# SINTESIS, UJI BIOAKTIVITAS DAN PENAMBATAN MOLEKUL TURUNAN KALIKS[4]-2-METILRESORSINARENA SEBAGAI ANTIMALARIA DAN ANTIOKSIDAN

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## INTISARI

Telah dilakukan sintesis, uji bioaktivitas, dan penambatan molekul turunan kaliks[4]-2-metilresorsinarena yaitu *C*-4-klorofenilkaliks[4]-2-metilresorsinarena (kaliks **A**), *C*-4-metoksifenilkaliks[4]-2-metilresorsinarena (kaliks **B**), dan *C*-4-dimetilaminofenilkaliks[4]-2-metilresorsinarena (kaliks **C**). Studi penambatan molekul dilakukan terhadap protein PfLDH dan PfENR. Sintesis dilakukan menggunakan metode refluks selama 24 jam dengan HCl 37% sebagai katalis dan etanol sebagai pelarut. Elusidasi struktur terhadap produk sintesis dilakukan berdasar analisis FTIR, $^{1}$H-NMR, dan LC-MS. Pengujian aktivitas sebagai antimalaria dilakukan secara *in vitro* terhadap *P. falciparum* FCR-3, sedangkan uji antioksidan dilakukan menggunakan metode penstabilan radikal DPPH.

Berdasarkan hasil penelitian diperoleh persen hasil kaliks **A**, **B**, dan **C** masing-masing sebesar 97, 95, dan 35%. Uji antimalaria terhadap *P. falciparum* FCR-3 menunjukkan bahwa kaliks **A** dan **C** aktif sebagai antimalaria dengan nilai $IC_{50}$ masing-masing 2,66 dan 13,83 μM, sedangkan kaliks **B** memiliki aktivitas sedang dengan nilai $IC_{50}$ sebesar 23,63 μM. Uji antioksidan menunjukkan bahwa kaliks **B** dan **C** bersifat antioksidan kuat ($IC_{50} \leq 100$ ppm), sedangkan kaliks **A** memiliki aktivitas sedang ($IC_{50} = 122{,}14$ ppm). Hasil penambatan molekul menunjukkan bahwa kaliks **A**, **B**, dan **C** memiliki kestabilan dan interaksi lebih baik terhadap PfENR dibandingkan dengan PfLDH. Penambatan terhadap PfENR menunjukkan nilai afinitas ikatan berturut-turut -7,8; -7,6; dan -8,0 kkal/mol, dan interaksi ikatan hidrogen dengan residu asam amino paling banyak adalah kaliks **A** (residu Thr367, Asn218, dan Ala219).

**Kata Kunci:** kaliks[4]-2-metilresorsinarena, antimalaria, antioksidan, PfENR

# *SYNTHESIS, BIOACTIVITY TEST AND MOLECULAR DOCKING OF CALIX[4]-2-METHYLRESORCINARENE DERIVATIVES AS ANTIMALARIAL AND ANTIOXIDANT AGENTS*

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## ABSTRACT

The synthesis, bioactivity assay and molecular docking of calix[4]-2-methylresorcinarene derivatives i.e., *C*-4-chlorophenylcalyx[4]-2-methylresorcinarene, *C*-4-methoxyphenylcalyx[4]-2-methylresorcinarene and *C*-4-dimethylaminophenylcalyx[4]-2-methylresorcinarene. Molecular docking studies against PfLDH and PfENR proteins have been conducted. The reaction was carried through the reflux method for 24 h using 37% HCl as the catalyst and ethanol as the solvent. The chemical structures of the synthesized products were confirmed by FTIR, $^{1}$H-NMR, and LC-MS analyses. The antimalarial activity assay was carried out against *P. falciparum* FCR-3, while the antioxidant assay was conducted using the DPPH method.

The results showed that calix **A**, **B**, dan **C** were obtained in 97, 95, and 35% yield, respectively. The antimalarial test against *P. falciparum* FCR-3 showed that calix **A** and **C** were active as antimalarials with $IC_{50}$ values of 2.66 and 13.83 µM, respectively, while calix **B** had a moderate activity with $IC_{50}$ value of 23,63 µM. Meanwhile, the antioxidant test showed that calix **B** and **C** showed strong antioxidants ($IC_{50} \leq 100$ ppm), while calix **A** showed moderate antioxidant activity ($IC_{50} = 122.14$ ppm). Molecular docking results showed that calix **A**, **B**, and **C** have better stability and interaction with PfENR compared to PfLDH. The against PfENR showed affinity energy values respectively of -7.8; -7.6; and -8.0 kcal/mol, and calix **A** had the most hydrogen bonding interaction with amino acid residues (Thr367, Asn218, and Ala219).

**Keywords:** calix[4]-2-methylresorcinarene, antimalarial, antioxidant, PfENR