

## DOCTORAL THESIS

### Integrating multi-omics to investigate the correlation between the quality and efficacy of ginseng

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## Abstract

Ginseng, the root and rhizome of *Panax ginseng* C. A. Mey. (Araliaceae), is one of the most famed dietary and medicinal herbs worldwide due to its multifaceted efficacies. Ginsenosides and carbohydrates are demonstrated the major bioactive components of ginseng. Ginseng materials are always formed under various conditions, e.g. different growth years or different post-harvest processing/handling manners. These conditions can impact chemical profiles and thereby cause different quality and efficacy of ginseng. To address this issue, it will be necessary to understand the correlation between the quality and efficacy of ginseng materials formed under different conditions. Previous studies have attempted to investigate how growth years and post-harvest processing/handling manners affect the quality and efficacy of ginseng. In the most of these cases, several chemical components and biological parameters were selected as the indicators for evaluating the quality and efficacy of ginseng, respectively. However, it has been well recognized that the therapy of ginseng is featured by “multiple components against multiple targets”. Therefore, several selected indicators may fail to comprehensively characterize the quality and efficacy of ginseng, thus cannot accurately reveal their correlations. Instead, holism-based approaches should be employed.

In this study, we integrated chemomics, metabolomics and gut microbiota genomics to investigate the correlation between the quality and efficacy of ginseng in the conditions of growth years, steam-processing and sulfur-fumigation. First, chemomics approach was developed to qualitatively and quantitatively determine major ginsenosides and carbohydrates (poly-, oligo- and monosaccharides) by ultra-high performance liquid chromatography-tandem triple quadrupole mass spectrometry (UHPLC-QqQ-MS/MS) and high performance liquid chromatography coupled with evaporative light scattering detector (HPLC-ELSD) for characterizing the overall quality of ginseng. Second, ultra-performance liquid chromatography-quadrupole time-of-flight mass spectrometry (UPLC-QTOF-MS/MS)-based metabolomics and 16S rRNA gene sequencing-based gut microbiota genomics coupled with biochemical parameters determination were

performed to evaluate anti-fatigue and anti-obesity activities of the different ginseng on animal models. Third, the obtained multi-omics data were processed by multivariate statistical analysis and then were integrated to discuss the correlation between the quality and efficacy of ginseng materials in different conditions.

The results indicated that: 1) ginseng with 4-6 growth years possessed different anti-fatigue activity in multiple targets due to the different effects of ginsenosides and carbohydrates on endogenous metabolism and gut microbiota; 2) steam-processing qualitatively and quantitatively altered ginsenosides and carbohydrates in ginseng, resulting in different anti-obesity activity between white ginseng and red ginseng, and the mechanisms potentially involve chemically structural/compositional specificity to gut microbiota; 3) SO<sub>2</sub> residual content caused by sulfur-fumigation did not correlate with the quality, efficacy and toxicity changes of sulfur-fumigated ginseng, more specifically, less SO<sub>2</sub> residue did not indicate higher quality, better efficacy nor weaker toxicity. The research provides scientific insights for guiding the clinical and dietary practice of ginseng and offers new methodology for comprehensively exploring the correlation between the quality and efficacy of herbal medicines.

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