## Studies on biological effects of plant lectins on animal cells and tissues

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Plant lectins have various biological effects on animal functions such as cell agglutination, mitosis, toxicity, cell growth inhibition, and anti-cancer and immunomodulatory effects. The involvement of lectins in our health and their relationship to degenerative disease is still an emerging science. The present study aimed to provide precise data for demonstrating the biological effects of plant lectin on animal cells and tissues.

To examine whether plant lectin could affect the gene expression of cytokines, gluconeogenic enzyme and transcription factor genes in mouse tissues and cultured cells, mRNA expression levels were measured by reverse transcription-polymerase chain reaction (RT-PCR) and quantitative real-time PCR (Q-PCR). The results indicated that Japanese mistletoe lectins (ML-J) increased the gene expression of proinflammatory cytokines interleukin (IL)-8, tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ) and IL-6 in Caco-2 cells at 10 ng/mL and TNF- $\alpha$ and IL-6 in the mouse duodenum at 10 µg/head. It was also found that ML-J caused increased (IL-8) cytokine production in Caco-2 cells with dose-dependently. To confirm the direct action of ML-J on Caco-2 cells through its carbohydrate-binding activity, an inhibition test was performed by lactose (200 mM), and the results showed that ML-J's action was carbohydrate-dependent. Intragastrically administered Lens culinaris agglutinin (LCA) at different concentration (20, 100 and 200 µg/head) and tomato lectin (TL) at 2 mg/head caused significantly down-regulation of Th1 cytokines IFN-y and pro-inflammatory cytokines TNF- $\alpha$ , IL-2, IL-12b and IL-1 $\beta$  in mouse intestine. The results suggest that LCA and TL have direct effects on modulation of the gene expression of Th1/Th2 balance to promote allergic activity and anti-inflammatory activity in vivo. The effects of LCA and TL on the gene expression of gluconeogenic enzymes in mouse tissues and Caco-2 cells, results indicated that LCA caused an up-regulation of the gene expression of the gluconeogenic enzymes glucose-6-phosphatase (G6Pase) and phosphoenolpyruvate carboxykinase (PEPCK) in mouse duodenum and in Caco-2 cells, whereas insulin had the opposite effect. The results also showed that LCA caused an increase in the intestinal gene expression of either hepatocyte nuclear factor (HNF)1a or HNF4a. TL caused an up-regulation of the gene expression of G6Pase and PEPCK in the mouse duodenum. The effects of methyl α-D-mannoside (MAM) on the change in gene expression in Caco-cell caused by LCA was examined, results indicated that up-regulated gene expression of G6Pase induced by LCA was attenuated by MAM. The up-regulation of PEPCK expression by LCA tended to be reduced in the presence of MAM. These findings suggest that LCA may have unfavorable effects. Therefore, lentil beans should be cooked well to remove bioactivity of LCA. This study provides the first example to show that a perorally administered plant lectin affects gene expression in the duodenum.

The present study provided some new information concerning the physiological effects of plant lectin on animal cells and tissues and suggested both of beneficial and deleterious effects. Elucidations of further biological effects of plant lectins will help to develop new strategies for maintain our health.