



Basic Methods and Ideas of TCM Quality Consistency Evaluation

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Abstract: The complexity of traditional Chinese medicine (TCM) itself determines that the quality evaluation of traditional Chinese medicine is more difficult than that of single-component chemical medicine. At present, the outbreak of COVID-19 has made the importance of traditional Chinese medicine well demonstrated. Traditional Chinese medicine has played an important role in fighting the epidemic and treating a series of other diseases. Therefore, we need to establish a comprehensive quality consistency evaluation system of traditional Chinese medicine as soon as possible to promote the better application of traditional Chinese medicine. This article expounds the basic methods and ideas of the quality consistency evaluation of traditional Chinese medicine, hoping to provide a good reference for researchers in this field.

Keywords: TCM quality; consistency evaluation; improvement of system; basic methods

1. Introduction

In recent years, with the continuous deepening of the modernization and internationalization of traditional Chinese medicine, the voice of calling for the establishment of a comprehensive quality consistency evaluation system of traditional Chinese medicine and the use of advanced quality consistency evaluation methods of traditional Chinese medicine is getting louder and louder. At home and abroad, a lot of manpower and material resources have been invested to study the basic methods of quality consistency evaluation of traditional Chinese medicine, and it is expected that a quality consistency evaluation method of traditional Chinese medicine that meets the needs of all aspects at this stage will be obtained.

At present, the conventional theories used in the quality consistency evaluation of traditional Chinese medicine include traditional Chinese medicine fingerprint research, biological activity detection analysis, Acousto-Optic Tunable Filter (AOTF), near-infrared spectroscopy analysis, etc.^[1] This article will introduce these three methods, especially the fingerprint of traditional Chinese medicine.

2. The present situation of quality consistency evaluation of traditional Chinese medicine

Nowadays, the content determination of a considerable number of medicinal materials and preparations in the Chinese Pharmacopoeia has not reached the control limit. Most of the preparations recorded in the Chinese Pharmacopoeia are compound prescriptions, which are only based on the content determination of single index components. At present, this evaluation model is not very perfect and it has certain shortcomings with a certain one-sidedness. And it is difficult to comprehensively control the quality of traditional Chinese medicine products.

3. The fingerprint of traditional Chinese medicine

The fingerprint of traditional Chinese medicine is to obtain accurate chemical components of traditional Chinese medicine on the basis of accurately understanding of the macro-system of traditional Chinese medicine and making full use of spectral and chromatographic analysis techniques. It is a method with great development potential, which is characterized by large amount of information, strong characteristics and strong integrity.^[2]

3.1 Classification of fingerprint of traditional Chinese medicine

Based on the differences in the source of the applied technology, the fingerprint of traditional Chinese medicine can be further subdivided, such as the fingerprint based on chemical theory (chromatographic fingerprint and spectral fingerprint belong to the category of chemical method), the fingerprint based on metabolic function and the fingerprint based on biological model (as shown in Figure 1). Among them, chemical fingerprint is the most widely used.

