DOCTORAL THESIS

Integrating metabolomics and glycomics for understanding the traditional usage of morindae officinalis radix

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ABSTRACT

Morindae Officinalis Radix (MOR), Bajitian in Chinese, is the dried root of *Morinda officinalis* F.C.How. (Rubiaceae). It is one of the most popular herbal medicines used in the southeast region of China. Various types of chemical constituents have been experimentally shown to be bioactive components of MOR, among which secondary metabolites and saccharides predominate. Pharmacological studies revealed MOR shows kidney tonifying, anti-osteoporosis, antidepressant, anti-inflammatory and antioxidant effect. Since 2002, MOR has been approved as a food supplement for daily healthcare, hence increasing consumption and demand for better quality of MOR. However, selection of MOR with superior quality is largely based on traditional experience which lacks scientific basis. For example, 3-4-year-old MOR is usually used without xylem; and processed MOR are believed to show different bioactivities. Therefore, to promote the rational utilization and ensure efficacy of MOR, overall qualitative and quantitative characterization of MOR in different traditional usage is needed. Anthraquinones, iridoid glycosides and oligosaccharides are the common reference compounds for chemical characterization of MOR. However, they are usually selectively characterized, which is not comprehensive enough in herbal quality evaluation. To deal with this, metabolomics targeting secondary metabolome and glycomics targeting glycome can be applied. And the integration of metabolomics and glycomics could be a promising approach to investigate overall chemical variations in MOR according to its traditional usage.

Therefore, in this study, chromatographic methods for metabololmics and glycomics were firstly developed to study the traditional usage of MOR. In Chapter 2, they were applied for studying chemical variation and differences in growth year and plant tissue of MOR. In Chapter 3, chemical differences in processed products of MOR were also studied using the established metabololmics and glycomics methods. Further bioactivity differences of them were studied by cell metabolomics with HEK 293 cells under high glucose microenvironment. Besides that, in Chapter 4, consumption method of not only MOR, but other herbal medicines were studied. Conventional boiling water extraction (BWE) and ultrasound-assisted extraction (UAE) were compared to understand their effects on polysaccharides.

For the study of growth year and tissues of MOR, the results showed that various types of bioactive components reached a maximum between 3-4 years of growth; and that xylem contained more potentially toxic constituents, but less bioactive components, than cortex. For the study of processing products, the results showed that secondary metabolome and glycome of raw MOR and other processing products was found qualitatively and quantitatively different. Contents of secondary metabolites were generally increased in processed products, while saccharides were decreased instead. Also, steamed MOR (F) seemed to show preventive effect of diabetic nephropathy and different MOR processing products had induced different metabolic changes on high glucose induced HEK 293 cells. In the study of extraction methods, the results showed that the polysaccharides from the herbal medicines by UAE were quantitatively and qualitatively different with those by BWE. The powerful extraction ability and polysaccharide degradation caused by ultrasound collectively contributed to these differences. It was revealed that not only the UAE conditions but also the polysaccharide structures could affect the extraction ability and polysaccharide degradation.

To conclude, metabolomics and glycomics were integrated in this study to investigate the variations in secondary metabolome and glycome in MOR. We had successfully applied these methods to study and provide scientific basis for traditional practice of MOR. We had proved that 3rd to 4th years of growth are the key period for the development of the biochemical signature of MOR. Xylem and cortex of MOR were qualitatively and quantitatively different and removing xylem could help to remove potentially toxic components. This study also provided scientific evidences for the justification of MOR and its processed products, as well as their metabolic effects on high glucose induced DN in HEK 293 cells. Besides, this study revealed both UAE parameters and structural properties of polysaccharides affects extraction recovery of polysaccharides in herbal medicines. Hence, we suggest UAE should be carefully considered before employing it in relevant chemical and pharmacological analysis.

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