Efek Ekstrak Etanol Buah Phaleria macrocarpa terhadap Penanda Kerusakan Mitokondria dan Profil Ekspresi Transporter Besi di Hati Tikus Model Hemosiderosis = Effect of Phaleria macrocarpa Fruit Ethanolic Extract on Mitochondrial Damage Marker and Iron Transporter Expressions Profile in the Liver of Hemosiderosis Rats

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Abstrak

Mitokondria merupakan organel yang memetabolisme besi secara ekstensif, sehingga menjadi target kerusakan yang diinduksi besi pada kondisi hemosiderosis. Produksi reactive oxygen species (ROS) yang tinggi di mitokondria dapat lebih meningkat saat ada besi bebas yang kemudian memicu reaksi Fenton. Produksi ROS yang tinggi dapat menyebabkan stres oksidatif, sehingga regulasi konsentrasi besi harus diatur dengan ketat. Phaleria macrocarpa diketahui mengandung senyawa aktif mangiferin yang telah terbukti memiliki aktivitas kelasi besi, namun belum diketahui apakah dapat bekerja di mitokondria. Penelitian ini bertujuan untuk mengetahui efektivitas ekstrak etanol buah Phaleria macrocarpa dalam melindungi mitokondria hati dari kerusakan akibat besi dan kaitannya dengan transporter influks dan efluks besi di hati tikus model hemosiderosis. Penelitian ini menggunakan organ hati tersimpan dari tikus Sprague-Dawleyjantan sebanyak 30 ekor yang dibagi secara acak ke dalam 6 kelompok, yaitu normal (N) dan kelompok hemosiderosis tanpa terapi (Fe), diterapi deferiprone 462,5 mg/kgBB (Fe+DFP), mangiferin 50 mg/kgBB (Fe+M), serta ekstrak etanol buah Phaleria macrocarpa dosis 100 mg/kgBB (Fe+PM100) dan 200 mg/kgBB (Fe+PM200). Dilakukan analisis kadar MnSOD, copy number mtDNA, dan analisis ekspresi mRNA DMT1, ZIP14, MFRN1, MFRN2, ABCB7, dan ABCB8 yang dilaporkan berperan dalam transpor besi ke dalam sel dan mitokondria. Hasil penelitian menunjukkan bahwa ekstrak Phaleria macrocarpa memengaruhi ekspresi gen transporter besi namun tidak dapat memperbaiki penanda kerusakan mitokondria pada organ hati hemosiderosis.

.....Mitochondria are organelles that metabolize iron extensively, making them targets for iron-induced damage. The high production of reactive oxygen species (ROS) in mitochondria can be further increased when there is free iron which then triggers the Fenton reaction. High ROS production can cause oxidative stress, so iron concentration regulation must be strictly regulated. Phaleria macrocarpa is known to contain the active compound mangiferin which has been shown to have iron chelation activity, but it is not yet known whether it can work in mitochondria. This study aims to determine the effectiveness of the ethanol extract of Phaleria macrocarpa fruit in protecting liver mitochondria from iron-induced damage and its relation to iron influx and efflux transporters in the liver of hemosiderosis rat models. This study used stored liver organs from 30 male Sprague-Dawley rats which were randomly divided into 6 groups, namely normal (N) and hemosiderosis groups without therapy (Fe), treated with deferiprone 462.5 mg/kgBW (Fe+DFP), mangiferin 50 mg/kgBW (Fe+M), and Phaleria macrocarpa fruit ethanolic extract at a dose of 100 mg/kgBW (Fe+PM100) and 200 mg/kgBW (Fe+PM200). Analysis of MnSOD levels, mtDNA copy number, and analysis of relative mRNA expression of DMT1, ZIP14, MFRN1, MFRN2, ABCB7, and ABCB8 were performed which were reported to play a role in iron transport into cells and mitochondria. The results showed that Phaleria macrocarpa extract has the potential to modulate the expression of iron

transporter genes but was not able to ameliorate the mitochondrial damage marker in hemosiderosis liver.