# SINTESIS ANALOG KURKUMIN MONOKETON BERBAHAN DASAR BENZILOKSIBENZALDEHIDA DAN AKTIVITASNYA SEBAGAI INHIBITOR TERHADAP α-AMILASE

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## INTISARI

Sintesis analog kurkumin monoketon berbahan dasar benziloksibenzaldehida, uji aktivitasnya sebagai inhibitor dan *molecular docking* terhadap enzim α-amilase telah dilakukan. Sintesis bahan dasar benziloksibenzaldehida dilakukan melalui reaksi eterifikasi Williamson pada senyawa hidroksibenzaldehida menggunakan pelarut DMF, $K_2CO_3$ sebagai basa, KI dan benzil klorida. Sintesis senyawa analog kurkumin dilakukan dengan reaksi Claisen-Schmidt antara dua jenis benziloksibenzaldehida yaitu 3-benziloksi-benzaldehida dan 4-benziloksibenzaldehida dengan tiga jenis keton yaitu aseton, siklopentanon dan sikloheksanon sehingga menghasilkan (1E,4E)-1,5-*bis*(3-(benziloksi)fenil)-1,4-pentadien-3-on (analog kurkumin A), (2E,5E)-2,5-*bis*(3-(benziloksi)benzilidin)siklopentanon (analog kurkumin B), (2E,6E)-2,6-*bis*(3-(benziloksi)benzilidin)sikloheksanon (analog kurkumin C), (1E,4E)-1,5-*bis*(4-(benziloksi)fenil)-1,4-pentadien-3-on (analog kurkumin D), (2E,5E)-2,5-*bis*(4-(benziloksi)benzilidin)siklopentanon (analog kurkumin E), (2E,6E)-2,6-*bis*(4-(benziloksi)benzilidin)sikloheksanon (analog kurkumin F). Hasil sintesis dianalisis strukturnya menggunakan spektrometer FTIR, LCMS/MS, $^{1}$H- dan $^{13}$C-NMR. Senyawa analog kurkumin dan akarbosa sebagai pembanding dilakukan uji aktivitas inhibisi terhadap enzim α-amilase serta ditentukan tipe inhibitornya. *Molecular docking* dilakukan untuk mengetahui jenis interaksi dan afinitas ikatan senyawa hasil sintesis dengan enzim α-amilase.

Hasil penelitian diperoleh 3-benziloksibenzaldehida dan 4-benziloksi-benzaldehida masing-masing menghasilkan *yield* sebesar 90,2 dan 88,8%. Sintesis analog kurkumin A, B, C, D, E dan F masing-masing menghasilkan *yield* sebesar 89,7; 97,4; 94,6; 97,3; 93,2 dan 78,1%. Uji aktivitas inhibisi menunjukkan empat senyawa analog kurkumin hasil sintesis memiliki aktivitas inhibisi lebih tinggi dari pada akarbosa yaitu senyawa analog kurkumin C, D, E dan F dengan nilai $IC_{50}$ masing-masing senyawa adalah 28,84; 19,05; 16,98 dan 19,95 µM. Senyawa analog kurkumin A dan B memiliki aktivitas inhibisi yang lebih rendah dari pada akarbosa dengan nilai $IC_{50}$ sebesar 33,11 dan 37,15 µM. Senyawa akarbosa memiliki nilai $IC_{50}$ sebesar 32,35 µM. Senyawa Analog kurkumin A, B, C, D, E, F dan akarbosa memiliki tipe penghambatan unkompetitif terhadap enzim α-amilase. *Molecular docking* senyawa analog kurkumin terhadap enzim α-amilase menunjukkan senyawa analog kurkumin A, B, C, D, E, dan F memiliki afinitas ikatan yang lebih rendah dari pada senyawa akarbosa.

Kata kunci: analog kurkumin, enzim α-amilase, benziloksibenzaldehida, *docking*.

# *SYNTHESIS OF MONOKETONE CURCUMIN ANALOGS FROM BENZYLOXYBENZALDEHYDE AND THEIR ACTIVITY AS INHIBITOR OF α-AMYLASE*

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## ABSTRACT

Synthesis of monoketone curcumin analogs from benzyloxybenzaldehyde, testing of its activity as inhibitor and molecular docking an α-amylase enzyme has been carried out. The synthesis of benzyloxybenzaldehyde base material was carried out through the Williamson etherification reaction on the hydroxybenzaldehyde compound using DMF as a solvent, $K_2CO_3$ as a base, KI and benzyl chloride. The synthesis of curcumin analogs compounds was conducted through the Claisen-Schmidt reaction between two types of benzyloksibenzaldehide (3-benzyloksibenzaldehyde and 4-benzyloksi-benzaldehyde) with three types of ketones (acetone, cyclopentanon and cyclohexanone) to produce (1E, 4E)-1,5-bis(3-benzyloxy))phenyl)-1,4-pentadient-3-one (curcumin analog A), (2E, 5E)-2,5-bis (3-(benzyloxy)benzylidine)cyclopentanone (curcumin analog B), (2E, 6E)-2,6-bis (3-(benzyloxy)benzylidine) cyclohexanone (curcumin analog C), (1E, 4E)-1,5-bis(4-(benzyloxy)phenyl)-1,4-pentadient-3-on (curcumin analog D), (2E, 5E)-2,5-bis(4-(benzyloxy)benzylidine)cyclopentanone (curcumin analog E), (2E, 6E)-2,6-bis (4-(benzyloxy)benzylidine))cyclohexanone (curcumin analog F). Furthermore, the results of the synthesis were analyzed using FTIR, LCMS/MS, $^{1}$H- and $^{13}$C-NMR spectrometers. The obtained curcumin analog was tested for its inhibitory activity against the α-amylase enzyme and determined the type of inhibitor. The inhibitory activity test of the α-amylase enzyme was also carried out on the acarbose as a comparison. Molecular docking was carried out to find out the type of interaction and the affinity of the bonds of the synthesized compound with the α-amylase enzyme.

The results showed that 3-benzyloxybenzaldehyde and 4-benzyloxy-benzaldehyde produced yields of 90.2 and 88.8%, respectively. Synthesis of curcumin analogs A, B, C, D, E and F yielded of 89.7; 97.4; 94.6; 97.3; 93.2 and 78.1%, respectively. The inhibitory activity of four curcumin analog compounds (C, D, E dan F) were higher that of the acarbose. On the contrary, the inhibitory activity of analog A and B was lower that of the acarbose. Curcumin analog compounds (A, B, C, D, E, and F) and acarbose have an uncompetitive inhibitory type of the α-amylase enzyme. Molecular docking study revealed that the curcumin analog compounds have lower binding affinity than that of acarbose.

Key words : curcumin analogs, α-amylase, benzyloxybenzaldehyde, docking.