British Journal of Nutrition (2017), **118**, 333–342
doi:10.1017/S0007114517002112

Effects of oral *Lactobacillus* administration on antioxidant activities and CD4+CD25+forkhead box P3 (FoxP3)+ T cells in NZB/W F1 mice

Bor-Show Tzang[1,2,3,4], Chung-Hsien Liu[5], Kuo-Ching Hsu[1], Yi-Hsing Chen[6,7], Chih-Yang Huang[8,9,10]† and Tsai-Ching Hsu[1,2,3]*

[1]*Institute of Biochemistry, Microbiology and Immunology, Chung Shan Medical University, Taichung 402, Taiwan, ROC*
[2]*Immunology Research Center, Chung Shan Medical University, Taichung 402, Taiwan, ROC*
[3]*Clinical Laboratory, Chung Shan Medical University Hospital, Taichung 402, Taiwan, ROC*
[4]*Department of Biochemistry, School of Medicine, Chung Shan Medical University, Taichung 402, Taiwan, ROC*
[5]*Department of Obstetrics and Gynecology, Chung Shan Medical University and Chung Shan Medical University Hospital, Taichung 402, Taiwan, ROC*
[6]*Research and Development Department, GenMont Biotech Incorporation, Tainan 741, Taiwan, ROC*
[7]*Institute of Biomedical Science and RongHsing Research Center for Translational Medicine, National Chung-Hsing University, Taichung 402, Taiwan, ROC*
[8]*Graduate Institute of Basic Medical Science, China Medical University, Taichung 404, Taiwan, ROC*
[9]*Graduate Institute of Chinese Medical Science, China Medical University, Taichung 404, Taiwan, ROC*
[10]*Department of Health and Nutrition Biotechnology, Asia University, Taichung 413, Taiwan, ROC*

(Submitted 3 May 2017 – Final revision received 17 July 2017 – Accepted 24 July 2017)

Abstract

Systemic lupus erythematosus (SLE) is an autoimmune disease that is characterised by a dysregulation of the immune system, which causes inflammation responses, excessive oxidative stress and a reduction in the number of cluster of differentiation (CD)4+CD25+forkhead box P3 (FoxP3)+ T cells. Supplementation with certain *Lactobacillus* strains has been suggested to be beneficial in the comprehensive treatment of SLE. However, little is known about the effect and mechanism of certain *Lactobacillus* strains on SLE. To investigate the effects of *Lactobacillus* on SLE, NZB/W F1 mice were orally gavaged with *Lactobacillus paracasei* GMNL-32 (GMNL-32), *Lactobacillus reuteri* GMNL-89 (GMNL-89) and *L. reuteri* GMNL-263 (GMNL-263). Supplementation with GMNL-32, GMNL-89 and GMNL-263 significantly increased antioxidant activity, reduced IL-6 and TNF-α levels and significantly decreased the toll-like receptors/myeloid differentiation primary response gene 88 signalling in NZB/W F1 mice. Notably, supplementation with GMNL-263, but not GMNL-32 and GMNL-89, in NZB/W F1 mice significantly increased the differentiation of CD4+CD25+FoxP3+ T cells. These findings reveal beneficial effects of GMNL-32, GMNL-89 and GMNL-263 on NZB/W F1 mice and suggest that these specific *Lactobacillus* strains can be used as part of a comprehensive treatment of SLE patients.

Key words: Systemic lupus erythematosus: Comprehensive treatment: *Lactobacillus paracasei* GMNL-32: *Lactobacillus reuteri* GMNL-89: *Lactobacillus reuteri* GMNL-263

Various studies have shown that elevated oxidative stress and decreased antioxidant activities are critical in the pathogenesis of systemic lupus erythematosus (SLE)[(1–3)]. Excessive oxidative stress damages lipids, proteins and DNA[(4,5)], and elicits autoantibodies in SLE patients, such as antibodies against oxidatively modified DNA and LDL[(6,7)]. Cytokines are also known to play direct roles in the disease pathogenesis of SLE[(8)]. SLE is characterised by a dysregulation of the immune system, which causes inflammation in multiple organs with diverse clinical manifestations[(9)]. Levels of IL-6 and TNF-α in serum are elevated in both lupus animal models and SLE patients. Studies of multiple animal SLE models have identified the critical role of the IL-6 pathway in SLE[(10–13)]. Indeed, evidence has correlated serum IL-6 level with disease activity or anti-double stranded

Abbreviations: DPPH, 1,1-diphenyl-2-picryl-hydrazyl; FoxP3, forkhead box P3; GMNL-32, *Lactobacillus paracasei* GMNL-32; GMNL-89, *Lactobacillus reuteri* GMNL-89; GMNL-263, *Lactobacillus reuteri* GMNL-263; MDA, malondialdehyde; MyD88, myeloid differentiation primary response gene 88; PI3K, phosphoinositide 3-kinase; SLE, systemic lupus erythematosus; TLR, toll-like receptor.

* **Corresponding author:** Dr T.-C. Hsu, fax +886 4 2324 8172, email htc@csmu.edu.tw
† Equal contribution as corresponding author.