STUDI PROFIL METABOLIT DAN *VIRTUAL SCREENING* EKSUDAT TANAMAN MANGROVE (*Avicennia marina* (Forsk.) Vierh.) SEBAGAI AGEN PENGHAMBAT ENZIM HMG-CoA REDUKTASE

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ABSTRAK

Latar Belakang: Eksudat *Avicennia marina* berpotensi sebagai sumber senyawa bioaktif inhibitor enzim HMG-CoA reduktase. Namun, metabolit yang berperan sebagai inhibitor belum teridentifikasi. Analisis profil metabolit menggunakan LC-HRMS dan *virtual screening* dilakukan untuk mengidentifikasi kandidat inhibitor HMG-CoA reduktase.
Tujuan: Mengetahui aktivitas inhibisi fraksi HEMWat eksudat *Avicennia marina* secara *in vitro*, metabolit berdasarkan LC-HRMS, dan kandidat inhibitor melalui *virtual screening*.
Metode: Eksudat *Avicennia marina* diekstraksi dengan air dan difraksinasi menggunakan HEMWat. Fraksi polar dan nonpolar diuji aktivitas inhibisi HMG-CoA reduktase secara *in vitro* dan dianalisis menggunakan LC-HRMS. Senyawa teridentifikasi diseleksi berdasarkan struktur 2D, kemudian dievaluasi menggunakan Lipinski's *Rule of Five*, BOILED-Egg, *molecular docking*, dan visualisasi interaksi molekuler.
Hasil: Fraksi polar dan nonpolar menghasilkan nilai IC_{50} sebesar 8032,86 ppm dan 6991,58 ppm, sedangkan Lovastatin sebesar 13,59 ppm. Analisis LC-HRMS mengidentifikasi 228 metabolit, dengan Karwinapthol B (16,03%; fraksi nonpolar) dan 6-[(1E)-3,4-dihydroxy-3-methyl-1-buten-1-yl]-7-methoxy-2H-chromen-2-one (17,57%; fraksi polar). *Virtual screening* menunjukkan L-α-PALMITIN, 2-(3,4-Dihydroxyphenyl)ethyl (4Z)-4-formyl-3-(2-oxoethyl)-4-hexenoate, dan Oleocanthal sebagai kandidat inhibitor terbaik dengan skor *docking* masing-masing −95,647; −84,046; dan −80,816. L-α-PALMITIN menunjukkan afinitas tertinggi dan berinteraksi dengan residu penting Glu559, Asp690, Lys691, dan Lys692.
Kesimpulan: L-α-PALMITIN merupakan kandidat inhibitor HMG-CoA reduktase paling potensial berdasarkan *virtual screening*.

Kata Kunci: Eksudat *Avicennia marina*, hiperkolesterolemia, HMG-CoA reduktase, profil metabolit, *virtual screening.*

METABOLITE PROFILING AND VIRTUAL SCREENING OF MANGROVE (*Avicennia marina* (FORSK.) VIERH.) EXUDATE AS AN HMG-CoA REDUCTASE INHIBITORY AGENT

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ABSTRACT

Background : *Avicennia marina* exudate has potential as a source of bioactive compounds that inhibit HMG-CoA reductase. However, the metabolites responsible for the inhibitory activity have not yet been identified. Metabolite profiling using LC-HRMS and virtual screening was performed to identify potential HMG-CoA reductase inhibitors.
Objective: To determine the inhibitory activity of HEMWat fractions of *Avicennia marina* exudate *in vitro*, identify metabolites based on LC-HRMS analysis, and determine potential inhibitors through *virtual screening*.
Methods: *Avicennia marina* exudate was extracted with water and fractionated using HEMWat. The polar and nonpolar fractions were evaluated for HMG-CoA reductase inhibitory activity in vitro and analyzed using LC-HRMS. The identified compounds were screened based on their 2D structures and subsequently evaluated using Lipinski's Rule of Five, BOILED-Egg, *molecular docking*, and molecular interaction visualization.
Results: The polar and nonpolar fractions yielded IC_{50} values of 8032.86 ppm and 6991.58 ppm, respectively, while Lovastatin showed an IC_{50} value of 13.59 ppm. LC-HRMS analysis identified 228 metabolites, with Karwinapthol B (16.03%; nonpolar fraction) and 6-[(1E)-3,4-dihydroxy-3-methyl-1-buten-1-yl]-7-methoxy-2H-chromen-2-one (17.57%; polar fraction) as the predominant metabolites. Virtual screening identified L-α-PALMITIN, 2-(3,4-Dihydroxyphenyl)ethyl (4Z)-4-formyl-3-(2-oxoethyl)-4-hexenoate, and Oleocanthal as the best inhibitor candidates, with docking scores of −95.647, −84.046, and −80.816, respectively. L-α-PALMITIN showed the highest affinity and interacted with the key residues Glu559, Asp690, Lys691, and Lys692.
Conclusion: L-α-PALMITIN was identified as the most promising HMG-CoA reductase inhibitor candidate based on *virtual screening*.

Keywords: *Avicennia marina* exudate, hypercholesterolemia, HMG-CoA reductase, metabolite profiling, virtual screening