

## INTISARI

Obesitas diangkat sebagai indikator prioritas kesehatan pada rencana pembangunan jangka menengah nasional 2020-2024 dengan target prevalensi obesitas 21,8% sampai akhir tahun 2024. Stres oksidatif yang disebabkan oleh obesitas dapat mengakibatkan kerusakan sel dan jaringan serta memicu munculnya penyakit degeneratif. Antioksidan membantu menetralkan radikal bebas dan mengurangi resiko komplikasi penyakit degeneratif. Antiobesitas bekerja sebagai penghambat lipase dan penekan nafsu makan pada SSP. Ekstrak *Curcuma aeruginosa* Roxb memiliki penghambatan terhadap lipase pankreas dan antioksidan. Belum ada penelitian yang menelusur sampai tingkat isolat pada kedua aktivitas tersebut.

Rimpang *Curcuma aeruginosa* Roxb diremaserasi dengan etanol 70% dan dilakukan isolasi dengan KCV dan KLTP. Proses isolasi senyawa dipandu oleh aktivitas penghambatan lipase pankreas dan antioksidan. Struktur dan nama isolat diidentifikasi menggunakan teknik spektroskopi meliputi MS, UV-Vis, FTIR dan NMR. Isolat dilakukan *molecular docking* dengan enzim lipase, reseptor 5-HT<sub>2c</sub>, TAAR-1, dan GLP-1. Isolat juga diprediksi profil *lipinski's rule of five* dan profil farmakokinetik ADMET (absorpsi, distribusi, metabolisme, ekskresi, dan toksisitas).

Isolat bioaktif penghambat lipase pankreas adalah 7-hydroxy-3,7,12-trimethyl-6,7,8,9,10,11-hexahydrobenzo [11,12] oxireno [1,4,5,6,11,12,13] cyclohepta [1,4] furan 2-one (FLEA.d9a) dan (6R,10S)-9-hydroxy-1,3,9-trimethyl-5,6,7,8,9,10,11,1-octahydro-2H-indeno [1,4] furan-2-one (FLEA.d9b) Isolat bioaktif antioksidan adalah zederone (FLE.a1) dan curcumenotone (FLE.a2). FLEA.d9b dan kontrol positif orlistat menunjukkan penghambatan lipase pankreas yang kuat (>80%) diikuti oleh FLEA.d9a menunjukkan aktivitas sedang (41%–80%). Aktivitas antioksidan isolat dievaluasi menggunakan uji DPPH, FRAP, dan ABTS. FLE.a1, FLE.a2 dan kontrol kuersetin menunjukkan aktivitas antioksidan yang kuat (IC<sub>50</sub> 50-100µg/mL) sampai sangat kuat (IC<sub>50</sub> <50µg/mL) pada ketiga metode. Isolat menunjukkan ikatan dengan residu asam amino penting pada protein target antiobesitas kecuali FLE.d9a tidak terikat Ser152 pada protein lipase 1LPB dan FLE.a1 tidak terikat Ser122 pada protein lipase 5ZUN. Pada prediksi profil farmakokinetik, semua isolat memenuhi kriteria *lipinski's rule of five* namun FLEA.d9a menunjukkan toksisitas AMES dan FLE.a2 menunjukkan sensitisasi kulit.

**Kata Kunci :** *Curcuma aeruginosa* Roxb, antiobesitas, penghambatan lipase pankreas, antioksidan, *molecular docking*

## ABSTRACT

Obesity was identified as one of the health priority indicators in the 2020-2024 national medium-term development plan, with a target of 21.8% prevalence in Indonesia by the end of 2024. Oxidative stress caused by obesity can cause cell and tissue damage and trigger the emergence of degenerative diseases. Antioxidants help neutralize free radicals and reduce the risk of complications from degenerative diseases. Antiobesity works as a lipase inhibitor and appetite suppressant in the CNS. *Curcuma aeruginosa* Roxb extract has inhibition of pancreatic lipase and antioxidants. There has been no research that has traced the level of isolates in these two activities.

*Curcuma aeruginosa* Roxb rhizome were remacerated with 70% ethanol solvent and the compounds were isolated with VLC and preparative TLC. The compound isolation process was guided by pancreatic lipase inhibitory and antioxidant activity. The structure and name of the isolate were identified using spectroscopic techniques including MS, UV-Vis, FTIR and NMR. The isolates were subjected to molecular docking with lipase enzymes, 5-HT<sub>2c</sub> receptor, TAAR-1, and GLP-1. Additionally, the isolated compound complied with Lipinski's rule of five and exhibited favorable ADMET properties.

The bioactive isolate of pancreatic lipase inhibitor are *7-hydroxy-3,7,12-trimethyl-6,7,8,9,10,11-hexahydrobenzo [11,12] oxireno [1,4,5,6,11,12,13] cyclohepta [1,4] furan 2-one* (FLEA.d9a) and *(6R,10S)-9-hydroxy-1,3,9-trimethyl-5,6,7,8,9,10,11,1-octahydro-2H-indeno [1,4] furan-2-one* (FLEA.d9b). Antioxidant bioactive isolates are *zederone* (FLE.a1) and *curcumenotone* (FLE.a2). FLEA.d9b and orlistat showed strong inhibition (>80%), followed by FLEA.d9a which showed moderate activity (41%–80%). The antioxidant activity of the isolates was evaluated using DPPH, FRAP, and ABTS assays. FLE.a1, FLE.a2, and quercetin showed strong (IC<sub>50</sub> 50-100µg/mL) to very strong (IC<sub>50</sub> <50µg/mL) antioxidant activity across all three methods. Isolates showed binding to important amino acid residues in anti-obesity target proteins except FLE.d9a and FLE.a1. Notably, FLE.d9a lacked interaction with Ser152 in the 1LPB lipase protein, and FLE.a1 lacked interaction with Ser122 in the 5ZUN lipase protein. In pharmacokinetic profile prediction, all isolates complied with Lipinski's rule of five but FLEA.d9a had AMES toxicity, and FLE.a2 had skin sensitization problems.

**Keywords:** *Curcuma aeruginosa* Roxb, antiobesity, lipase pancreatic inhibitor, antioxidant, molecular docking