INTISARI

POTENSI NEUROPROTEKTIF EKSTRAK *CINNAMOMUM VERUM* TERHADAP MEMORI SPASIAL DAN EKSPRESI mRNA TNF-α PADA HIPOKAMPUS TIKUS MODEL STROKE ISKEMIA GLOBAL TRANSIEN

Latar Belakang: Pada cedera iskemia/reperfusi (I/R) serebral, terjadi kerusakan sekunder akibat kembalinya aliran darah ke otak setelah periode iskemia, salah satunya melalui proses inflamasi yang ditandai dengan meningkatnya sitokin proinflamasi seperti *tumor necrosis factor*-α (TNF-α) di hipokampus. Kerusakan jaringan pada hipokampus dapat menurunkan fungsi memori spasial. Ekstrak *Cinnamomum verum* memiliki efek antiinflamasi pada model penyakit neurologis, tetapi efeknya pada model stroke iskemia global transien belum banyak diketahui.

Tujuan: Penelitian ini bertujuan untuk mengkaji aktivitas neuroprotektif ekstrak *Cinnamomum verum* terhadap fungsi memori spasial dan ekspresi mRNA TNF-α pada hipokampus tikus model stroke iskemia global transien yang diinduksi dengan *bilateral common carotid artery occlusion* (BCCAO).

Metode: Tikus wistar jantan (n=25) dibagi ke dalam lima kelompok (n=5) yaitu kelompok *Sham operation* (SO), kelompok BCCAO tanpa pemberian ekstrak (BCCAO), serta kelompok BCCAO dengan pemberian ekstrak *Cinnamomum verum* dosis 100 mg/kgBB (C100), 200 mg/kgBB (C200), dan 400 mg/kgBB (C400). BCCAO dilakukan dengan menjepit arteria carotis communis selama 20 menit kemudian dilepas. Memori spasial diuji dengan Morris *water maze* (MWM). Tikus diterminasi 8 hari setelah BCCAO untuk mengambil jaringan hipokampus. Ekspresi mRNA TNF-α dianalisis dengan RT-PCR.

Hasil: Kelompok BCCAO memiliki jarak tempuh untuk mencapai *platform* di hari ke-4 *learning phase* MWM (14.159±3.432) dan ekspresi mRNA TNF-α (0,89±0,02) yang lebih panjang dan lebih tinggi secara signifikan ($p<0,05$) daripada kelompok SO. Setelah pemberian ekstrak *Cinnamomum verum*, jarak hari ke-4 *learning phase* MWM kelompok C100 (5.552±2.804), C200 (6.414±3.534), dan C400 (6.743±4.495) lebih pendek secara signifikan ($p<0,05$) dibanding kelompok BCCAO. Ekspresi mRNA TNF-α pada kelompok C100 (0,78±0,05) dan C200 (0,73±0,06) lebih rendah secara signifikan ($p<0,05$) daripada kelompok BCCAO, sementara pada kelompok C400 (0,83±0,08) cenderung menurun mendekati SO.

Kesimpulan: Ekstrak *Cinnamomum verum* memperbaiki fungsi memori spasial dan menurunkan ekspresi mRNA TNF-α pada hipokampus tikus dengan BCCAO.

Kata kunci: *Cinnamomum verum*, cedera I/R serebral, memori spasial, TNF-α

ABSTRACT

NEUROPROTECTIVE POTENTIAL OF CINNAMOMUM VERUM EXTRACT ON SPATIAL MEMORY AND TNF-α mRNA EXPRESSION IN THE HIPPOCAMPUS OF TRANSIENT GLOBAL ISCHEMIC STROKE MODEL IN RAT

Background: In cerebral ischemia/reperfusion (I/R) injury, secondary damage occurs due to the return of blood flow to the brain after a period of ischemia, one of which is through an inflammatory process characterized by increased proinflammatory cytokines such as tumor necrosis factor-α (TNF-α) in the hippocampus. Damage in the hippocampus can impair spatial memory function. Cinnamomum verum extract is anti-inflammatory in neurological disease models, but its effects in transient global ischemic stroke models are not well known.

Objective: This study aims to examine the neuroprotective activity of Cinnamomum verum extract on spatial memory function and TNF-α mRNA expression in the hippocampus of rats with transient global ischemic stroke induced by bilateral common carotid artery occlusion (BCCAO).

Methods: Male Wistar rats (n=25) were divided into five groups (n=5): Sham operation (SO), BCCAO without extract administration (BCCAO), and BCCAO with Cinnamomum verum extract administration at doses of 100 mg/kgBW (C100), 200 mg/kgBW (C200), and 400 mg/kgBW (C400). BCCAO was performed by clamping the common carotid arteries for 20 minutes and then releasing it. Spatial memory was tested using the Morris water maze (MWM). The rats were terminated 8 days after BCCAO to collect hippocampal tissue. TNF-α mRNA expression was analyzed by RT-PCR.

Results: The BCCAO group had a significantly higher distance traveled to reach the platform on day 4 of the MWM learning phase (14,159±3,432) and TNF-α mRNA expression (0,89±0,02) than the SO group ($p<0.05$). After administration of Cinnamomum verum extract, the distance on day 4 of the MWM learning phase in the C100 (5,552±2,804), C200 (6,414±3,534), and C400 (6,743±4,495) groups was significantly shorter than in the BCCAO group ($p<0.05$). TNF-α mRNA expression in the C100 (0.78±0.05) and C200 (0.73±0.06) groups was significantly lower than in the BCCAO group ($p<0.05$), while in the C400 group it tended to decrease, approaching that of the SO group.

Conclusion: Cinnamomum verum extract improved spatial memory function and decreased TNF-α mRNA expression in the hippocampus of rats with BCCAO.

Keywords: *Cinnamomum verum*, cerebral I/R injury, spatial memory, TNF-α