Efek ekstrak Etanol Acalypha indica L., terhadap respon inflamasi pada patogenesis NAFLD Tikus : analisis molecular docking, dan ekspresi TLR9, Nuclear factor kappa B, dan TNF alpha = The effects of Acalypha indica L. Ethanolic Extract on inflammatory response in rat NAFLD pathogenesis : molecular docking analysis and expression of TLR9, Nuclear factor kappa B and TNF alpha

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Abstrak

Komplikasi penyakit perlemakan hati non-alkoholik (PHNA) ditemukan pada 67% populasi memenuhi kriteria sindrom metabolik. Acalypha indica L. (AI) adalah herbal yang telah diketahui memiliki efek anti-oksidan, dan anti-inflamasi. Penelitian ini bertujuan membuktikan efek AI terhadap mekanisme pertahanan imun yang dibawa. Penelitian dilakukan dengan molecular docking terhadap senyawa AI pada TLR9, NFB, TNF, dan perubahan histopatologik hati. Model hewan steatohepatitis pada tikus Sprague-Dawley didapat dari induksi diet tinggi fruktosa, dan kolesterol (DTFK) selama 12 minggu. Terapi diberikan selama 8 minggu. Dua puluh lima tikus dibagi ke dalam 5 kelompok: Normal (K1), DTFK (K2), DTFK+AI, 400 mg (K3), kombinasi AI, 400 mg +gemfibrozil (Gem) 31 mg (K4) dan Gem 31 mg (K5) masing-masing per kgBB. Molecular docking untuk mengidentifikasi interaksi antara molekul hidrogen senyawa AI dengan residu asam amino TLR9, NFB, TNF. Perubahan morfologi hati dinilai dengan cara skoring. Analisis statistik yang dilakukan adalah uji Kruskall Wallis post hoc Mann Whitney, dilanjutkan dengan uji korelasi Spearman. Hasil molecular docking menunjukkan, selain senyawa flavonoid, ditemukan senyawa alkaloid beta-sitosterol, dan stigmasterol yang dapat berikatan dengan ketiga marker inflamasi dengan nilai binding energy terbaik. Senyawa lain dasycarpidan-1-methanol, acetate (ester), fenofibrate, quinine. Pemberian AI menurunkan hipertrofi (p=0,031), steatosis makrovesikular (p=0,018), fokus inflamasi (p=0,005). Pemberian AI juga menurunkan ekspresi TLR9 (p=0,009), NFB (p=0,009), TNF (p=0,009), akan tetapi tidak sebaik pemberian kombinasi AI+Gem.

.....Complications of non-alcoholic fatty liver disease (NAFLD) include 67% of the criteria for metabolic syndrome. Acalypha indica L., (AI) which is one of a herbal plant had been known as anti-oxidant and anti-inflammatory effects. The effect of AI for therapy investigated by looking of the immune defense mechanisms. This researched was assessed by molecular docking approached on TLR9, NFB, TNF expression and liver morphological changes. Animal models of steatohepatitis were collected from high-fructose and cholesterol diet (HFCD) of Sprague-Dawley rats for 12 weeks and followed by therapy for 8 weeks. There were 5 groups from twenty five researched rats, include normal group (K1), HFCD group (K2), HFCD group supplemented with 400 mg Acalypha indica L. (K3), combination between 400 mg AI.+gemfibrozil (Gem) 31 mg (K4) and Gem 31 mg/kg (K5) in kgBW, respectively. The results of molecular docking were carried out by assessing the interaction between hydrogen molecules of AI compounds and amino acid residues in TLR9, NFB, TNF. Morphological changes were assessed by scoring system. Statistical analyzed used Kruskall Wallis with post hoc Mann Whitney test continued by Spearman correlation test. The molecular docking analysis showed that, an alkaloid compounds were found besides the flavonoid compounds that can bind to the binding pocket of inflammatory markers with the best binding

energies. Other compounds, there are dasycarpidan-1-methanol, acetate (ester), fenofibrate and quinine. Supplementation of AI would reduced hypertrophy (p=0.031), macrovesicular steatosis (p=0.018), inflammation foci (p=0.005) and also decreased of TLR9 (p=0.009), NFB (p=0.009), TNF (p=0.009) expression, but not as good as the combination of AI+Gem.