SINTESIS DAN UJI AKTIVITAS TURUNAN NITROFENILKALIKS[4]-2-METILRESORSINARENA SEBAGAI SENYAWA ANTIOKSIDAN DAN ANTIMALARIA SERTA PENAMBATAN MOLEKUL TERHADAP RESEPTOR *Pf*LDH

Siti Astika Nisa
20/466491/PPA/06057

INTISARI

Sintesis, uji aktivitas dan penambatan molekul turunan nitrofenilkaliks[4]-2-metilresorsinarena sebagai senyawa antioksidan dan antimalaria telah dilakukan. Senyawa turunan kaliks[4]-2-metilresorsinarena disintesis dalam satu tahap reaksi melalui reaksi siklokondensasi dengan mereaksikan resorsinol dan aldehida aromatik, yaitu 2-nitrobenzaldehida, 3-nitrobenzaldehida dan 4-nitrobenzaldehida. Reaksi dilakukan dengan menggunakan metode refluks dalam pelarut etanol dan katalis asam klorida 37%. Senyawa hasil sintesis dikarakterisasi menggunakan spektrometer FTIR, ^{1}H-NMR, ^{13}C-NMR, dan LC-MS. Uji aktivitas antioksidan dilakukan dengan metode DPPH (2,2-difenil-1-pikrilhidrazil), sedangkan uji aktivitas antimalaria dilakukan secara *in vitro* terhadap *Plasmodium falciparum* 3D7. Studi penambatan molekul dilakukan menggunakan perangkat lunak Autodock Vina terhadap reseptor *Pf*LDH.

Hasil penelitian menunjukkan bahwa senyawa *C*-2-nitrofenilkaliks[4]-2-metilresorsinarena (2NK), *C*-3-nitrofenilkaliks[4]-2-metilresorsinarena (3NK) dan *C*-4-nitrofenilkaliks[4]-2-metilresorsinarena (4NK) telah berhasil disintesis. Senyawa 2NK, 3NK dan 4NK memiliki persen hasil berturut-turut sebesar 86,4; 78,6 dan 95,7%. Senyawa 2NK, 3NK dan 4NK memiliki aktivitas antioksidan dengan nilai IC_{50} 116,10; 135,85 dan 93,76 µg/mL, sehingga senyawa 2NK dan 3NK dikategorikan moderat sedangkan senyawa 4NK dikategorikan kuat sebagai senyawa antioksidan. Uji aktivitas antimalaria terhadap 2NK, 3NK dan 4NK menghasilkan nilai IC_{50} berturut-turut 2,35; 1,68 dan 1,79 µM, sehingga senyawa-senyawa tersebut tergolong aktif sebagai antimalaria. Penambatan molekul yang dilakukan terhadap reseptor *P. falciparum lactate dehydrogenase* (*Pf*LDH) menunjukkan bahwa senyawa 2NK, 3NK dan 4NK memiliki nilai afinitas ikatan berturut-turut -5,1; -6,1; -6,0 kkal/mol serta memiliki interaksi spesifik berupa ikatan hidrogen terhadap residu asam amino Arg109, Thr101 dan Lys102 pada situs aktif reseptor.

Kata kunci: antimalaria, antioksidan, kaliks[4]resorsinarena, *Pf*LDH, *Plasmodium falciparum* 3D7

SYNTHESIS AND ACTIVITY TESTS OF NITROPHENYLCALIX[4]-2-METHYLRESORCINARENE AS ANTIMALARIAL AND ANTIOXIDANT AGENTS AND MOLECULAR DOCKING AGAINST PfLDH RECEPTOR

Siti Astika Nisa
20/466491/PPA/06057

ABSTRACT

Synthesis, activity test and molecular docking of nitrophenylcalix[4]-2-methylresorcinarene derivatives as antimalarial and antioxidant agents have been carried out. Calix[4]-2-methylresorcinarene derivatives were synthesized in one step reaction through cyclocondensation reaction by reacting resorcinol and aldehydes, i.e., 2-nitrobenzaldehyde, 3-nitrobenzaldehyde and 4-nitrobenzaldehyde. The reaction was carried out through the reflux method with ethanol and hydrochloric acid 37% as the solvent and catalyst, respectively. The synthetic products were characterized using FTIR, ^{1}H-NMR, ^{13}C-NMR, and LC-MS spectrometers. The antioxidant test was conducted using DPPH (2,2-diphenyl-1-picrylhydrazyl) method while the antimalarial activity test was carried out *in vitro* against *Plasmodium falciparum* 3D7.

The results showed that the *C*-2-nitrophenylcalix[4]-2-methylresorcinarene (2NK), *C*-3-nitrophenylcalix[4]-2-methylresorcinarene (3NK) and *C*-4-nitrophenylcalix[4]-2-methylresorcinarene (4NK) compounds were successfully synthesized. Compounds 2NK, 3NK and 4NK had 86.4, 78.6 dan 95.7% yield, respectively. Compounds 2NK, 3NK and 4NK had antioxidant activity with IC_{50} values of 116.10, 135.85 and 93.76 µg/mL, therefore, 2NK and 3NK compounds were categorized as moderate while 4NK was categorized as a strong antioxidant compound. The antimalarial activity test of 2NK, 3NK and 4NK gave IC_{50} values of 2.35, 1.68 and 1.79 µM, therefore, these compounds are classified as active as antimalarial compounds. Molecular docking performed against the *P. falciparum lactate dehydrogenase* (*Pf*LDH) receptor showed that the 2NK, 3NK and 4NK compounds had negative binding affinity values of -5.1; -6,1; 6,0 kcal/mol and had specific interactions in the form of hydrogen bonds to the amino acid residues Arg109, Thr101 and Lys102 in the active site of the receptor.

Keywords: antimalarial, antioxidant, calix[4]resorcinarene, *Pf*LDH, *Plasmodium falciparum* 3D7