# INTISARI

Diabetes melitus (DM) merupakan kondisi dimana tubuh penderitanya tidak dapat memproduksi insulin dengan baik. Kurkumin dilaporkan memiliki aktivitas antidiabetes dengan menghambat α-glukosidase. Namun kurkumin memiliki profil farmakokinetik yang buruk. Untuk memperbaiki hal tersebut dilakukan modifikasi struktur. Penelitian ini bertujuan untuk mengetahui potensi senyawa analog kurkumin seri dibenziliden-sikloheksanon sebagai agen antidiabetes berdasarkan pengujian *in-silico* serta mensintesis senyawa yang memiliki nilai prediksi terbaik. Metode *in-silico* meliputi *virtual screening, pharmacophore modeling, molecular docking* terhadap protein *crystal structure of the N-terminal subunit of human maltase-glucoamylase in complex with acarbose* (PDB ID: 2QMJ), dan *molecular dynamics*. Kemudian tiga senyawa analog kurkumin yang diprediksi berpotensi sebagai agen antidiabetes disintesis menggunakan *starting material* keton siklik dan aromatik aldehid dengan suasana asam menggunakan metode *microwave-assisted*.

Hasil *virtual screening* menunjukkan bahwa seluruh senyawa analog kurkurmin menunjukkan hasil yang cukup baik, mematuhi aturan Lipinski (kecuali senyawa A119), aman, dan tidak toksik. Berdasarkan *pharmacophore modeling*, senyawa A106, A107, dan A115 memiliki kemiripan struktur dengan model, sedangkan hasil *molecular docking* menunjukkan senyawa A119, A117, dan A115 memiliki energi ikatan yang terendah dengan -10,74; -9,21; dan -9,02 kkal/mol, yang mana akan dilanjutkan analisisnya pada *molecular dynamics* dan sintesis. Hasil *molecular dynamics* menunjukkan kompleks yang stabil yang dibuktikan dengan nilai RMSD, RMSF, Rg, SASA, ikatan hidrogen, dan MM/PBSA. Sintesis senyawa A115 dan A117 menghasilkan rendemen 86,55 dan 52,86% pada kondisi asam dengan suhu 80 °C selama 60 menit. Namun, senyawa A119 masih menghasilkan senyawa campuran. Penelitian ini diharapkan dapat digunakan untuk penelitian lanjutan *in-vitro* dan *in-vivo* untuk mengetahui potensi senyawa analog kurkumin sebagai agen antidiabetes.

**Kata Kunci**: antidiabetes, *molecular docking*, *molecular dynamics*, senyawa analog kurkumin, sintesis senyawa organik

# *ABSTRACT*

*Diabetes mellitus (DM) is a condition where the body cannot produce insulin. Curcumin is reported to have antidiabetic activity by inhibiting α-glucosidase. However, curcumin has a poor pharmacokinetic profile. To improve this, structural modification is carried out. This study aims to determine the potential of dibenzyliden-cyclohexanone series curcumin analog compounds as antidiabetic agents based on in-silico testing and to synthesize compounds that have the best predictive value. In-silico methods include virtual screening, pharmacophore modeling, molecular docking against the protein crystal structure of the N-terminal subunit of human maltase-glucoamylase in complex with acarbose (PDB ID: 2QMJ), and molecular dynamics. Then, three curcumin analog compounds predicted to have potential as antidiabetic agents were synthesized using cyclic ketone and aromatic aldehyde starting materials in an acidic atmosphere using a microwave-assisted method.*

*The virtual screening showed that all kurkurmin analog compounds showed good results, obeyed Lipinski's rule (except compound A119), were safe, and non-toxic. Based on pharmacophore modeling, compounds A106, A107, and A115 have structural similarity with the model. At the same time, molecular docking results show compounds A119, A117, and A115 have the lowest binding energy with -10.74, -9.21, and -9.02 kcal/mol, which will continue their analysis in molecular dynamics and synthesis. The molecular dynamics results show a stable complex as evidenced by the RMSD, RMSF, Rg, SASA, and hydrogen bond values. Synthesis of compounds A115 and A117 produced yields of 86.55 and 52.86% under acidic conditions with a temperature of 80 ℃ for 60 minutes. However, compound A119 produced a mixed compound. This research is expected to be used further in-vitro and in-vivo to determine the potential of curcumin analog compounds as antidiabetic agents.*

***Keywords**: antidiabetes, molecular docking, molecular dynamics, curcumin analog compounds, organic compound synthesis*