STUDI PROFIL METABOLIT DAN *VIRTUAL SCREENING* EKSUDAT TANAMAN MANGROVE (*Avicennia marina* (Forsk.) Vierh.) SEBAGAI AGEN PENGHAMBAT ENZIM PANCREATIC LIPASE

AHLA AMANINA
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ABSTRAK

Latar Belakang: Obesitas meningkat secara signifikan dalam beberapa tahun terakhir. Penghambatan enzim *pancreatic lipase* menjadi alternatif terapi untuk mengurangi penyerapan lemak. Avicennia marina memiliki senyawa metabolit sekunder yang dapat menurunkan profil lipid, namun aktivitas penghambatan enzim *pancreatic lipase* oleh eksudat *Avicennia marina* belum diketahui.

Tujuan Penelitian: Tujuan penelitian dilakukan untuk mengetahui aktivitas fraksi HEMWat dari ekstrak eksudat *Avicennia marina* sebagai penghambat enzim *pancreatic lipase* secara *in vitro, virtual screening,* dan kajian farmakokinetika.

Metode: Metode fraksinasi HEMWat dilakukan menggunakan pelarut n-heksana, etil asetat, metanol, dan air. Uji *in vitro* aktivitas inhibisi enzim *pancreatic lipase*, pengujian profil metabolit menggunakan LC-HRMS, dan *virtual screening* dilakukan kombinasi kajian farmakokinetika dan *molecular docking*.

Hasil: Profil metabolit mengidentifikasi 324 senyawa, hasil filtrasi senyawa tanpa senyawa sintetis terdapat 228 senyawa, filtrasi tanpa struktur terdapat 148 senyawa, kemudian filtrasi senyawa duplikasi terdapat 88 senyawa yang dilakukan *virtual screening* farmakokinetika dengan Lipinski rule of five dan boiled egg plot, setelah proses data mining diperoleh 82 senyawa dilakukan *molecular docking*. Nilai IC50 fraksi polar, nonpolar, dan kontrol positif secara berturut-turut yaitu 47,46; 399,57; 8,32. Hasil senyawa terbaik berdasarkan score docking terbaik yaitu senyawa L-α-PALMITIN memiliki potensi sebagai antiobesitas, namun memiliki aktivitas yang lebih rendah dibandingkan senyawa kontrol positif yaitu orlistat.

Kesimpulan: Berdasarkan studi in vitro nilai IC50 terbaik pada fraksi polar sebesar 47,46 ppm, sedangkan pada in silico kajian farmakokinetika dan score docking terbaik, senyawa L-α-PALMITIN berpotensi sebagai penghambat enzim *pancreatic lipase*.

Kata Kunci*: Eksudat Avicennia marina. enzim pancreatic lipase, obesitas, antiobesitas, virtual screening.*

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ABSTRACT

Background: Obesity has increased significantly in recent years. Inhibition of pancreatic lipase is an alternative therapy for reducing fat absorption. Avicennia marina contains secondary metabolites that can lower lipid profiles; however, the pancreatic lipase-inhibiting activity of Avicennia marina exudate remains unknown.

Aim: The objective of this study was to determine the activity of the HEMWat fraction from Avicennia marina exudate extract as a pancreatic lipase inhibitor through in vitro testing, virtual screening, and pharmacokinetic analysis.

Methods: The HEMWat fractionation was performed using n-hexane, ethyl acetate, methanol, and water as solvents. In vitro testing of pancreatic lipase inhibitory activity, metabolite profiling using LC-HRMS, and virtual screening were conducted in combination with pharmacokinetic studies and molecular docking.

Results: The metabolite profile identified 324 compounds; after filtering out synthetic compounds, 228 compounds remained; after filtering out compounds without known structures, 148 compounds remained; followed by filtering out duplicate compounds, leaving 88 compounds that underwent pharmacokinetic virtual screening using Lipinski's Rule of Five and the boiled egg plot; after data mining, 82 compounds were selected for molecular docking. The IC50 values for the polar fraction, nonpolar fraction, and positive control were 47.46, 399.57, and 8.32, respectively. Based on the best docking score, the top compound, L-α-PALMITIN, showed potential as an anti-obesity agent; however, its activity was lower than that of the positive control, orlistat.

Conclusion: Based on the in vitro study, the best IC50 value in the polar fraction was 47.46 ppm, while in the in silico pharmacokinetic analysis and based on the best docking score, the compound L-α-PALMITIN has potential as an inhibitor of pancreatic lipase.

Keywords: Anti-obesity, Avicennia marina exudate, obesity, pancreatic lipase, virtual screening.