mol and for *PfHsp90* protein, are -4.68; -6.33; and -5.26 kcal/mol. Based on the moleclar doking study, polycilclic γ-lactam **B** was synthesiszed and tested for be synthesized and tested for antiplasmodial activity. The polycyclic γ-lactam **B** was successfully synthesized in three reaction steps and the yield percentages of 97, 80, and 86%, respectively. The antiplasmodial activity assay by in vitro showed that the polycyclic γ-lactam **B** compound had an IC_{50} value of 97.726 g/mL and was categorized as less active against *Plasmodium falciparum* strain 3D7.

Keyword: Antiplasmodial test, Molecular docking, *Plasmdoum falciparum*, Polycylic lactam