

DOCTORAL THESIS

Pharmacognostical studies on Heshouwu (*Polygoni Multiflori Radix*): textual research, quality evaluation and processing chemistry investigation

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ABSTRACT

Heshouwu, derived from the tuberous root of *Polygonum multiflorum* Thunb., has been widely used in Traditional Chinese Medicine for centuries. It has a purgative effect when unprocessed, while used as a tonic after processing, and according to historical records, *heshouwu* should be steamed and sun-dried nine times to generate processed materials.

Up until recently, three aspects of *heshouwu* have not been sufficiently studied. First, it is necessary to understand the history of *heshouwu*, including the emergence in the literature, the descriptions of its appearance, its effects and controversies, as well as the evolution of *heshouwu*'s processing. As historical texts open a window to the past and clarify the issues of important clinical concern in the modern world, historical *bencao* (materia medica) literature research should be conducted. Second, in commercial herbal markets, *heshouwu* is divided into different grades based on morphological features of size and weight. A heavier weight and larger size command a higher price, and both sellers and buyers accept this grading. However, two questions arise: Does the existing grading system accurately represent the quality of the herb? If not, is there another system, or are there other morphological criteria, that could be used to reliably represent quality? Lastly, while *heshouwu* has been processed for hundreds of years, including the present, the chemistry of that processing has not been well studied.

To address these issues, this study is divided into four parts. First, a systematic review of the text and illustrations in historical *bencao* literature is conducted. The *bencao* literature study illustrates the origin, botanical

characteristics, actions and processing of *heshouwu*, as well as the origin and historical evolution of *baishouwu* (“white *heshouwu*”).

To assess the inherent quality of various grades and to explore whether the existing grading system of *heshouwu* accurately represent quality, we firstly analyze the chemical profiles in three different commercial grades of *heshouwu* raw materials, using UPLC-QTOF-MS/MS and UPLC-QqQ-MS/MS. The results reveal that production regions and specifications both influence the chemical constituents of *heshouwu*, but the influence of production regions is even more evident. Differences in the constituents among production regions are relatively large, while there are no significant differences among the existing commercial grades.

As the relationship between bioactive components and morphological features can be found by analyzing the distribution patterns of chemical components in different tissues, in order to find other reliable morphological indicators of quality furtherly, a method combining laser microdissection (LMD), UPLC-QTOF-MS/MS and UPLC-QqQ-MS/MS is applied in the third part of this study. The results indicate that, *heshouwu* with broader cork and phloem, as seen in a transverse section, are typically of better quality as these parts are where the bioactive components accumulate.

In the fourth part of this study, targeted and untargeted metabolomics analyses using UPLC-QTOF-MS/MS and UPLC-QqQ-MS/MS are integrated to investigate the processing chemistry of *heshouwu*. The results demonstrate that processing by nine cycles of steaming and drying can qualitatively and quantitatively alters the chemical profile of *heshouwu*, which suggests that the nine cycles might be necessary for the preparation of processed *heshouwu*.

The historical *bencao* literature research, chemical basis for quality evaluation, as well as processing chemistry investigation of *heshouwu* have been conducted in depth in this study. The results will be helpful in providing scientific basis of *heshouwu*'s application.

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