PENENTUAN ANALOG KURKUMIN TERBAIK DARI 5-BROMO-2-HIDROKSIBENZALDEHIDA MELALUI PENAMBATAN MOLEKUL PADA PROTEIN *Plasmodium falciparum* LACTATE DEHYDROGENASE (PfLDH) DAN SARCO/ENDOPLASMIC RETICULUM Ca^{2+}-ATPASE (SERCA), SINTESIS SERTA UJI AKTIVITAS SEBAGAI ANTIMALARIA

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INTISARI

Penelitian ini bertujuan untuk mengetahui pengaruh penambahan gugus bromo pada senyawa analog kurkumin dengan variasi keton berupa aseton (1,5-bis(5-bromo-2-hidroksibenzilidin)penta-1,4-dien-3-on/analog kurkumin **A**), siklopentanon (2,5-bis(5-bromo-2-hidroksibenzilidin)siklopentanon/analog kurkumin **B**), dan sikloheksanon (2,6-bis(5-bromo-2-hidroksibenzilidin)sikloheksanon/analog kurkumin **C**) terhadap aktivitas antimalaria melalui penambatan molekul pada protein PfLDH dan SERCA dengan PDB ID: 1U4O dan 2EAU menggunakan software AutoDock Vina 1.1.2. Sintesis analog kurkumin **C** dengan interaksi terbaik dari 5-bromo-2-hidroksibenzaldehida dan sikloheksanon dalam etanol menggunakan katalis NaOH. Senyawa prekursor 5-bromo-2-hidroksibenzaldehida diperoleh dari reaksi 2-hidroksibenzaldehida dengan $KBrO_3$, HBr 47%, dan asam asetat glasial. Karakterisasi analog kurkumin C dilakukan dengan FTIR, DI-MS/MS, ^{1}H-NMR, dan analisis elemental. Uji aktivitas antimalaria secara *in vitro* dilakukan terhadap parasit *P. falciparum strain* FCR-3.

Hasil penelitian menunjukkan adanya penambahan gugus bromo pada analog kurkumin **C** dapat meningkatkan aktivitas pada residu asam amino protein PfLDH berupa Met30, Ile31, Ser245, dan Thr97 dengan nilai afinitas ikatan -8,1 kkal mol^{-1} serta protein SERCA pada residu asam amino Gln56, Gln108, dan Asp59 dengan nilai afinitas ikatan -9,0 kkal mol^{-1}. Senyawa analog kurkumin **C** berhasil disintesis berupa padatan berwarna oranye dengan rendemen sebesar 34,78%. Senyawa analog kurkumin **C** terbukti sangat aktif sebagai antimalaria dengan nilai IC_{50} 1,83 µg/mL dibandingkan senyawa kurkumin dengan nilai IC_{50} 6,51 µg/mL pada uji *in vitro* terhadap *P. falciparum strain* FCR-3.

Kata kunci: analog kurkumin, antimalaria, penambatan molekul, PfLDH, SERCA.

DETERMINATION OF THE BEST CURCUMIN ANALOGUE FROM 5-BROMO-2-HYDROXYBENZALDEHYDE THROUGH MOLECULAR DOCKING ON *Plasmodium falciparum* LACTATE DEHYDROGENASE (PfLDH) AND SARCO/ENDOPLASMIC RETICULUM Ca^{2+}-ATPASE (SERCA) PROTEINS, SYNTHESIS WITH ACTIVITY TEST AS ANTIMALARIAL

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ABSTRACT

This study aims to determine the effect of bromo group substituted curcumin analogue compounds with ketone variations in the form of acetone (1,5-bis(5-bromo-2-hydroxybenzylidine)penta-1,4-dien-3-one/curcumin analogue **A**), cyclopentanone (2,5-bis(5-bromo-2-hydroxybenzylidine)cyclopentanone/curcumin analogue **B**), and cyclohexanone (2,6-bis(5-bromo-2-hydroxybenzylidine) cyclohexanone/curcumin analogue **C**) against PfLDH and SERCA proteins as antimalarial through molecular docking with PDB ID: 1U4O and 2EAU using AutoDock Vina 1.1.2 software. Synthesis of curcumin analogue **C** with the best interaction from 5-bromo-2-hydroxybenzaldehyde and cyclohexanone in ethanol using NaOH catalyst. The precursor compound 5-bromo-2-hydroxybenzaldehyde was obtained from the reaction of 2-hydroxybenzaldehyde with KBrO3, HBr 47%, and glacial acetic acid. The characterization of curcumin analogue **C** was carried out by FTIR, DI-MS/MS, ^{1}H-NMR, and elemental analysis. Antimalarial activity test using in vitro against *P. falciparum* strain FCR-3 parasite.

The results of this research showed that the bromo group substituted curcumin analogue **C** could increase the activity on amino acid residues of PfLDH protein in the form of Met30, Ile31, Ser245, and Thr97 has binding affinity value of -8.1 kcal mol^{-1} and SERCA protein on amino acid residues Gln56, Gln108, and Asp59 with binding affinity value of -9.0 kcal mol^{-1}. Curcumin analogue **C** compound has been successfully synthesized to produce orange solid with yield of 34.78%. Curcumin analogue **C** compound proved to be very active as an antimalarial compound and its IC_{50} was 1.83 g/mL compared to curcumin compound with IC_{50} value of 6.51 g/mL by in vitro test against *P. falciparum* strain FCR-3.

Keyword: curcumin analogue, antimalarial, molecular docking, PfLDH, SERCA.