

Pengaruh Pemberian Ekstrak Herba Ciplukan terhadap Inflamasi dan Fibrosis pada Model Tikus Skleroderma dengan Penyakit Paru Interstitial = Effect of Ciplukan Herb Administration on Inflammation and Fibrosis in Scleroderma Rat Model with Interstitial Lung Disease

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Abstrak

Sklerosis sistemik atau skleroderma adalah suatu penyakit jaringan ikat yang dimediasi imun yang ditandai dengan fibrosis kulit dan organ dalam serta vaskulopati. Penyebab kematian utama pada sklerosis sistemik adalah penyakit paru interstitial. Pengobatan penyakit paru interstitial pada sklerosis sistemik saat ini belum memuaskan. Herba ciplukan (*Physalis angulata*) merupakan salah satu terapi alternatif yang potensial dan terbukti dapat memperbaiki fibrosis kulit pada pasien sklerosis sistemik namun data pada manifestasi paru belum ada. Penelitian ini bertujuan untuk menilai efek herba ciplukan dalam mencegah dan memperbaiki inflamasi dan fibrosis paru pada model tikus sklerosis sistemik dan mencari dosis optimal ciplukan untuk memperbaiki fibrosis. Penelitian ini terbagi dalam 2 tahap yaitu tahap kuratif fibrosis (tahap 1) dan tahap preventif inflamasi dan fibrosis (tahap 2). Pada tahap 1, 33 tikus (*Rattus norvegicus*) galur Sprague-Dawley 1012 minggu dibagi dalam 6 kelompok yaitu kelompok yang mendapat bleomisin dan ciplukan (dosis 50, 100, 150, dan 200 mg/kg), bleomisin dan salin, dan kontrol negatif. Bleomisin diberikan subkutan per hari selama 14 hari dan ciplukan atau salin diberikan mulai hari ke-21 selama 30 hari lalu hewan diterminasi. Fibrosis dinilai dengan derajat fibrosis dan luas fibrosis pada histopatologi, kadar hidroksiprolin, TGF- dan MMP13 jaringan paru. Pada tahap 2, 36 ekor tikus dibagi dalam 6 kelompok yaitu 2 kelompok yang mendapat bleomisin dan ciplukan (50 dan 100 mg/kgBB) dan 2 kelompok bleomisin dan salin. Tiga kelompok diterminasi di H14 dan 3 kelompok di H51. Pada tahap 2, bleomisin dan ciplukan diberikan bersamaan selama 14 hari pertama. Luaran yang dinilai di H14 adalah kadar IL-6 paru, jumlah leukosit dari BAL dan skor inflamasi paru secara histopatologi. Luaran yang dinilai di H52 adalah derajat fibrosis dan luas fibrosis, kadar hidroksiprolin, TGF- dan MMP13 paru. Kadar IL-6, TGF- dan MMP 13 dinilai dengan ELISA dari jaringan paru, Hidroksiprolin dinilai dari jaringan paru dengan metode kolorimetri. Pada tahap 1 terdapat perbedaan luas fibrosis yang secara statistik bermakna antara kelompok yang mendapat ciplukan dosis 100, 150, dan 200 mg/kgBB dibandingkan kelompok bleomisin. Tidak terdapat perbedaan skor fibrosis antara kelompok yang mendapat ciplukan 50, 100, dan 150 mg/kgBB dengan kontrol negatif. Tidak terdapat perbedaan hidroksiprolin antara kelompok yang mendapat ciplukan dengan kontrol negatif. Tidak terdapat perbedaan kadar TGF- dan MMP13 yang secara statistik bermakna antar kelompok. Pada tahap 2 penelitian tidak didapatkan perbedaan kadar IL-6, jumlah leukosit cairan BAL dan skor inflamasi yang bermakna antar kelompok dan tidak terdapat perbedaan skor fibrosis, luas fibrosis, kadar hidroksiprolin, TGF- dan MMP13 antar kelompok. Sebagai simpulan ekstrak ciplukan memiliki efek kuratif untuk menurunkan luas fibrosis paru dengan dosis optimal 100 mg/kgBB. Ciplukan tidak memiliki efek preventif terhadap inflamasi dan fibrosis.

.....Systemic sclerosis or scleroderma is an immune mediated connective tissue disease which is manifested by fibrosis on skin and internal organ and vasculopathy. Interstitial lung disease (ILD) is the main cause of death of systemic sclerosis however the treatment of ILD in systemic sclerosis is still unsatisfactory.

Ciplukan (*Physalis angulata*) herb is a potential alternative treatment for systemic sclerosis and has been proven to improve skin sclerosis in systemic sclerosis patients however the study on its effect on lung has been lacking. The aim of this study is to evaluate the effect of ciplukan herb for treating and preventing inflammation and fibrosis in systemic sclerosis animal model and to find out its optimal dose in improving lung fibrosis. This study was done in 2 stages. For the first stage (treatment of fibrosis), 33 Sprague-Dawley rats aged 1012 weeks were divided into 6 groups (4 groups were given bleomycin and ciplukan extract dose 50,100,150, and 200 mg/kgBW, respectively, bleomycin and saline and negative control). Bleomycin was given subcutaneously daily for 14 days and ciplukan or saline were given from day 21 until the next 30 days and then the animals were sacrificed. At the end of observation, degree of fibrosis and width of fibrosis from lung histopathology, hydroxyproline, TGF-, and MMP13 levels were analyzed. For the second stage (prevention), 36 rats were divided into 6 groups (bleomycin and ciplukan dose 50 and 100 mg/kgBW, and bleomycin only). Three groups were sacrificed after 14 days of observation for evaluation of IL-6 level in lung tissue, leucocyte count on BAL fluid and inflammation score. Three groups were sacrificed after 51 days observation and were analyzed for degree of fibrosis and width of fibrosis from lung histopathology, hydroxyproline, TGF-, and MMP13 levels. For the second stage, bleomycin and ciplukan were given simultaneously for 14 days. IL-6, TGF-, and MMP13 levels were measured using ELISA methods while hydroxyproline was analyzed using colorimetric method. From the stage 1, there was a significant reduction in width of lung fibrosis on groups receiving bleomycin and ciplukan dose 100, 150, and 200 mg/kgBW compared with bleomycin group. There was no difference of fibrosis score among groups who received ciplukan 50,100, and 150 mg/kgBW compared to the negative control. There was no difference of hydroxyproline among groups who received ciplukan compared with negative control. There was no difference of TGF-, and MMP13 levels among groups. From the stage 2, there were no difference of IL-6 levels, BAL leukocyte count and inflammation score among groups after 14 days and no difference of fibrosis score, extension of fibrosis, hydroxyproline, TGF- and MMP13 levels among groups after 51 days observation. As a conclusion, ciplukan herb has a role as a treatment of fibrosis to reduce extent of lung fibrosis with optimal dose of 100 kg/BW but shows no effect on prevention of lung inflammation and lung fibrosis.