INTISARI

Reaksi multikomponen modifikasi amidoalkilasi dilakukan dengan mencampurkan tiga senyawa secara bersamaan. Metode ini berkembang ke arah anti-tuberkulosis karena produk hasil sintesis mempunyai ikatan CO-NH yang memiliki aktivitas biologis. Tuberkulosis (TB) merupakan penyakit infeksi yang disebabkan bakteri *M. Tuberculosis*. Resistensi bakteri diantaranya *Multidrugs Resistant-TB* (MDR-TB) dan *Extensively drug Resistant-TB* (XDR-TB) terhadap obat anti-TB menjadi masalah baru dalam pengobatan. Penelitian ini bertujuan untuk mensintesis senyawa klorobenzil-formamid menggunakan metode reaksi multikomponen yang kemudian diuji aktivitasnya sebagai anti-TB. Senyawa klorobenzil-formamid memiliki kemiripan struktur dengan Isoniazid karena mempunyai ikatan CO-NH pada strukturnya.

Senyawa klorobenzaldehid (2-klorobenzaldehid, 4-klorobenzaldehid, 2,4-diklorobenzaldehid, atau 2,6-diklorobenzaldehid) direaksikan dengan formamida melalui *amidoalkylation* dengan reduktor $NaBH_4$ dan/atau asam format. Senyawa hasil sintesis diidentifikasi dengan elusidasi struktur menggunakan metode spektroskopi (^{1}H-NMR, ^{13}C-NMR, FTIR) dan GC-MS. Uji aktivitas antituberkulosis menggunakan metode *Microplate Alamar Blue Assay* (MABA) dan media *Middlebrook* 7H9-7H11 dengan seri konsentrasi 1000-1,954 µg/Ml terhadap bakteri *M. tuberculosis* strain H_{37}Rv.

Hasil penelitian menunjukkan bahwa produk berhasil disintesis menggunakan reaksi multikomponen metode asam format dengan nilai %rendemen 36,5%(LR-107-K4), 42%(LR-137-K8), 7,3%(LR-130-K12) dan 3%(LR-131-K16). Elusidasi struktur menunjukkan kemurnian 100% menggunakan GC-MS dan analisis FTIR, ^{1}H-NMR dan ^{13}C-NMR mengkonfirmasi struktur senyawa. Hasil uji aktivitas antituberkulosis senyawa target didapatkan nilai KHM LR-107-K4, LR-137-K8 dan LR-131-K16 sebesar 1000 µg/mL, sedangkan LR-130-K12 sebesar 500 µg/mL. Senyawa hasil sintesis dengan $NaBH_4$ tidak membentuk senyawa target, akan tetapi memiliki nilai KHM 1000 µg/mL untuk LR-107-K17, 500 µg/mL untuk LR-137-K18, LR-130-K19 dan 250 µg/mL untuk LR-131-K20. Nilai KBM 1000 µg/mL didapatkan untuk senyawa LR-131-K20. Senyawa target memiliki aktivitas antituberkulosis, akan tetapi pada konsentrasi yang tinggi serta tidak lebih poten dibandingkan dengan INH (2 µg/mL) sebagai kontrol obat.

KATA KUNCI : klorobenzil-formamid, antituberkulosis, reaksi multikomponen, elusidasi struktur, KHM, KBM.

ABSTRACT

The multicomponent amidoalkylation reaction is done by mixing three compounds simultaneously. This method develops in the direction of anti-tuberculosis because the synthesized product has a CO-NH bond that has biological activity. Tuberculosis (TB) is an infectious disease caused by M. tuberculosis. Bacterial resistance including Multidrugs Resistant-TB (MDR-TB) and Extensive drug Resistant-TB (XDR-TB) against anti-TB drugs is a new problem in treatment. This study aims to synthesize chlorobenzyl-formamide compounds using multicomponent reaction methods which are then tested for their activity as anti-TB. The chlorobenzyl-formamide compound has a similar structure with Isoniazid because it has a CO-NH bond in its structure.

Chlorobenzaldehyde compounds (2-chlorobenzaldehyde, 4-chlorobenzaldehyde, 2,4-dichlorobenzaldehyde, or 2,6-dichlorobenzaldehyde) are reacted with formamide through amidoalkylation with the reducing agent NaBH4 or formic acid. The synthesized compounds were identified by structural elucidation using spectroscopic methods (^{1}H-NMR, ^{13}C-NMR, FTIR) and GC-MS. The antituberculosis activity test used the Microplate Alamar Blue Assay (MABA) method and the Middlebrook 7H9-7H11 media with a concentration series of 1000-1,954 µg / mL against M. tuberculosis bacteria strain H37Rv.

The results showed that the product was successfully synthesized using a multicomponent reaction with formic acid with yield of LR-107-K4, LR-137-K8, LR-130-K12, LR-131-K16 are 36.5%, 42%, 7.3% and 3% respectively. Structure elucidation showed 100% purity using GC-MS and FTIR, ^{1}H-NMR and ^{13}C-NMR confirmed the structure of the compound. The results of the antituberculosis activity test of the target compound obtained a MIC are 1000 µg / mL for LR-107-K4, LR-137-K8 and LR-131-K16 , while compound LR-130-K12 was 500 µg / mL. Synthesized compounds with NaBH4 do not obtain the target compounds, but have MIC value 1000 µg / mL for LR-107-K17, 500 µg / mL for LR-137-K18, LR-130-K19 and 250 µg / mL for LR-131-K20. 1000 µg / mL MBC value was obtained for the LR-131-K20 compound. The target compound has antituberculosis activity, but at high concentrations but are less potent than INH (2 µg / mL) as drug control.

KEY WORDS: chlorobenzyl-formamide, antituberculosis, multicomponent reaction, elucidation structure, KHM, KBM.