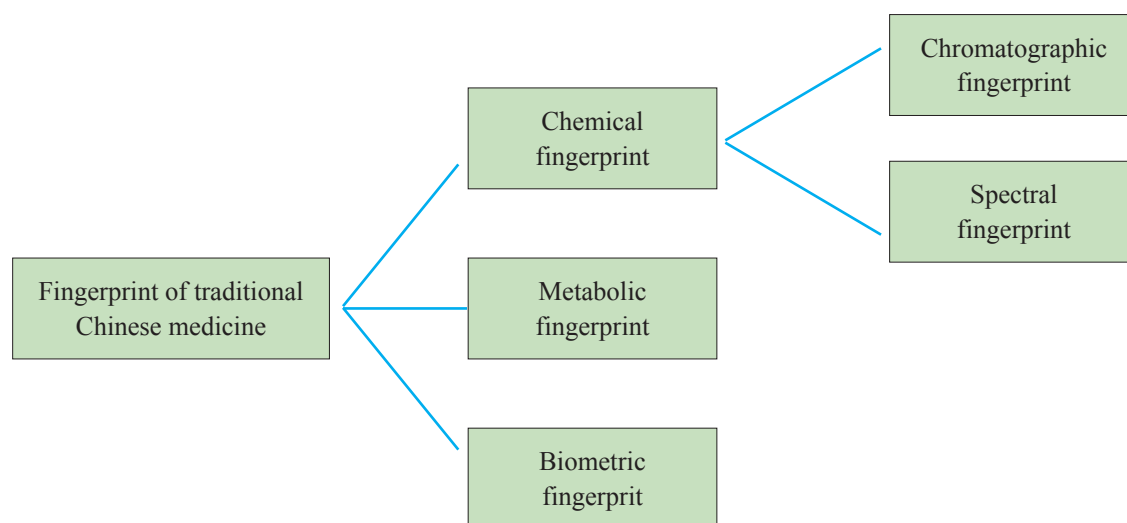


Figure 1. Classification of fingerprint of traditional Chinese medicine

3.2 Quantitative fingerprint of traditional Chinese medicine

3.2.1 Function of quantitative fingerprint of traditional Chinese medicine

Based on the engineering cybernetics proposed by older generation scientists such as Qian Xuesen, the first step in the application of fingerprint of traditional Chinese medicine is to achieve qualitative identification of the chemical composition of the system. And then obtain the accurate content range of important fingerprint components. This is the primary task of quantitative fingerprint of traditional Chinese medicine. At present, the functions of fingerprint of traditional Chinese medicine are as follows.^[3]

(1) It can show the additive characteristics of the chemical fingerprint in terms of quantity. In the case of $S_m \geq 0.90$, the overall linear characteristics of the system are very obvious. (2) All raw materials and preparations of traditional Chinese medicine have standard preparations and have standard quantitative fingerprints. Standard preparations should play an important role in promoting a more standardized and scientific system for the processing quality of traditional Chinese medicine. (3) Considering the controllability of traditional Chinese medicine, the macro-qualitative and macro-quantitative analysis of traditional Chinese medicine can be performed from the perspective of the overall fingerprint. (4) The pattern of formulation of traditional Chinese medicine standard preparation can be based on the quantitative fingerprint of a single raw material of traditional Chinese medicine to realize the direct evaluation of the effectiveness of the preparation medicine, which plays a role of source control in excluding unqualified raw materials. (5) One of the best representatives of the overall concept of traditional Chinese medicine in my country is the quantitative fingerprint of traditional Chinese medicine, which is of great value in processing workshops and clinical use, especially in quantitative prescription. (6) Controlling the effect of all raw materials and preparations of traditional Chinese medicine in order to maintain their balance and stability is the conventional use of the system fingerprint quantitative research method of the dual-standard spectrum and three-solid chromatographic column.

3.2.2 Realization mode of fingerprint of traditional Chinese medicine

At present, there are three main modes for realizing the fingerprint of traditional Chinese medicine, namely index quantitative amplitude control and full fingerprint qualitative mode, activity quantitative spectrum correlation mode and quantitative fingerprint, macro qualitative and macro quantitative mode.

3.2.3 System quantitative fingerprint method (SQFM)

SQFM can not only identify the genus of traditional Chinese medicine, but also quantitatively measure the overall chemistry. The quantitative study of systematic fingerprint limits the physical consistency of the overall effect of traditional Chinese medicine from the perspective of the system, which is consistent with the reality of the globality and diversity of traditional Chinese medicine. At the same time, this method is also the theoretical basis for reasonably dealing with drawbacks, and has become the most critical method to limit the consistency and stability of traditional Chinese medicine materials based on chemical theory. SQFM theory is the most typical research theory and core achievement of Professor Sun Guoxiang, from a small number of data testing theories to a variety of data models. Its development process is also gradually advanced: through refinement and conciseness, and the key indicators are quantified and highlighted. It is the most outstanding achievement in the study of the quality consistency evaluation of traditional Chinese medicine.^[4]

