

# Efek Ekstrak Etanol *Centella asiatica* (Linn.) Terhadap Depression-Like Behavior, Neuroinflamasi, dan Plastisitas Sinap Pada Tikus Obes Yang Diinduksi Diet Tinggi Lemak dan Fruktosa = The Effect of *Centella Asiatica* (Linn.) Ethanolic Extract on Depression-Like Behavior, Neuroinflammation and Synaptic Plasticity in Obese Rats Induced by High-Fat And Fructose Diet

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## Abstrak

Penelitian ini bertujuan untuk mengonfirmasi keterkaitan obesitas akibat diet tinggi lemak serta fruktosa dan pemberian ekstrak etanol *C. asiatica* (CA) terhadap kemunculan depression-like behavior. Parameter penelitian meliputi kadar IL-6 hipokampus sebagai penanda neuroinflamasi, kadar BDNF, serta protein sinaptik PSD-95 dan SYN1 pada region of interest (ROI) hipokampus, yaitu CA1, CA2, dan DG. Evaluasi tingkah laku dilakukan dengan instrumen Open Field Test (OFT), Elevated Plus Maze (EPM), dan Forced Swim Test (FST). Tikus Sprague-Dawley jantan dibagi menjadi empat kelompok dengan kombinasi DTLF dan pemberian CA. DTLF berkontribusi dengan sangat signifikan ( $p < 0,0001$ ) terhadap perbedaan kadar IL-6 antar kelompok, namun tidak dengan pemberian CA. Neuroinflamasi tidak terbukti dan pemberian CA cenderung tidak memperbaiki kondisi tersebut. Efek negatif obesitas akibat DTLF ditunjukkan pada rendahnya kadar BDNF kelompok obesitas ( $p < 0,0001$ ), dimana kelompok tersebut juga cenderung memiliki PSD-95 dan SYN1 yang lebih rendah pada sebagian besar ROI hipokampus. Perbedaan PSD-95 paling signifikan ditemukan pada area dentate gyrus ( $p < 0,0001$ ). Pemberian CA cenderung memperbaiki kadar BDNF, SYN1 pada seluruh ROI, serta PSD-95 hanya pada area CA1 dan CA2. Depression-like behavior secara deskriptif muncul akibat obesitas akibat DTLF pada seluruh uji, dan pemberian CA cenderung memperbaikinya yang dibuktikan pada instrumen OFT dan EPM.

.....This study aims to confirm the relationship between obesity caused by a high-fat and fructose diet and the administration of *C. asiatica* (CA) ethanol extract to the emergence of depression-like behaviour. The research parameters included hippocampal IL-6 levels as a marker of neuroinflammation, BDNF levels, and synaptic proteins PSD-95 and SYN1 in the region of interest (ROI) of the hippocampus, namely CA1, CA2, and DG. Behavioural evaluation was conducted using the Open Field Test (OFT), Elevated Plus Maze (EPM), and Forced Swim Test (FST) instruments. Male Sprague-Dawley rats were divided into four groups with combined DTLF and CA administration. DTLF contributed significantly ( $p < 0.0001$ ) to the difference in IL-6 levels between groups, but not CA administration. Neuroinflammation was not evident and CA administration tended not to improve the condition. The negative effect of obesity due to DTLF was shown in the low BDNF levels of the obese group ( $p < 0.0001$ ), which also tended to have lower PSD-95 and SYN1 in most hippocampal ROIs. The most significant difference in PSD-95 was found in the dentate gyrus area ( $p < 0.0001$ ). CA administration tended to improve the levels of BDNF, SYN1 in all ROIs, and PSD-95 only in the CA1 and CA2 areas. Depression-like behaviour descriptively appeared due to obesity caused by DTLF in all tests, and CA administration tended to improve it as evidenced in the OFT and EPM instruments.