UNIVERSITI TEKNOLOGI MARA

NEUROPROTECTIVE EFFECT OF NANOPARTICLE-BOUNDED BRAIN DERIVED NEUROTROPHIC FACTOR (BDNF) IN RATS WITH EXPERIMENTAL HAEMORRHAGIC STROKE

SAYYIDAH MARYAMUL AZRA ZUL RAMLI

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.

Name of Student	:	Sayyidah Maryamul Azra Zul Ramli
Student I.D. No.	:	2015789217
Programme	:	Master of Medical Science (Anatomy) – MD757
Faculty	:	Medicine
Thesis Title	:	Neuroprotective Effect of Nanoparticle-Bounded Brain Derived Neurotrophic Factor (BDNF) in rats with Experimental Haemorrhagic Stroke.
Signature of Student	:	……..
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ABSTRACT

Brain-derived neurotrophic factor (BDNF) plays an essential role in brain plasticity and repair. At the same time, nanoparticle (NPs) poly (lactic-co-glycolic acid) (PLGA) has been proven either in-vivo or in-vitro as potential carriers for drugs across the BBB, with advantages of enhanced drug efficiency and safety. This study was aimed to investigate the neuroprotective effect of BDNF-PLGA nanoparticles on experimental haemorrhagic stroke (HS) in rats. Sprague-Dawley rats were divided into 6 groups; group 1, sham operation while group 2 to 6 were induced with HS. 15 minutes after induced, all groups were treated with respective formulations intravenously: groups 1 and 2 were treated with saline; group 3 was treated with empty PLGA NPs; group 4 with PLGA NPs coated with surfactant; group 5 with BDNF-loaded PLGA NPs and group 6 with BDNF-loaded PLGA NPs coated with surfactant. Behavioural assessments were performed after treatment on days 1, 3 and 7. On day 7, rats were sacrificed, and brain was taken for histological and immunohistochemical analysis. Caspase-3 staining showed that treatment with BDNF-loaded PLGA NPs exhibited significant lower in apoptosis compared with other HS groups. Groups 2, 3 and 4 demonstrated a significant increase in glial cells when compared to BDNF treated groups. Rats treated with BDNF-loaded PLGA NPs also exhibited low expression of synaptophysin. Open field test showed that treatment with BDNF-loaded PLGA NPs produced high score in rearing and total distance travelled indicating improvement in locomotor activity. BDNF NPs treated group showed improved rotarod performance indicating improvement in their motor learning and coordination. Rats treated with BDNF-loaded PLGA NPs also exhibited increased grip strength as evidence of motor neuroprotection. Hence, BDNF-loaded PLGA NPs may have neuroprotective effect on experimental HS in rats.

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