3.3 The control mode of standard preparation of traditional Chinese medicine based on fingerprint of traditional Chinese medicine

At the present stage, the added fingerprint of Chinese Pharmacopoeia is the basis for the consistency evaluation of the effect of traditional Chinese medicine. It is an effective method to evaluate the consistency of the quality of traditional Chinese medicine by establishing a standard preparation limitation theory based on the system quantitative fingerprint research model.

3.3.1 Basic control mode of fingerprint of traditional Chinese medicine

In the new edition of the *Chinese Pharmacopoeia*, the full chemical fingerprint content distribution of the standard fingerprint pattern, that is, the identification of the similarity of the proportional distribution, has been realized. The fingerprint control mode of traditional can be divided into two levels. The first level is the characteristic fingerprint of remote control, which is realized on the basis of overall qualitative analysis through system adaptability inspection, system unified change, and system correction method quantification. The second level is the near-controlling standard fingerprint, which is realized on the basis of overall quantification through the standard preparation control method, standard fingerprint pattern method, and standard pattern correction method.

The first level is the characteristic fingerprint of remote control, which is realized on the basis of overall qualitative analysis through the investigation of system adaptability, the change of system unification and the quantitative method of system correction.

The second level is the standard fingerprint of near-control, which is realized on the basis of overall quantification through standard preparation control method, standard fingerprint atlas method and standard map correction method.

3.3.2 Control mode of standard preparations of traditional Chinese medicine

The core template for ensuring the effectiveness of traditional Chinese medicine is to combine the standard preparation of traditional Chinese medicine with the quality control of traditional Chinese medicine. This systematic project has achieved a high degree of consistency in the raw materials and quality of traditional Chinese medicine. We must make full use of the standard formulation control mode to carry out important innovations in the overall layout. Therefore, the index of “fingerprint test” is added here, and the index $Sm \geq 0.90$ is used to judge the authenticity of the effect of traditional Chinese medicine, and $80\% \leq Pm \leq 120\%$ to control the overall component content. It is recommended to control the critical range of high content index components.

3.3.3 The core control method of the current Chinese medicine quality consistency evaluation system is the systematic fingerprint quantification method

The collection of traditional Chinese medicine chemical fingerprints constitutes a single system. The current focus is to determine the size of the system's fingerprint capacity based on the chemical fingerprint characteristics of traditional Chinese medicine drugs and the exertion of drug effects. The planning of the material consistency of the overall drug effect of traditional Chinese medicine from the perspective of the system is a major feature of the systematic fingerprint quantification method, which is highly consistent with the current macro situation of traditional Chinese medicine. It is the primary core method that constitutes the consistency control of chemical substances in traditional Chinese medicine.

3.3.4 Determination method and formula of dissolution of traditional Chinese medicine solid preparation

① Determination of the dissolution of each component in the pharmacodynamic indexes; ② UV automatic control method; ③ UV full fingerprint dissolution determination method. The formula used is as follows:

$$F_2 = 501 \text{ g} \left\{ \left[1 + \frac{1}{n} \sum_{i=1}^n (R_i - T_i)^2 \right]^{-0.5} \times 100 \right\}$$

3.3.5 Determination of multi-component BE of traditional Chinese medicine

The existing more commonly used methods for the determination of multi-component BE of traditional Chinese medicine are the multi-angle combination method and the biological method that associates the efficacy through the same efficacy. The multi-faceted theory is often applied to the analysis of bioequivalence. It can effectively combine the chemical structure and drug effect in the fingerprint of traditional Chinese medicine. It can also combine the chemical structure, drug mechanism and the effect of clinical application.^[5] The bioequivalence study of traditional Chinese medicine preparations can also be achieved through biological evaluation, that is, the bioequivalence study of traditional Chinese medicine can be conducted through biological evaluation methods with the same therapeutic effect and related therapeutic effects.

