Available online at www.sciencedirect.com

ScienceDirect

Chinese Journal of Natural Medicines 2016, **14**(3): 0177–0184

Chinese Journal of Natural Medicines

·Review·

The spectrum-effect relationship—a rational approach to screening effective compounds, reflecting the internal quality of Chinese herbal medicine

ZHU Chun-Sheng, LIN Zhi-Jian, XIAO Ming-Liang, NIU Hong-Juan, ZHANG Bing*

School of Chinese Pharmacy, Beijing University of Chinese Medicine, Beijing 10029, China

Available online 20 Mar., 2016

[ABSTRACT] Since the chromatographic fingerprint was introduced, it has been accepted by many countries to assess the quality and authenticity of Chinese herbal medicine (CHM). However, solely using the chromatographic fingerprint to assay numerous chemicals is not suitable for the assessment of the whole internal quality and pharmacodynamics of CHM. Consequently, it is necessary to develop a rational approach to connecting the chromatographic fingerprint with effective components to assess the internal quality of CHM. For this purpose, a spectrum-effect relationship theory was proposed and accepted as a new method for the assessment of CHM because of its potential use to screen effective components from CHM. In this paper, we systematically reviewed the application of the spectrum-effect relationship theory in the research of CHM, including research mentality, different chromatographic analysis techniques, data processing technologies, and structure determination.

[KEY WORDS] Chinese herbal medicine; Chromatographic fingerprint; Spectrum-effect relationship

[CLC Number] Q5 **[Document code]** A **[Article ID]** 2095-6975(2016)03-0177-08

Introduction

Nowadays, there has been a growing interest in Chinese herbal medicine (CHM) due to its long-standing clinical use and reliable therapeutic efficacy in the prevention and treatment of human diseases. Correspondingly, identification, authentication, and quality control of CHM attract more attention [1-3]. However, currently methods for quality assessment cannot fulfill the practical requirements for the internal quality assessment of CHM because it consists of a myriad of chemicals and the therapeutic effect of CHM is attributed to the interactions of multiple phytochemicals [2, 4-5], which is different from chemically synthetic drug. Thus, it is required to develop a rational way to establish an effective quality evaluation system, which would not only ensure the efficacy, safety and stability of CHM products, but also embody the holistic concept of CHM [6].

Comparing with other methods, the chromatographic fingerprint analysis of herbal medicine represents a comprehensive qualitative approach to species authentication, internal quality evaluation and stability test of CHM. Hence, it emerges and is accepted as a powerful tool to evaluate and control the quality of CHM [2, 7-8]. The chromatographic fingerprint is accepted by the World Health Organization and other countries as an identification and quality evaluation technique for herbal medicines [9-12]. Generally, major constituents in the chromatographic fingerprint are considered as markers in the quality assessment of CHM, regardless of their effectiveness [13-15]. Unfortunately, it is far from sufficient to find out which components are the active ones that play the leading role in treatment response. That being said, the chromatographic fingerprint only improves the quality control and standardization, but is deficient in determining the efficacy of CHM [16].

So it is imperative and urgent to strengthen the fingerprint-effect study to discern the relationship between chromatographic fingerprint and pharmacodynamics efficacy of CHM, establish integrated evaluation system, and finally find the main effective components in fingerprint reflecting

[Received on] 12-Apr.-2015

[Research funding] This work was supported by Ministry of Education Research Fund for the Doctoral Program (20130013120001 and 20120013130002); Beijing University of Chinese Medicine Young Teachers of Special Autonomy Issue (2013-QNJSZX008); Beijing University of Chinese Medicine Scientific Research Innovation Team (2011-CXTD-014).

[*Corresponding author] E-mail: zhangbing6@263.net

The authors have declared no conflict of interest.

the therapeutic effects of CHM. In order to tackle with this problem and provide a better method, a new theory called the spectrum-effect relationship was first systematically proposed by Li *et al*. in 2002 [17]. Being the advanced stage of fingerprint research, the spectrum-effect relationship can illustrate the relationship between fingerprint and pharmacodynamic effects through multiple statistical analysis methods and help establish the CHM efficacy material basis, which can truly reflect the internal quality of CHM. Comparing with the traditional extraction and separation, it has advantages of less time and solvent consumption, low operating costs, and little pollution to the environment [18]. More important, when applied in holistic research of CHM, the spectrum-effect relationship theory conforms to the integral view of TCM. For these reasons, it has become one of the best methods for CHM internal quality evaluation.

