

ABSTRACT

Mechanism of Torbangun (*Coleus amboinicus*) Stem Extract on Uric acid-Oxonic acid Induced Nephropathy in Wistar Rats (*Rattus norvegicus*)

Introduction. Torbangun (*Coleus amboinicus*, CA) extracts are known to have anti-oxidant activity, anti-platelet aggregations, anti-bacterial, anticancer and anti-inflammation.

Aim. The purposed to study the mechanism of *Coleus amboinicus* (CA) stem extracts in Wistar rats with uric acid-oxonic acid induced nephropathy, by analyzing the levels of Glutathione Peroxidase (GPx) activity, Interleukin-1 β (IL-1 β), Transforming growth factor- β 1 (TGF- β 1) expression and macrophage CD 68 (ED-1).

Method. Fifty-six male Wistar rats (*Rattus norvegicus*), 3 months with 150-200 g body weight, were allocated into four groups (n=14). The control group received placebo, treatment group were administered orally with uric acid 1,5% and oxonic acid 2% (P1) and received 500 mg/kg BW of the CA stem extracts (P2) and received 5 mg/kg BW quercetin (P3) by oral, respectively for 35 days. Blood serums collected for analysis of cystatin C (Cys-C), creatinine and BUN concentrations. All groups were sacrificed to collect kidney organ for measuring of GPx activity, IL-1 β expression, TGF- β 1 expression was conducted by Avidin-Horseradish Peroxidase (HRP) Sandwich-ELISA. Kidney organ was collected to histopathological analyzed by Hematoxylin-eosin and Periodic Acid Schiff staining. Immunohistochemistry is conducted for identification of CD 68 expression. The levels of GPx, IL-1 β , TGF- β 1, CD 68 and Cys-C concentrations were analyzed by statistic independent test.

Results. *Coleus amboinicus* (CA) stem extract by Thin Layer Chromatography has a relative fraction of flavonoids, terpenes, saponins, polyphenols and alkaloids. By *in silico* analyzed, quercetin as a marker compound of CA stem extract has stronger bind to the TGF- β 1receptor (PDB code: 4X0M) than its of 3WA_601 ligand. Induction with uric acid- oxonic acid for 35 days has proven to causes nephropathy with indicated of elevated BUN, creatinine and cystatin-C levels and necrotic lesions of tubular membrane and glomerular kidney, in P1, P2, and P3 groups. The research results showed that CA stem extract at a dose of 500 mg/kg BW decreased the activity of GPx, IL-1 β expressions and CD 68 not significantly ($p > 0.05$) and increased of TGF- β 1 expression significantly ($p \leq 0.05$) in P2 and P3 groups than the P1 group. This study was concluded that torbangun stem extract is proven to inhibit on uric acid-induced nephropathy, however, a mechanism of that inhibitory activity could not explain clearly in this research.

Keywords: *Coleus amboinicus*, Wistar rat, nephropathy, *in silico*, mechanism of action