

Application and Practice of Traditional Chinese Medicine Characteristic Technology Inheritance in Research and Development of Traditional Chinese Medicine Preparations in Medical Institutions

Xiu CHENG¹, Hai ZHAO², Shujie KOU¹, Mingqin CHEN², Liang YANG^{2*}

1. Changshun People's Hospital, Guizhou Province, Changshun 550700, China; 2. The Second Affiliated Hospital of Guizhou University of Traditional Chinese Medicine, Guiyang 550002, China

Abstract Medical institution preparations play an important role in the development of hospitals, being one of the main forms of traditional Chinese medicine clinical characteristic medication, as well as an important carrier for the inheritance and innovation of traditional Chinese medicine. In recent years, the research and development of traditional Chinese medicine preparations has become a hot spot in the research and development of preparations by medical institutions. Traditional Chinese medicine preparations prepared by traditional processes and their entrusted preparation matters have changed from the current licensing management to filing management. The registration model of traditional Chinese medicine preparations has undergone significant changes, emphasizing more on real data and evaluation results from the objective world, respecting traditional medication experience, and emphasizing the inheritance and innovative development of traditional technological experience. In the process of following teachers in the inheritance project of traditional Chinese medicine, we combined the inheritance of traditional Chinese medicine characteristic technology with the research and development practice of traditional Chinese medicine preparations in medical institutions, and focused on the analysis and discussion of technical problems such as prescription screening, dosage form selection, process route design and clinical observation of traditional Chinese medicine preparations, hoping to provide reference for scholars in the same field of traditional Chinese medicine.

Key words Inheritance of traditional Chinese medicine characteristic technology; Traditional Chinese medicine preparation; Medical institutions; Practical analysis

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Traditional Chinese medicine preparations in medical institutions occupy an important position in the development of hospitals, and are one of the main forms of clinical characteristic drugs of traditional Chinese medicine. They have many advantages such as curative effect and price, and are also an important carrier for the characteristic inheritance and innovative development of traditional Chinese medicine. Traditional Chinese medicine preparations in medical institutions are mostly summarized by veteran doctors of traditional Chinese medicine with rich clinical experience for many years, and represent the characteristics and advantages of a hospital, a department and a famous doctor, playing an active role in establishing famous hospitals, famous doctors and famous departments.

The inheritance projects of traditional Chinese medicine characteristic technology are an important measure for China to vigorously cultivate high-level talents of traditional Chinese

medicine, maintain and carry forward the characteristic advantages of traditional Chinese medicine, and promote the coordinated development of Chinese herbs and traditional Chinese medicine cause. In 2021, Guizhou Administration of Traditional Chinese Medicine first incorporated the inheritance of traditional Chinese medicine characteristic technology into the special inheritance plan of traditional Chinese medicine, and simultaneously brought teaching staff to lower-level medical institutions to carry out integrated linkage and resource sharing, so as to realize joint accelerated development. As students of The Third Batch of Traditional Chinese Medicine Famous Doctors Inheritance Project in Guizhou Province, we studied the identification, preparation and processing of traditional Chinese medicine with teachers. In the special practice of the inheritance and innovative development of medical institution preparations under the filing system, the technical problems such as prescription selection, dosage form selection, process research and clinical data collection were analyzed and discussed in preparation research, in order to attract more attention and promote the inheritance and innovative development of traditional Chinese medicine.

Prescription Evaluation

Medical institution preparations are fixed prescription preparations prepared by medical institutions for their own use according to the clinical needs of their own units^[1]. The definition contains several meanings. In specific, the subject objects are medical

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Xiu CHENG (1984–), female, P. R. China, associate chief pharmacist, devoted to traditional Chinese medicine and ethnic medicine resources and clinical research.

* Corresponding author. Liang YANG (1983–), male, associate chief pharmacist, devoted to evaluation of the effectiveness and safety of traditional Chinese medicine (ethnic medicine) and clinical research on medical institution preparations. E-mail: brightnet@qq.com.

