The Role of an Athanolic Extract of Andrographis Paniculata Leaves on Doxorubicin-Induced Cardiac and Renal Toxicity in Healthy Rats = Peran Ekstrak Etanol Daun Andrographis Paniculata pada Jantung dan Ginjal Tikus yang Diinduksi Doxorubicin

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Abstrak

Doxorubicin (DOX) dilemahkan oleh toksisitas jantung dan ginjal meskipun efektif melawan kanker. Walaupun dexrazoxane tersedia untuk mengatasi toksisitas DOX, efektivitasnya terbatas, begitu pula obat konvensional seperti beta-blocker dan statin. Penelitian ini menyelidiki efek perlindungan ekstrak etanol daun Andrographis panikulata (EEAP) terhadap toksisitas jantung dan ginjal yang diinduksi oleh DOX pada tikus sehat dengan fokus pada mekanisme anti-inflamasi dan mitokondria. Sebanyak 30 ekor (5 kelompok) tikus Sprague Dawley diaklimatisasi selama 2 minggu. Kelompok normal mendapat saline (ip) selama 4 minggu. Kelompok DOX menerima doxorubicin (4mg/kg/minggu). Kelompok perlakuan (DOX+EEAP) menerima doksorubisin dan ekstrak daun Andrographis Paniculata dengan dosis bervariasi (125, 250, 500 mg/kg/hari) secara oral selama 4 minggu. Setelah darah dan organ (jantung, ginjal) dikumpulkan, darah dianalisis untuk elektrolit (kalsium dan natrium). Jaringan dianalisis sebagai penanda inflamasi (NF-B, IL-1, NLRP-3), fungsi mitokondria (PGC1-, TFAM), dan gambaran histopatologis yang menggunakan pewarnaan hematoxylin dan eosin (H&E) serta pewarnaan trikrom Masson. Kadar kalsium jantung juga diukur. Pengobatan bersama EEAP menurunkan natrium dan kalsium plasma dan kadar penanda inflamasi IL-1 dan NLRP-3 di jaringan jantung dan ginjal tetapi tidak menunjukkan efek signifikan pada ekspresi PGC1- dan TFAM dibandingkan dengan kelompok DOX. Selain itu, kadar kalsium jantung berkurang. Lebih lanjut, konsentrasi NF-B berkurang sedikit oleh EEAP dibandingkan dengan kelompok DOX saja. EEAP kemungkinan besar terlindungi dari peradangan yang disebabkan oleh DOX yang mengarah pada pemulihan histologi jantung dan ginjal menjadi normal. Efek perlindungan EEAP dalam penelitian ini dimediasi, setidaknya sebagian, oleh modulasi jalur NF-B/NLRP3/IL-1.

.....Doxorubicin (DOX), despite its effectiveness against cancer, is compromised by cardiac and renal toxicity. While dexrazoxane exists for DOX toxicity, its effectiveness is limited, as are conventional drugs like beta-blockers and statins. This study investigates the protective effects of an ethanolic extract of Andrographis paniculata leaves (EEAP) against DOX-induced cardiac and renal toxicity in healthy rats, focusing on anti-inflammatory and mitochondrial mechanisms. 30 Sprague Dawley rats (5 groups) were acclimatized for 2 weeks. The normal group received saline (ip) for 4 weeks. The DOX group received only doxorubicin (4mg/kg/week). Treatment groups (DOX+EEAP) received doxorubicin and varying doses (125, 250, 500 mg/kg/day) of Andrographis paniculata leaf extract orally for 4 weeks. After sacrifice, blood and organs (heart, kidneys) were collected. Blood was analysed for electrolytes (calcium and sodium). Tissues were analysed for inflammatory markers (NF-B, IL-1, NLRP-3), mitochondrial function (PGC1-, TFAM), and histopathological features using hematoxylin and eosin (H&E) or Masson’s trichrome stain. Cardiac calcium levels were also measured. EEAP co-treatment lowered plasma sodium and calcium, decreased levels of inflammatory markers (IL-1 and NLRP-3) in heart and kidney tissues, but showed no significant effect on PGC1- and TFAM expression compared to the DOX group. Additionally, cardiac calcium levels

were reduced. Further, NF-B concentration was slightly reduced by EEAP compared to the DOX only group. EEAP likely protected against DOX-induced inflammation, leading to a restoration of normal heart and kidney histology. EEAP's protective effects in this study were mediated, at least in part, by modulation of the NF-B/NLRP3/IL-1 pathway.