

INTISARI

Tuberkulosis (TB) memakan jutaan korban di dunia setiap tahun, dan bentuk-bentuk TB yang resisten terhadap obat terus bermunculan. Hal ini menjadi pendorong pentingnya penemuan obat TB baru. Berdasar pada studi terdahulu, senyawa kurkumin dan turunannya (analog) menunjukkan aktivitas antibakteri. Pada penelitian ini akan dilakukan sintesis senyawa analog kurkumin A-154 (2,6-Bis(2',4'-diklorobenziliden)-sikloheksanon) serta dilakukan uji afinitas senyawa analog kurkumin tersebut dengan protein target TB.

Sintesis senyawa analog kurkumin dilakukan melalui kondensasi aldol menggunakan metode *microwave-assisted organic synthesis* (MAOS) menggunakan starting material berupa 2,4-Diklorobenzaldehid dan Sikloheksanon dengan rasio mol ekuivalen 2:1 dan katalis HCl. Hasil sintesis diuji kemurniannya melalui uji jarak lebur dan KLT, lalu senyawa dielusidasi menggunakan spektrometer GC-MS, FTIR, ¹H-NMR, dan ¹³C-NMR. Uji afinitas anti-TB dilakukan secara *in silico* dengan metode penambatan molekul pada protein MtDHFR, lalu dianalisis afinitasnya berdasarkan perbandingan energi ikatan dan visualisasi interaksi protein-ligan hasil penambatan molekul dengan ligan alami dan beberapa antifolat.

Senyawa analog kurkumin yang dihasilkan berupa kristal kuning senyawa 2,6-Bis(2',4'-diklorobenziliden)-sikloheksanon dengan rendemen 38,63%, tergolong murni dengan jarak lebur 158,2-159,0 °C, dan penampakan bercak tunggal pada KLT menggunakan eluen etil asetat:heksan (1:9 v/v). Hal ini diperjelas melalui data spektrum GC-MS, FTIR, ¹H-NMR dan ¹³C-NMR. Hasil penambatan molekul menunjukkan bahwa senyawa memiliki afinitas terhadap protein target yang ditandai oleh ikatan spesifik yang mirip dengan ligan alami dan antifolat lain, nilai energi ikatan terendah yang dimiliki senyawa A-154 terhadap protein MtDHFR adalah -7,77 kkal/mol.

Kata Kunci : analog kurkumin, anti-tuberkulosis, kurkumin, *microwave-assisted organic synthesis*, penambatan molekul

ABSTRACT

Tuberculosis (TB) claims millions of lives worldwide each year, and drug-resistant forms of TB continue to emerge. This underscores the urgent need for the discovery of new anti-TB drugs. Based on previous studies, curcumin and its derivatives (analogues) have shown antibacterial activity. In this study, the synthesis of a curcumin analogue compound A-154 (2,6-Bis(2',4'-dichlorobenzylidene)-cyclohexanone) was carried out, followed by an affinity test of the synthesized analogue against a TB target protein.

The curcumin analogue was synthesized via aldol condensation using the microwave-assisted organic synthesis (MAOS) method, with 2,4-dichlorobenzaldehyde and cyclohexanone as the starting materials in a 2:1 molar ratio and HCl as the catalyst. The purity of the synthesized compound was tested using melting point analysis and thin-layer chromatography (TLC), and then the compound was elucidated using GC-MS, FTIR, ¹H-NMR, and ¹³C-NMR spectroscopy. Anti-TB affinity was evaluated *in silico* using molecular docking against the MtDHFR protein, with affinity determined based on binding energy comparisons and visualization of protein-ligand interactions compared to the natural ligand and several antifolates.

The synthesized curcumin analogue was obtained as a yellow crystalline compound, identified as 2,6-Bis(2',4'-dichlorobenzylidene)-cyclohexanone, with a yield of 38.63%, relatively pure as indicated by a melting point of 158.2–159.0 °C, and a single spot on TLC using ethyl acetate:hexane (1:9 v/v) as the eluent. These findings were supported by spectral data from GC-MS, FTIR, ¹H-NMR, and ¹³C-NMR. Molecular docking results showed that the compound had good affinity for the target protein, evidenced by specific interactions similar to those of the natural ligand and other antifolates, the lowest binding energy of compound A-154 against MtDHFR protein was -7.77 kcal/mol.

Keywords: curcumin analog, anti-tuberculosis, curcumin, microwave-assisted organic synthesis, molecular docking