UNIVERSITI TEKNOLOGI MARA

NEUROPROTECTIVE EFFECTS OF ETHANOLIC EXTRACT OF *Centella asiatica* (CAE) ON METHAMPHETAMINE-INDUCED NEUROTOXICITY

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MSc

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AUTHOR'S DECLARATION

I declare that the work in this thesis was carried out in accordance with the regulations of Universiti Teknologi MARA. It is original and is the results of my own work, unless otherwise indicated or acknowledged as referenced work. This thesis has not been submitted to any other academic institution or non-academic institution for any degree or qualification.

I, hereby, acknowledge that I have been supplied with the Academic Rules and Regulations for Post Graduate, Universiti Teknologi MARA, regulating the conduct of my study and research.

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ABSTRACT

Plant-derived antioxidants are known as promising therapeutic agent due to its effectiveness and minimal side effects. Till today limited natural-derived antioxidant is available to attenuate neurotoxicity induced by psychostimulant drug, methamphetamine (METH). Persistence and long term abuse of METH promotes loss of dopaminergic neurons which eventually results in neurodegenerative disorders including Parkinson's disease (PD). A traditional medicinal herb, *Centella asiatica* or pegaga has been well studied to exert neuroprotective and antioxidant properties. Herein, we examined potential neuroprotective effects of ethanolic extract of *Centella asiatica* (CAE) on METH-induced neurotoxicity, *in vitro all-trans* retinoic acid (RA) differentiated human neuroblastoma, SH-SY5Y cells and *in vivo* Sprague-Dawley rat model. The RA-differentiated SH-SY5Y cells was used to resemble dopaminergic neuronal-like cells. Cytotoxicity, neurotoxicity as well as neuroprotective effects of CAE were measured via 3-(4,5- dimethylthiazol-2-yl)-5-(3-carboxymethoxypheyl)-2-(4-sulfophenyl)-2H-tetrazolium, MTS assay against METH-treated SH-SY5Y cells. Results showed that CAE significantly decreased the viability of the undifferentiated SH-SY5Y cells in concentration-dependent manner. In addition, CAE (1mg/mL) significantly increased the viability of neuron cells and did not caused toxic effects on cells. CAE at concentrations of 100pg/mL and 1mg/mL conferred significant neuroprotective effects against METH- induced neuronal-cell death. Meanwhile, through *in vivo* Sprague-Dawley rat model, neuroprotective effects of CAE on PD-like symptom was evaluated through behavioural test. Further, involvement of manganese superoxide dismutase (SOD2) and microRNA, miR-34a in brain as antioxidant and neuroprotection biomarker was measured by Quantitative Real-time Polymerase Chain Reaction (qPCR). CAE treatment significantly improved the motor performance of METH-treated rats as evaluated on vertical pole test and narrow beam test. Gene expression showed that upregulation of SOD2 and miR-34a, suggest mechanism by which CAE exerts its neuroprotective mechanisms against METH-induced neurotoxicity. In conclusion, therefore we postulate that CAE could be promising neuroprotective effects in *in vitro* and *in vivo* rat model of METH-induced neurotoxicity.

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