

**UNIVERSITI TEKNOLOGI MARA**

**SUPPRESSION OF LPS-STIMULATED  
BV2 MICROGLIAL CELLS AND  
ATTENUATION OF MEMORY  
DEFICIT IN MICE BY  
LACTOBACILLI-FERMENTED MILK**

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Thesis submitted in fulfillment  
of the requirements for the degree of  
**Master of Science**

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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 result 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.

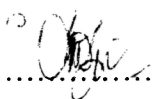
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## ABSTRACT

Neuroinflammation has been implicated as a common cause of neurodegenerative disease including Alzheimer's disease (AD). It results primarily from the activation of microglia that produces neurotoxic mediators and pro-inflammatory cytokines leading to neuronal death. Currently, research support nutritional interventions that include foods enriched with antioxidants to prevent AD and there is an increasing interest in the use of probiotics as a neuroprotective agent. In the present study, the protective effect of six lactobacilli strains (LAB 1, LAB 9, LAB 10, LAB 11, LAB 12 and LABPC) fermented in three different milk types [soymilk (SM-LAB), cow's milk (CM-LAB) and goat's milk (GM-LAB)] against lipopolysaccharide (LPS)-induced neuroinflammation in microglial BV2 cells was determined *in vitro*. The ability of the lactobacilli-fermented milk types to prevent memory deficit in LPS-induced mice was also investigated. Anti-inflammatory response against nitric oxide (NO) and CD40 expression was measured in BV2 cells. Mice were orally administered with SM-LAB, CM-LAB or GM-LAB for 28 days and learning and memory behavior were assessed using Morris water maze test. Brain tissues were used to measure acetylcholinesterase (AChE) activity, antioxidative activity, lipid peroxidation activity [malondialdehyde (MDA)], nitrosative stress parameters (NO), meanwhile, serum was collected for cytokine analysis (MCP-1, IL-1 $\beta$  and IL-6). In general, all the lactobacilli strains fermented in soymilk (SM-LAB 1, 9, 10, 11, 12 and SM-LABPC) and goat's milk (GM-LAB 1, 9, 10, 11, 12 and SM-LABPC) significantly ( $p < 0.05$ ) inhibited NO production without affecting cell viability. In cow's milk, only CM-LAB 9 and CM-LABPC decreased the NO level. However, the CD40 expression level was not significantly affected. Administration of CM-LAB, GM-LAB and SM-LAB (LAB 9 and LABPC) attenuated LPS-induced memory deficit as shown by the Morris water maze test. Furthermore, lactobacilli fermented in all milk types enhanced the level of antioxidant enzymes; SOD, GSH, and GPx and substantially reduced MDA level in LPS-induced mice. For AChE activity, only CM-LAB and GM-LAB significantly ( $p < 0.05$ ) reduced AChE level, while only SM-LAB significantly ( $p < 0.05$ ) increased catalase activity. The cytokines were reduced in SM-LAB, but for CM-LAB and GM-LAB, the effects of unfermented milk (UCM and UGM) were even greater. In conclusion, results from the present study suggest the ameliorating effect of lactobacilli-fermented milk on LPS-induced neuroinflammation and memory deficit to be mediated via anti-inflammatory, inhibition of AChE and antioxidative activities. Dietary interventions with probiotics fermented milk have the potential to prevent neuroinflammation and improve memory in AD.

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