論　文　内　容　要　旨

Metabolomic and transcriptional study of plant-derived lactic acid bacteria enhancing bioactivities of medicinal plant extracts

（生薬発酵産物の生物活性を高める植物乳酸菌の

メタボローム解析と転写研究）

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Fermentation is a valuable biotechnology that can be exploited to develop novel plant-based foods with improved health promoting properties. Plant fermentation process by LAB involves the decomposition and/or bioconversion of complex phytochemicals into bioavailable and bioactive compounds via action of microbial enzymes like glycosyl hydrolase, phenolic acid decarboxylase, reductase and esterase that concentrates functional microbial metabolites with beneficial consequences for human health. In this study, the bioactivities of the aqueous extracts of three medicinal herbs Paeonia Radix Alba (dried root of *Paeonia lactiflora* Pall), Mentha (*Mentha arvensis* Linné var. *piperascens* Malinvaud) and Gardenia fructus (the fruit of *Gardenia jasminoides* J. Ellis) were evaluated after fermentation with plant-derived lactic acid bacteria strains like *L. brevis* 174A, *L. plantarum* SN13T and *P. pentosaceus* LP28. . The bioactive metabolites released in each extract after fermentation were also determined. The whole genome sequence of *L. plantarum* SN13T was used to identify the putative genes encoding the associated enzymes of these metabolic pathways. Finally, the transcription profile of these genes were compared in each medicinal extract.

The fermentation of Paeonia extract with strains like *L. brevis* 174A and *L. plantarum* SN13T were found to significantly reduce the production of lipopolysaccharide (LPS) induced inflammatory mediators like nitric oxide (NO), intracellular reactive oxygen species (ROS) and cytokines IL-6 and TNF-α and their gene expressions in RAW 264.7 cells. In case of Mentha extract, it was found that fermentation with the strain SN13T could effectively increase its bioactivity against the LPS stimulated cells, but the strain LP28 could not. The strain SN13T was also found to increase the potential of Gardenia fructus extract to inhibit the inflammatory mediators and their gene expressions. HPLC analysis revealed that the fermentation of Paeonia extract by SN13T and 174A led to metabolism of gallic acid into pyrogallol. In Mentha extract, dihydrocaffeic acid was produced by SN13T from rosmarinic via caffeic acid. Meanwhile, the fermentation of Gardenia extract by SN13T metabolized geniposide to produce genipin. In the whole genome sequence of *L. plantarum* SN13T (GenBank accession no. AP019815.1), genes encoding putative metabolic enzymes: decarboxylase; ß-glucosidases; esterase; and reductase; that could be involved in the fermentation of Paeonia; Gardenia; and Mentha extracts were identified as *ubiD*; *pbg9* and *bglH3*; *ceh*; *hcrA* and *hcrB*; respectively. The SN13T genes *ubiD*; *pbg9*; and *hcrB* encoding putative metabolic enzymes decarboxylase; ß-glucosidase; and reductase were specifically overexpressed in Paeonia; Gardenia; and Mentha extracts respectively. Moreover, transcription of these genes in each extract was time-dependent, which also correlated with the emergence of metabolites in the fermented extract and their subsequent bioactivities, i.e., during early hours of fermentation in Paeonia extract, while only after 8 hours in Mentha and Gardenia extracts. In conclusion, this study emphasize that medicinal plant extracts can be conveniently exploited as fermentation media for plant-derived LAB to develop functional food with enhanced bioactive properties.