The intestinal target involved in the actions of Sambucus williamsii Hance on bone protection

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Abstract:

Introduction: Osteoporosis is a chronic and long-term skeletal metabolic disease. Our previous study revealed the bone beneficial effects of *Sambucus williamsii* Hance (SWH), a fork medicine that has been used in China for thousands of years on bone and joint diseases. However, the in-house pharmacokinetics results concluded that the level of major components lignans in SWH treated serum was too low to be detected. As oral administration is a regular way for Chinese medicine, we hypothesis that SWH might exert bone protective effects via intestinal targets. This study aimed to determine how SWCA modulates bone metabolism via intestinal targets.

Materials and Methods: A metabonomics were carried out to identify the endogenous metabolites changes that were related to intestine or gut microbiota due to the administration of SWH, and to verity the metabolites by ovariectomized rats and cells studies.

Results: Our study indicated that SWH effectively restored the changes of 26 metabolites induced byestrogen-deficiency in OVX rats, among them, tryptophan was related to gut microbiota and intestine. In vitro, SWH suppressed the synthesis of serotonin, one of the two major metabolites of tryptophan, by inhibiting protein expression of tryptophan hydroxylase 1 (TPH-1), the synthetic rate-limiting enzyme of serotonin in intestine, in RBL-2H3 cells (tph-1 gene high expressing cells). In vivo, it decreased serum levels of serotonin, suppressed the protein expression of TPH-1 in the colon, and reversed the gene and protein expressions of FOXO1 and ATF4 in the femur in OVX rats.

Conclusions: These findings indicated that the bone protective effects of SWH were mediated by gut-derived serotonin via intestinal target TPH-1.