3.3.6 Safety control method of traditional Chinese medicine

The safety control method of traditional Chinese medicine should be realized from finding effective ingredients through basic research, accelerating the research of modernization of traditional Chinese medicine, establishing a perfect quality evaluation system of traditional Chinese medicine, perfecting the supervision mechanism of adverse reaction of traditional Chinese medicine, and establishing standardized production enterprises. ^[6]

4. Biological activity detection method

Biological activity measurement is also called bioassay. It uses the in vivo test of the whole animal body or the in vitro test of isolated organs, tissues, cells, etc. to achieve the purpose of determining the nature and biological activity of the drug, which in turn reflects its clinical function and potency. method.

4.1 Commonly used bioassay methods

Compared with the traditional Chinese medicine fingerprint method, the application of the biological activity detection method in the evaluation of the consistency of traditional Chinese medicine is still relatively limited, and the scope of use is not wide. At present, there are few commonly used bioassay methods, among which the method of evaluating the content of markers is widely used. ^[7]

4.2 Feasibility of biological activity detection method in the consistency evaluation of traditional Chinese medicine quality

From the perspective of the composition of substances and the effects of production methods on drugs, compared with chemical drugs, traditional Chinese medicine has a more complex composition of its own components, a wider active composition, and an unclear effective composition and toxicity mechanism of drugs. It is close to biological medicine. At present, some people have proposed a new method of quality control of traditional Chinese medicine based on biological activity detection methods. For example, Yan Dan and others, taking Huanglian as the object, from the perspective of original identification, routine inspection, chemical analysis and bioassay, concentrated common technologies, fully elaborated the development process of their working reference products, and formed a more suitable biometric method. ^[8]

4.3 Research progress of biological activity detection methods

Since the beginning of the 21st century, the development of biological activity detection methods has become faster and faster. Some of these methods have been included in the Chinese Pharmacopoeia and become statutory detection standards and judgment methods; while other methods have not yet been included in the Pharmacopoeia, but Now it is also maturing.

5. Acousto-optic tunable filter near-infrared spectroscopy technology

Near-infrared spectroscopy (NIRS) ^[9] reflects the group frequency or dual-frequency absorption of the tensile vibration of hydrogen-containing groups such as C-H, O-H, N-H, and S-H in most organic substances in the near-infrared spectrum, which has been widely applied in the medical field. At present, near-infrared spectroscopy analysis technology has been fully integrated into computer technology and metrology, which provides good prospects for development. It may play an important role in the process of evaluating the consistency of traditional Chinese medicine.

Now, acousto-optic tunable filter near-infrared spectroscopy technology is the latest near-infrared technology. The US FDA has used this technology as a standard detection method.

In the current stage of Chinese medicine production in China, the production of Chinese herbal decoction still lacks an effective online monitoring technology. The production process still relies on experience to determine the processing level of Chinese medicine, which is very unfavorable for the construction of Chinese medicine consistency evaluation system. Therefore, it is necessary to apply Acousto-Optic Tunable Filter-near infrared spectroscopy technology to the processing of decoction pieces to achieve strict quality control in the production process of decoction pieces. ^[10]

6. Conclusion

This article gives a more comprehensive introduction to the basic methods and ideas of the consistency evaluation of traditional Chinese medicine, and gives a detailed review of the three commonly used methods, especially the fingerprint of traditional Chinese medicine. Compared with the other two methods, the fingerprint method of traditional Chinese medicine has broader development prospects and is more suitable for the actual situation facing traditional Chinese medicine. The fingerprint method of traditional Chinese medicine can effectively promote the development of consistency

evaluation of traditional Chinese medicine and make traditional Chinese medicine play a greater role in clinical treatment.

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