The spectrum-effect relationship is considered as a potential method to determine effective components in complex mixtures and reflect the internal quality of herbal medicine. Being widely used in the field of CHM, it is indispensable in the process of modernization and internationalization of CHM. In this paper, we will review various aspects about spectrum-effect relationship, including research ideas, analysis methods, data processing techniques, and some prominent results generated in recent years to provide ideas and references for screening the CHM effective components that are accurately reflecting the internal quality of CHM.

Research mentality and method of the spectrum-effect relationship

To date, there has been no unified research mentality on how to handle the spectrum-effect relationship. Therefore, it is the key to find an effective and available method. Concern has recently been expressed along with the deepening of research on the spectrum-effect relationship, and a prototype has come up.

The process of spectrum-effect relationship study on CHM is divided into three steps: The first step is to get a reliable chromatographic fingerprint which has a high separation degree and a clear concentration distribution of chemical components, i.e., to acquire the so-called “spectrum”. Meanwhile, it is needed to get the pharmacodynamic information on CHM and relevant efficacy data mostly obtained in studies at animal, cellular and molecular levels. The second step is to link the given peaks in the chromatographic fingerprint to the pharmacodynamic effects of CHM, which means taking together preliminary results of “spectrum” and “effect”, in order to screen effective components from all the chemical components of CHM by processing the data obtained in step one and build the spectrum-effect relationship model. The final step is to identify the structures of effective components to help build a quality evaluation system, which can accurately reflect the therapeutic effect and inner quality of CHM based on the chromatographic fingerprint [19-23] (Fig. 1). The spectrum-effect relationship study provides a powerful method and insights for the quality control on CHM as well as the screening of effective components. Through the above process, investigation of relationships between chromatographic fingerprint and pharmacodynamic activities makes the evaluation of the differences in internal quality and pharmacodynamic activities of CHM possible. Therefore, combining the fingerprint with effective components can be used as one of the criteria on evaluation of the true effectiveness of CHM.

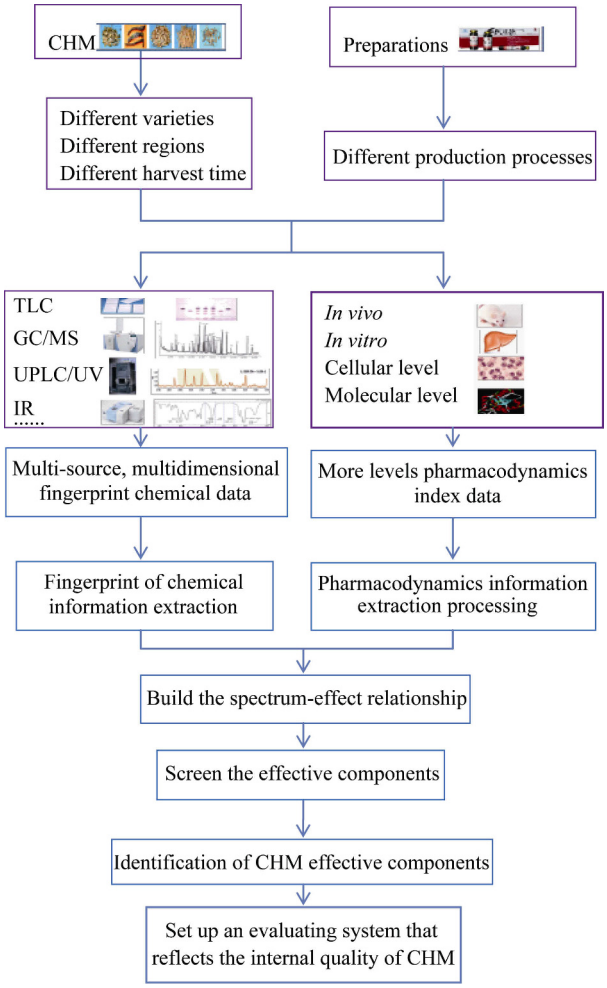

Fig. 1 Schematic presentation of spectrum-effect relationship study on CHM

Technologies involved in spectrum-effect relationship study

Technologies used to construct chromatographic fingerprint

Considering that the spectrum-effect relationship research of CHM is based on the chromatographic fingerprint, it is important to establish a suitable analytical method to generate a fingerprint that can reflect chemical ingredients of CHM as much as possible. There are several analytical separation techniques widely used in this field, including high performance liquid chromatography (HPLC), gas chromatography (GC), ultra performance liquid chromatography (UPLC), chromatography combined with mass