

## ABSTRAK

Ikbal, Ahmad. 2016. Pengaruh Lama Pemberian Kurkumin terhadap Penurunan Ekspresi TGF- $\beta$  Jaringan Hati pada Tikus Model Fibrosis Akibat Induksi Karbon Tetraklorida (CCl4). Tugas Akhir, Program Studi Kedokteran Fakultas Kedokteran Universitas Brawijaya Malang. Pembimbing: (1) dr. Supriono, Sp.PD-KGEH. (2) Dr. dr. Wisnu Barlianto, M.Si. Med, Sp.A (K).

TGF- $\beta$  atau *Transforming Growth Factor*  $\beta$  adalah sitokin yang paling berperan dalam fibrosis hati. Injuri hepatosit mengaktifkan TGF- $\beta$  dan TGF- $\beta$  memediasi *hepatic stellate cell* (HSC) serta mengaktifkan fibroblas untuk penyembuhan injuri hepatosit, termasuk pembentukan miofibroblas dan deposisi matriks ekstraseluler, sehingga terjadi kondisi fibrosis hati. Kurkumin telah terbukti memiliki efek hepatoprotektif karena kandungan antioksidannya dapat menekan stres oksidatif serta menghambat perubahan HSC menjadi miofibroblas, sehingga dapat menekan produksi TGF- $\beta$ . Penelitian ini bertujuan untuk mengetahui pengaruh lama pemberian kurkumin terhadap penurunan ekspresi TGF- $\beta$  jaringan hati pada tikus model fibrosis akibat paparan CCl4 pada minggu ke-2, 5, dan 9. Sampel adalah tikus Wistar jantan yang dibagi menjadi 8 kelompok, terdiri dari kontrol negatif (KN), kontrol positif (KP), kelompok perlakuan dengan lama pemberian kurkumin selama 2 minggu (KP2) dan kelompok kontrolnya (KK2), kelompok perlakuan dengan pemberian kurkumin selama 5 minggu (KP5) dan kelompok kontrolnya (KK5), kelompok perlakuan dengan pemberian kurkumin selama 9 minggu (KP9) dan kelompok kontrolnya (KK9). Dari hasil penghitungan, didapatkan rerata ekspresi TGF- $\beta$  jaringan hati sebagai berikut (sel), KN=4,4; KP=36,825; KP2=4,3; KK2=65,375; KP5=7,575; KK5=94,525; KP9=22,225; dan KK9=22,525. Dari hasil penelitian ini, didapatkan perbedaan yang bermakna antara 8 kelompok perlakuan ini (*one way ANOVA*  $p=0,000$ ). Uji korelasi Pearson menunjukkan bahwa terdapat korelasi negatif antara lama pemberian kurkumin dengan penurunan ekspresi TGF- $\beta$  jaringan hati dengan angka koefisien korelasi sebesar 0,741 dan angka signifikansinya sebesar 0,006. Uji regresi linier menunjukkan bahwa perlakuan berpengaruh sebesar 54,8% terhadap penurunan ekspresi TGF- $\beta$  jaringan hati. Kesimpulan dari penelitian ini adalah semakin lama pemberian kurkumin, semakin kecil penurunan ekspresi TGF- $\beta$  jaringan hati.

Kata Kunci: Fibrosis hati, Karbon Tetraklorida, Kurkumin, TGF- $\beta$ , *Transforming Growth Factor*  $\beta$ .

## ABSTRACT

Ikbal, Ahmad. 2016. **The Effect of Duration of Curcumin Therapy on the Decreasing Expression of TGF- $\beta$  in Rat's Liver Tissue Induced by Carbon Tetrachloride (CCl4).** Final Assignment, Medical Program, Faculty of Medicine, Brawijaya University. Supervisors: (1) dr. Supriono, Sp.PD-KGEH. (2) Dr. dr. Wisnu Barlianto, M.Si. Med, Sp.A (K).

TGF- $\beta$  or *Transforming Growth Factor  $\beta$*  is cytokine that has the most major role in liver fibrosis. The injury of hepatocyte gives stimulus to TGF- $\beta$  activation and it mediates hepatic stellate cell (HSC), activates fibroblast for hepatocyte healing, including myofibroblast formation and extracellular matrix deposition, so that liver fibrosis is occurred. Curcumin is proven for its hepatoprotective effect produced by its antioxidant composition able to suppress oxidative stress, inhibit the transformation of HSC into myofibroblast, and results in the suppression liver tissue TGF- $\beta$  expression. This study is aimed to test the effect of the duration of curcumin therapy on the decreased expression of TGF- $\beta$  in rat's liver tissue induced by carbon tetrachloride in week-2, 5, and 9 of curcumin administration. Samples are taken from male Wistar rat which is divided into 8 groups that consist of negative control (KN), positive control (KP), the curcumin-given treatment group for 2 weeks (KP2) and it's control (KK2), the curcumin-given treatment group for 5 weeks (KP5) and it's control (KK5), and the curcumin-given treatment group for 9 weeks (KP9) and it's control (KK9). The results of quantification are as follows (cell), KN=4,4; KP=36,825; KP2=4,3; KK2=65,375; KP5=7,575; KK5=94,525; KP9=22,225; dan KK9=22,525. The result of this experiment shows that there is a significant difference between the 8 groups of samples (One Way ANOVA  $p=0,000$ ) with normal and homogenous data distribution. Pearson correlation shows that there is a negative correlation between the duration of curcumin treatment and the decreasing expression of TGF- $\beta$  in rat's liver tissue, with correlation coefficient in the amount of 0,741 and significancy in the amount of 0,006. Linear regression test shows that the treatment gives 54,8% contribution to the decreasing of TGF- $\beta$ 's expression in liver tissue. In conclusion, the longer of duration of curcumin therapy given, the smaller amount of decreasing TGF- $\beta$ 's expression in rat's liver tissue will be.

Keywords: Liver fibrosis, Carbon Tetrachloride (CCl4), Curcumin, TGF- $\beta$ , *Transforming Growth Factor  $\beta$* .

