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Prediksi Aktivitas Kulit Alpukat Kultivar Alligator, Pangeran dan Mentega Terhadap Neuropati Diabetik Menggunakan Bioinformatika, Machine Learning, Metabolomik, dan Kemometrika
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INTISARI

Alpukat (*Persea americana* Mill.) merupakan salah satu buah yang sering dikonsumsi dan diolah oleh masyarakat. Pengolahan buah tersebut menghasilkan limbah berupa biji dan kulit buah yang seringkali tidak dimanfaatkan lebih lanjut. Kulit alpukat mengandung senyawa fenolik termasuk flavonoid yang berpotensi sebagai sumber antioksidan alami untuk melawan penyakit akibat stres oksidatif. Penelitian ini bertujuan untuk mengetahui senyawa yang terkandung dalam kulit alpukat melalui studi metabolomik dan kemometrika serta prediksi mekanismenya dalam terapi neuropati perifer diabetik melalui pendekatan bioinformatika dan *machine learning*.

Studi literatur dan *online database* (CMAUP dan KNApSAcK) dilakukan untuk memperoleh data senyawa kulit alpukat dan dianalisis dengan pendekatan bioinformatika dan *machine learning* untuk memprediksi senyawa yang berpotensi aktif serta target dan jalur aksi potensial terkait mekanisme aksi terhadap neuropati perifer diabetik. Analisis *untargeted metabolomics* dilakukan terhadap kulit alpukat dari 3 kultivar berbeda untuk membandingkan senyawa yang terkandung pada masing-masing kultivar berdasarkan hasil pengujian aktivitas antioksidan serta korelasinya terhadap total fenolik dan flavonoid berdasarkan kemometrika.

Studi *network pharmacology* terintegrasi *machine learning* mengidentifikasi 16 senyawa aktif dengan protein kunci ESR1 dan AKR1B1, yang berpotensi dalam terapi neuropati perifer diabetik melalui jalur *AGE-RAGE signaling pathway*, *insulin resistance*, dan *TNF signaling pathway*. Studi *molecular docking* menunjukkan hasil afinitas ikatan senyawa epigalokatekin-3-kumarat yang kuat dengan protein target AKR1B1 (-10,31 kcal/mol) yang mendukung potensinya dalam terapi neuropati perifer diabetik. Ekstrak metanol kultivar "Alligator," "Mentega," dan residu kultivar "Pangeran" memiliki aktivitas penangkapan radikal bebas DPPH tertinggi yang berkorelasi positif dengan kandungan fenolik berdasarkan analisis *principal component analysis*. Analisis *untargeted metabolomic* berhasil mengkonfirmasi 7 senyawa serupa dengan dengan hasil *network pharmacology* yakni epikatekin, asam klorogenat, asam neoklorogenat, asam kriptoklorogenat, kuersetin, vitexin, dan cinchonain yang memiliki aktivitas sebagai antioksidan, antidiabetes, antiinflamasi, antiapoptosis, dan efek neuroprotektif dalam terapi neuropati perifer diabetik.

Kata kunci: *Persea americana* Mill., antioksidan, bioinformatika, fitokimia, neuropati perifer diabetik

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ABSTRACT

Avocado (*Persea americana* Mill.) is a widely consumed and processed fruit, yet its processing generates waste in the form of seeds and peels, which are often underutilized. Avocado peels contain phenolic including flavonoid compounds with potential as natural antioxidants to combat diseases associated with oxidative stress. This research aims to identify the compounds contained in avocado peels through metabolomic and chemometric studies and to predict their mechanisms in diabetic peripheral neuropathy therapy through bioinformatics and machine learning approaches.

A literature review and online database analysis were conducted to compile data on compounds in avocado peels, followed by bioinformatics and machine learning analyses to predict potentially active compounds, their targets, and potential pathways related to the mechanism of action in diabetic peripheral neuropathy. Untargeted metabolomic analysis was performed on avocado peels from three different cultivars to compare the compounds present in each cultivar, based on their antioxidant activity and correlations with total phenolic and flavonoid content using chemometric approaches.

Integrated network pharmacology with machine learning identified 16 active compounds targeting key proteins ESR1 and AKR1B1, which are potentially effective in treating diabetic peripheral neuropathy through the AGE-RAGE signaling pathway, insulin resistance, and TNF signaling pathway. Molecular docking studies revealed a strong binding affinity of epigallocatechin-3-coumarate to the target protein AKR1B1 (-10.31 kcal/mol), supporting its potential in diabetic neuropathy therapy. The methanol extracts of the "Alligator," "Mentega," and residue of "Pangeran" cultivars have the highest DPPH radical scavenging activity, which positively correlates with phenolic content based on principal component analysis. Untargeted metabolomic analysis successfully confirmed 7 compounds similar to those found in network pharmacology, namely epicatechin, chlorogenic acid, neochlorogenic acid, cryptochlorogenic acid, quercetin, vitexin, and cinchonain, which have activities as antioxidants, antidiabetic, anti-inflammatory, anti-apoptotic, and neuroprotective effects in the therapy of diabetic peripheral neuropathy.

Keywords: *Persea americana* Mill., antioxidant, bioinformatics, phytochemical, diabetic peripheral neuropathy