

SINTESIS ANALOG KURKUMIN SIMETRIS DARI TURUNAN HIDROKSIBENZALDEHIDA DAN UJI AKTIVITASNYA SEBAGAI INHIBITOR ENZIM α -AMILASE SERTA EFEK SINERGISITASNYA DENGAN ASAM FERULAT

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INTISARI

Senyawa 2,6-bis(4-hidroksi-3-metoksibenzilidin)sikloheksanon (analog kurkumin **A**), senyawa 2,6-bis(4-hidroksibenzilidin)sikloheksanon (analog kurkumin **B**), dan senyawa 2,6-bis(3-hidroksibenzilidin)sikloheksanon (analog kurkumin **C**) telah berhasil disintesis. Uji aktivitas senyawa analog kurkumin **A**, **B**, dan **C** sebagai inhibitor enzim α -amilase dan efek sinergisitasnya dengan asam ferulat telah dilakukan. Sintesis senyawa analog kurkumin berlangsung melalui reaksi Claisen-Schmidt antara turunan hidroksibenzaldehida (vanilin, 4-hidroksi benzaldehida, dan 3-hidroksibenzaldehida) dengan sikloheksanon dalam suasana asam. Struktur senyawa hasil sintesis dikonfirmasi dengan Spektrofotometer FTIR, *Direct Inlet*-MS, Spektrometer ^1H - dan ^{13}C -NMR.

Hasil penelitian diperoleh analog kurkumin **A** berupa padatan berwarna kuning dengan rendemen 65,03% dan titik leleh 178-179 °C, analog kurkumin **B** berupa padatan berwarna hijau pucat dengan rendemen 67,35% dan titik leleh 288-289 °C, dan analog kurkumin **C** berupa padatan berwarna oranye dengan rendemen 66,34% dan titik leleh 211-213 °C. Senyawa analog kurkumin **A**, **B**, dan **C** berpotensi sebagai inhibitor enzim α -amilase dengan aktivitas inhibisi tertinggi masing-masing 32,52; 87,69; dan 69,30% pada konsentrasi 1 mM dengan nilai IC_{50} 12,14; 2,54 dan 3,73 mM. Senyawa analog kurkumin **B** memiliki aktivitas inhibisi terbaik 87,69% dan nilai IC_{50} 2,54 mM. Uji sinergisitas menunjukkan bahwa kombinasi senyawa analog kurkumin **A** dan asam ferulat dengan perbandingan 1:1 memberikan efek sinergis ringan-sedang dengan nilai IC_{50} sebesar 2,43 mM. Kombinasi senyawa analog kurkumin **B** dan asam ferulat memberikan aktivitas inhibisi optimum pada perbandingan 2:1 dengan nilai IC_{50} sebesar 1,27 mM dan menghasilkan efek sinergis ringan-sedang. Kombinasi senyawa analog kurkumin **C** pada semua perbandingan memberikan efek antagonis.

Kata kunci: analog kurkumin, antidiabetes, enzim α -amilase, asam ferulat.

**SYNTHESIS OF SYMMETRIC CURCUMIN ANALOGUES FROM
HYDROXYBENZALDEHYDE DERIVATIVES AND THEIR ACTIVITY
ASSAY AS INHIBITOR OF α -AMYLASE ENZYME AND ITS
SYNERGISM EFFECT WITH FERULIC ACID**

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ABSTRACT

Compounds of 2,6-bis(4-hydroxy-3-methoxybenzylidene)cyclohexanone (curcumin analogue **A**), 2,6-bis(4-hydroxybenzylidene)cyclohexanone (curcumin analogue **B**), and 2,6-bis(3-hydroxybenzylidene)cyclohexanone (curcumin analogue **C**) have been successfully synthesized. Activity assay of curcumin analogues **A**, **B**, and **C** as inhibitor α -amylase enzyme and synergism effect with ferulic acid have also been carried out. The synthesis of curcumin analogues has been performed through Claisen-Schmidt reaction between hydroxybenzaldehyde derivatives (vanillin, 4-hydroxybenzaldehyde, and 3-hydroxybenzaldehyde) and cyclohexanone in acid condition. The structures of the products were elucidated by FTIR Spectrophotometer, Direct Inlet-Mass Spectrometer, ^1H -, and ^{13}C -NMR Spectrometer.

The results showed that curcumin analogue **A** was obtained as yellow solid in 65.03% yield with m.p. of 178-179 °C, curcumin analogue **B** was yielded as pale green solid in 67.35% with m.p. of 288-289 °C and curcumin analogue **C** was produced in 66.34% as orange solid with m.p. of 211-213 °C. The results of inhibition activities of α -amylase enzyme showed that curcumin analogues **A**, **B**, and **C** were potential as an α -amylase enzyme inhibitor with the inhibition activity at concentration 1 mM of 32.52; 87.69; and 69.30% and IC_{50} of 12.31; 2.54; and 3.73 mM respectively. Curcumin analogue **B** was the best inhibitor α -amylase enzyme with inhibition activity of 87.69% and IC_{50} of 2.54 mM. The results of the synergistic assay showed that the combination of curcumin analogue **A** and ferulic acid (1:1) indicates a moderate to slight synergism effect with IC_{50} of 2.43 mM. The combination of curcumin analogue **B** and ferulic acid (2:1) had the optimum of inhibition activity with IC_{50} of 1.27 mM and gave a moderate to slight synergism effect. The combination of curcumin analogue **C** had an antagonism effect in all concentration ratios.

Keywords: curcumin analogue, antidiabetic, α -amylase enzyme, ferulic acid.