ABSTRAK

Demensia dapat disebabkan karena kematian neuron otak akibat stres oksidatif. Rimpang kunyit (*Curcuma longa* Linn) mengandung kurkumin yang memiliki efek antioksidatif dan neuroprotektif. Tujuan umum penelitian ini adalah untuk mengembangkan ekstrak rimpang kunyit sebagai sediaan pencegah demensia. Tujuan khususnya adalah untuk mengkaji mekanisme *in vivo* ekstrak rimpang kunyit *(C. longa* L.) terstandar kurkumin pada tikus *Sprague Dawley* model demensia yang diinduksi trimetiltin (TMT) dengan: (1) mengamati memori spasial melalui uji Morris *water maze*, (2) mengukur penanda stres oksidatif melalui pengamatan biokimiawi kadar MDA plasma dan otak, kadar glutation (GSH), aktivitas glutation peroksidase (GPx), superoksid dismutase (SOD), dan katalase (CAT) otak, (3) pengamatan histologik dengan menghitung estimasi jumlah total sel pyramidal hippocampus di daerah CA1 dan CA2-CA3 dengan metode stereologi serta pengamatan semikuantitatif imunohistokimia ekspresi protein *caspase-3* di daerah tersebut.

Penelitian ini menggunakan tikus *Sprague Dawley*, umur sekitar 2 bulan, berat 180-200 g, dibagi menjadi 6 kelompok perlakuan, masing-masing kelompok terdiri dari 10 ekor. Kelompok normal (KN) diberi larutan CMC-Na per oral (p.o) dan injeksi salin intraperitoneal (i.p); Kelompok Kontrol Sakit (KS) diberi larutan CMC-Na p.o dan injeksi larutan TMT dalam salin 0,9% i.p; Kelompok Kontrol Positif (KP) diberi sitikolin dosis 200 mg/kg p.o dan injeksi TMT; dan kelompok ekstrak rimpang kunyit terstandar kurkumin (ERKTK) yang diberi variasi dosis yaitu100 mg/kg BB (E100), 200 mg/kgBB (E200), 300 mg/kg BB (E300) dan juga injeksi TMT. ERKTK dan sitikolin diberi mulai hari 1 sampai hari 28, sedangkan injeksi TMT diberikan dosis tunggal pada hari ke 8 perlakuan. Uji Morris *water maze* (MWM) dilakukan mulai hari ke 29 sampai hari 35. Setelah itu hewan uji diambil darahnya melalui sinus orbitalis, kemudian dikorbankan untuk diambil otaknya. Hemispherium cerebri kiri untuk pengamatan biokimiawi dan hemispherium cerebri kanan diambil hippocampusnya untuk pengamatan histologik. Hasil uji memori spasial dianalisis statististik dengan uji *one-way repeated measures analysis of variance* (ANOVA). Data hasil uji biokimiawi dan histologik dianalisis statistik dengan uji *one-way* ANOVA atau Kruskall Wallis. Untuk mengetahui perbedaan di antara 2 kelompok dilanjutkan dengan uji Tukey HSD atau Mann Whitney dengan tingkat signifikansi 0,05.

Ekstrak rimpang kunyit terstandar kurkumin (ERKTK) dosis 200 mg/kg BB dapat meningkatkan memori spasial tikus *Sprague Dawley* model demensia yang terpapar TMT. Berdasarkan pengamatan biokimiawi ERKTK 200 mg/kg BB dapat mencegah peningkatan kadar MDA plasma dan otak, meningkatkan aktivitas GPx, SOD, CAT serta kadar GSH otak, dan mencegah penurunan estimasi jumlah total sel pyramidal serta peningkatan ekspresi *caspase*-3 di daerah CA2-CA3 hippocampus. Tikus yang diberi ERKTK dosis 200 mg/kg BB menunjukkan hasil uji MWM, uji biokimiawi, dan imunohistokimia *caspase*-3 yang hampir sama dengan tikus yang diberi sitikolin.

Kata kunci: demensia; *Curcuma longa* Linn.; TMT; MDA; antioksidan; hippocampus; *caspase*-3

ABSTRACT

Dementia seems to primarily implicate oxidative stress-induced neuronal death in the brain. Turmeric (*Curcuma longa* L.) contains curcumin which has anti-oxidative and neuro-protective effects. The general objective of this research is to develop the extract of turmeric as a preventive preparation of dementia. The specific objective of this research is to study the *in vivo* mechanism of standardized turmeric rhizome extract on *Sprague Dawley* rat model of dementia induced by TMT, by : (1) observing spatial memory with the Morris water maze test; (2) measuring oxidative stress markers i.e, malondialdehyde (MDA) levels of plasma and brain, levels of glutathion (GSH), activities of glutathion peroxidase (GPx), superoxide dismutase (SOD), and catalase (CAT) of brain; (3) calculating the estimation of the total number of pyramidal cells in the hippocampal area CA1 and CA2- CA3 by stereology method and semiquantitavely calculating the protein expression of *caspase*-3 in the such areas.

Sixty adult male Sprague-Dawley rats (195-215 g) were randomly divided into six groups consisting of 10 rats for each group. The groups are N group (normal group), which received oral CMC-Na solution and intra-peritoneal injection of 0.9% saline; T group (control group), which was given oral CMC-Na solution and intra-peritoneal injection of TMT chloride dissolved in 0,9% saline; positive control group, which was treated with oral 200 mg/kg bw of citicoline solution and TMT chloride injection; and E100, E200, E300 groups, which were treated with oral 100 mg/kg BW, 200 mg/kg BW, and 300 mg/kg BW, respectively, of turmeric rhizome extract, besides intra-peritoneal injection of TMT chloride. The turmeric rhizome extract and citicoline solutions were given at day 1 up to day 28 of experiment, whereas the TMT chloride injection given as a single dose of 8 mg/kg bw was administered at day 8 of experiment. Morris water maze test were carried out one day after the day of the last treatment of the rats (i.e. day 29) and the test lasted for 7 days. At day 36 the blood were taken from orbital sinus, afterthat all rats were sacrificed and the cerebrums were then dissected out from the skull. The left cerebral hemispheres were used for biochemical observation whereas the right one were used for histological examination. The spatial memory test were analyzed statistically with one way repeated measures ANOVA. Data of biochemical and histological test were analyzed by one way ANOVA or Kruskal Wallis test followed by Tukey HSD or Mann Whitney test with 0.05 significance level .

Standardized turmeric extract dose of 200 mg / kg BW improved spatial memory of *Sprague Dawley* rat models of dementia exposed by TMT. This dose lowered the levels of MDA plasma and brain, increased the activities of GPx, SOD, CAT and the levels of GSH of brain. In addition, 200 mg/ kg BW of turmeric extract administration on rats might partially hindered the deficits of pyramidal cells and the increases of caspase-3 expression in the CA2-CA3 region. To some extent these effects seemed to be comparable to those of citicoline.

Keywords: dementia; *Curcuma longa* L.; TMT; MDA; antioxidant, hippocampus, *caspase*-3