INTISARI

Prevalensi hipertensi pada penduduk umur ≥18 tahun di Indonesia mengalami peningkatan dari sebelumnya dan diperkirakan akan terus meningkat. Obat-obatan sintetis memegang porsi besar dalam terapi farmakologis hipertensi, salah satunya obat golongan ACE inhibitor. Namun, obat-obatan tersebut memiliki potensi efek samping dan memakan biaya yang relatif tinggi. Alternatif hipertensi pun muncul dari senyawa bahan alam, salah satunya tanaman kunyit (*Curcuma longa*) yang mengandung kurkumin. Kurkumin memiliki aktivitas sebagai antihipertensi, salah satunya melalui penghambatan enzim ACE. Namun, kurkumin memiliki bioavailabilitas dan stabilitas yang rendah. Maka, dilakukan modifikasi struktur menjadi senyawa analog kurkumin. Eksplorasi potensi senyawa analog kurkumin secara khusus dilakukan terhadap senyawa 2,6-bis-(4'-bromobenziliden)-sikloheksanon (senyawa analog kurkumin A137). Penelitian ini bertujuan untuk menelusuri potensi dan menguji aktivitas senyawa analog kurkumin 2,6-bis-(4'-bromobenziliden)-sikloheksanon) sebagai penghambat *Angiotensin Converting Enzyme*.

Penelitian ini terdiri dari pengujian *in silico* dan *in vitro* terhadap senyawa analog kurkumin 2,6-bis-(4'-bromobenziliden)-sikloheksanon. Uji *in silico* dilakukan dengan metode penambatan molekuler menggunakan program MOE untuk memprediksi interaksi antara senyawa dengan protein ACE. Uji aktivitas dilakukan secara *in vitro* menggunakan kit untuk mengonfirmasi adanya aktivitas penghambatan. Hasil uji *in vitro* berupa nilai aktivitas enzimatik dan persen penghambatan yang selanjutnya dianalisis secara statistika.

Hasil studi *in silico* menunjukkan bahwa senyawa analog kurkumin 2,6-bis-(4'-bromobenziliden)-sikloheksanon memiliki interaksi dengan ACE dengan model interaksi yang mirip dengan ramipril. Senyawa tersebut mampu berinteraksi dengan kofaktor Zn dan residu asam amino pada situs aktif ACE, yaitu Tyr523. Hasil studi *in vitro* menunjukkan bahwa senyawa analog kurkumin 2,6-bis-(4'-bromobenziliden)-sikloheksanon memiliki aktivitas enzimatik sebesar 6,0973±1,7712 mU dan persen penghambatan sebesar 85,5445±4,3071%. Senyawa tersebut memiliki aktivitas penghambatan yang signifikan terhadap ACE. Aktivitas penghambatan ACE oleh senyawa tersebut pun superior terhadap ramipril. Senyawa tersebut memiliki potensi penghambatan enzim ACE yang dapat dipertimbangkan untuk pengembangan alternatif obat antihipertensi.

Kata Kunci: 2,6-bis-(4'-bromobenziliden)-sikloheksanon, senyawa analog kurkumin A137, ACE, penambatan molekuler, uji aktivitas penghambatan ACE

ABSTRACT

The prevalence of hypertension among individuals aged ≥18 years in Indonesia has increased from previous levels and is expected to continue rising. Synthetic drugs play a significant role in the pharmacological therapy of hypertension, including drugs classified as ACE inhibitors. However, these drugs have the potential for side effects and come with relatively high costs. Alternatives for hypertension treatment have emerged from natural compounds, including turmeric (Curcuma longa) containing curcumin. Curcumin exhibits antihypertensive activity, one of which is through ACE inhibition. However, curcumin has low bioavailability and stability. Therefore, structural modification of curcumin into curcumin analogs has been carried out. The exploration of the potential of curcumin analog compounds was specifically carried out on the compound 2,6-bis-(4'-bromobenzylidene)-cyclohexanone (curcumin analog A137). This study aimed to investigate the potential and evaluate the activity of the curcumin analog 2,6-bis-(4'-bromobenzylidene)-cyclohexanone as Angiotensin Converting Enzyme inhibitor.

This study consisted of in silico and in vitro testing of the curcumin analog 2,6-bis-(4'-bromobenzylidene)-cyclohexanone. In silico testing was conducted using molecular docking method with the MOE program to predict the interaction between the compound and the ACE protein. Activity testing was performed in vitro using a kit to confirm the presence of inhibitory activity. The results of the in vitro test were in the form of enzymatic activity value and percentage of inhibition, which were then statistically analyzed.

The results of the in silico study showed that curcumin analog 2,6-bis-(4'-bromobenzylidene)-cyclohexanone has the potential to interact with ACE similar to ramipril. The compound was able to interact with Zn cofactor and amino acid residues at the ACE active site, namely Tyr523. The results of the in vitro study showed that the curcumin analog 2,6-bis-(4'-bromobenzylidene)-cyclohexanone had an enzyme activity of 6.0973±1.7712 mU and a percent inhibition of 85.5445±4.3071%. The compound has significant inhibitory activity against ACE. The ACE inhibitory activity of the compound was also superior to ramipril. The compound has ACE inhibitory potential that can be considered for the development of alternative antihypertensive drugs.

***Keywords**: 2,6-bis-(4'-bromobenzylidene)-cyclohexanone, curcumin analog A137, ACE, molecular docking, ACE inhibition activity test*