SINTESIS SENYAWA ANALOG KURKUMIN MONOKARBONIL ASIMETRIS SERTA PENAMBATAN MOLEKUL DENGAN TARGET PROTEIN Pf-DHFR-TS SEBAGAI ANTIMALARIA

Nur Hidayah
17/414640/PA/18140

INTISARI

Telah dilakukan sintesis senyawa analog kurkumin monokarbonil asimetris serta penambatan molekul sebagai antimalaria. Sintesis analog kurkumin monokarbonil asimetris dilakukan melalui dua tahap reaksi yaitu sintesis benzalaseton dilanjutkan kondensasi benzalaseton dengan benzaldehid tersubstitusi. Senyawa benzalaseton **A** [(E)-4-(4-hidroksil-3-metoksifenil) but-3-en-2-on] dan benzalaseton **B** [(E)-4-(2-hdroksifenil)but-3-en-2-on] dihasilkan dari reaksi antara vanilin dan salisilaldehid dengan aseton dalam pelarut etanol dengan katalis basa NaOH 8% (b/v) dengan pengadukan selama 24 jam. Sintesis senyawa analog kurkumin monokarbonil asimetris **AKMA 1** [1-(3-metoksi-4-hidroksifenil)-5-(4-metoksifenill)-penta-1,4-dien-3-on] dihasilkan dari reaksi benzalaseton **A** dengan senyawa *p*-anisaldehid dan senyawa analog kurkumin monokarbonil asimetris **AKMA 2** [1-(2-hidroksifenil)-5-(3-4-dimetoksifenill)penta-1,4-dien-3-on] dibuat dari benzalaseton **B** dengan senyawa veratraldehid. Kedua senyawa **AKMA 1** dan **AKMA 2** diperoleh melalui reaksi dengan perbandingan (1:1) dengan pelarut etanol dan menggunakan katalis basa NaOH 8% (b/v) dengan pengadukan selama 24 jam. Elusidasi struktur terhadap produk hasil sintesis dilakukan dengan spektrometer FTIR, GC/LC-MS dan ^{1}H-NMR. Senyawa **AKMA 1** dan **AKMA 2** diuji aktivitasnya sebagai senyawa antimalaria secara *in silico* terhadap protein *Pf*-DHFT-TS dan dilakukan analisis ADMET untuk mengetahui aktivitas biologisnya secara oral.

Hasil penelitian diperoleh masing-masing benzalaseton **A** dan **B** dengan rendemen 58,6% dan 54,57% sedang **AKMA 1** dengan rendemen 83,87% dan **AKMA 2** dengan rendemen 61,29%. Hasil uji aktivitas melalui penambatan molekul menunjukkan bahwa **AKMA 1** dan **AKMA 2** memiliki aktivitas antimalaria yang lebih baik dengan nilai energi afinitas -7,03 kkal/mol dan -7,64 kkal/mol yang lebih rendah dibanding ligan asli atau kurkumin. Hasil prediksi ADMET menunjukkan **AKMA 1** dan **AKMA 2** bersifat *non toxic* dan memenuhi standar *Lipinski's rule* sehingga dapat berdifusi pasif ke dalam sel dan dapat dikonsumsi secara oral.

Kata kunci: analog kurkumin monokarbonil asimetris, antimalaria, benzalaseton, penambatan molekul

SYNTHESIS OF ASYMMETRIC MONOCARBONYL CURCUMIN ANALOGUE COMPOUNDS AND MOLECULAR DOCKING WITH TARGETING Pf-DHFR-TS PROTEIN AS AN ANTIMALARIAL

Nur Hidayah
17/414640/PA/18140

ABSTRACT

Synthesis of asymmetric monocarbonyl curcumin analogue compounds and molecular docking as antimalarial have been carried out. Synthesis of asymmetric monocarbonyl curcumin analogues was carried out in a two-step reaction, namely synthesis of benzalacetone followed by condensation of benzalacetone with substituted benzaldehyde. Benzalacetone **A** [(E)-4-(4-hydroxyl-3-methoxyphenyl) but-3-en-2-one] and benzalacetone **B** [(E)-4-(2-hydroxyphenyl)but-3-en- 2-on] were made from the reaction of vanillin and salicylaldehyde with acetone in ethanol solvent with a base catalyst of 8% (w/v) NaOH with stirring method for 24 hours. Synthesis of the asymmetric monocarbonyl curcumin analogue **AKMA 1** [1-(3-methoxy-4-hydroxyphenyl)-5-(4-methoxyphenyl)-penta-1,4-diene-3-one] was made from the reaction of benzalacetone **A** with compound p-anisaldehyde and asymmetric monocarbonyl curcumin analogue **AKMA 2** [1-(2-hydroxyphenyl)-5-(3-4-dimethoxyphenyl)penta-1,4-diene-3-one] was made from benzalacetone **B** with veratraldehyde. The two compounds of **AKMA 1** and **AKMA 2** were obtained by reaction in a ratio (1:1) with ethanol as a solvent and using a base catalyst of 8% (w/v) NaOH with stirring for 24 hours. Structural elucidations of the synthesized product were carried out using FTIR, GC/LC-MS and ^{1}H-NMR spectrometers. Compounds **AKMA 1** and **AKMA 2** were tested for their activity as antimalarial compounds against Pf-DHFT-TS protein and ADMET analysis was performed to determine their biological activity orally.

The results showed that benzalacetone **A** and **B** were produced in yield of 58.6% and 54.57%, while **AKMA 1** and **AKMA 2** was yielde in 83.87% and 61.29% respectively. The results of the activity test through molecular docking showed that **AKMA 1** and **AKMA 2** had better antimalarial activity with affinity energy values of -7.03 kcal/mol and -7.64 kcal/mol which were lower than the original ligand or curcumin. ADMET prediction results show that **AKMA 1** and **AKMA 2** are non-toxic and conform Lipinski's rule standards so that they can diffuse passively into cells and can be consumed orally.

Keyword: antimalarial, asymmetric monocarbonyl curcumin analogue, benzalacetone, molecular docking