institutions; the management departments are approved by provincial food and drug administrations; the clients are patients in hospitals who ask for drugs for their own use; the prescriptions are characterized by fixed prescriptions; and the prescriptions are not available in the market. Most hospitals are conducting research on patent medicines based on clinically safe and effective prescriptions. Following points should be paid attention to when screening prescriptions: ① Innovation: In the face of existing varieties in the fiercely competitive market, creativity and novelty must be considered in prescription screening of preparations in hospitals. If hospitals can apply for a patent, it is best to form patent protection to avoid repeated development of the same prescription. When publishing articles and applying for topics in preclinical research, we should pay attention to the confidentiality of prescriptions to avoid losing the opportunity of patent application. Moreover, we should note that "different dosage forms with the same prescription as those already available on the market" are not allowed to be filed. ② Resource protection: Original medicinal materials in prescriptions should be considered to be conducive to resource protection and sustainable development. For some hospital formulations contain "pangolin", which is a national first-class protected animal, and the inclusion of which in the 2020 edition of pharmacopoeia has been cancelled, experts who use this drug as a raw material to declare hospital preparations will have more considerations. ③ Simplification and reduction: At the beginning of clinical formulation, it can be targeted at multiple syndromes, and even treat different diseases simultaneously. If a hospital wants to position a type of formula for the treatment of a specific syndrome of a certain disease, it should be simplified and reduced according to the theory of traditional Chinese medicine to form a formula with perfect compatibility, limited herbs, and specific function, which can greatly reduce the difficulty of research and development and save funds. For example, some clinical formulas have 20 to 30 herbs and a wide range of treatments, and if they can be simplified to less than 20 herbs, the prescriptions will be specialized and targeted at the main syndrome, often achieving better therapeutic effects. ④ Fixed composition: According to the document of the General Administration, "prescriptions should have a usage history of more than 5 years in medical institutions"^[2], and some research materials can be exempted. According to the meaning of this sentence, experts in Guizhou Province require that the herbs, processed product categories and dosages of prescriptions should be as consistent as possible, especially within the 3 years prior to application. Therefore, after determining the composition, it is recommended to form agreed prescriptions, which should be recorded by hospitals' medical departments and bundled in computers to ensure consistency in the prescriptions issued by different physicians. ⑤ Prescription dosage: Whether the dosages are within the ranges of the statutory standard daily dosages is also one of the important criteria for experts to evaluate whether to waive some information. Meanwhile, for medicinal materials that have been proven to be toxic by statutory standards or modern toxicology, special

attention should be paid to the 18 opposites and 19 fears, otherwise the research difficulties, contents, time and funding will significantly increase. ⑥ Name specification: Herbs in prescriptions should be arranged in the order of monarch, minister, assistant, and guide, and used in correct names according to *Chinese Pharmacopoeia*. For varieties not included in *Chinese Pharmacopoeia*, the correct names in local standards should be used. Meanwhile, attention should be paid to names of processed products. Herbs that require special processing should be clearly indicated. For example, "hawthorn" should be written as "pure hawthorn" instead of "raw hawthorn"^[3], and "Radix Scutellariae" should be written as "Radix Scutellariae slices".

Traditional Process Technology

Thoughts on dosage forms

Clinical preparations are the foundation and basis for pharmaceutical research. Whether they come from ancient preparations, empirical preparations, or hospital agreed prescriptions, their origins are mostly decoction. In the research and development of preparations in medical institutions, the collection of historical data about the use of prescriptions for more than 5 years can be decoction, or preparations made by doctors after one-on-one prescription and special adjustment. It is suggested that during clinical observation, decoction should be gradually changed to dosage forms to be developed, so as to control the dosages and processes of prescriptions in the later research.

Thoughts on processes

The preparation of traditional Chinese medicine depends on the traditional Chinese medicine theory, and Chinese herbs as raw materials are processed according to certain specifications into medicines which can effectively prevent and treat diseases. Medical institutions in Guizhou Province implement registration management for traditional Chinese medicine preparations prepared using traditional processes, including two requirements: "traditional processes and traditional dosage forms"^[4]. "Traditional Chinese medicine preparations have the characteristics of complex ingredients, weak basic research, unclear effective ingredients, and multiple target effects"^[5], so based on clinical practical use, validation research is conducted on clinically effective and safe traditional preparation processes. Meanwhile, modern scientific research methods are applied to the optimization of traditional process conditions, and inheritance and innovation are the key points of process thinking. In addition, in the selection of "excipients", experts will evaluate whether excipients affect traditional processes and evaluate whether they comply with the application of traditional processes to prepare traditional Chinese medicine formulations under the filing system, which also needs to be noted.

Quality Standards and Stability

The study of drug quality standards is one of the important contents of the research on traditional Chinese medicine hospital preparations. Adopting modern methods and technologies such as

traditional Chinese medicine chemistry and analytical chemistry, inspection methods and standard formulation contents can be ultimately established. Such study more reflects the progress of modern pharmaceutical research, while the pre-treatment research of medicinal materials is often overlooked. The sources of traditional Chinese medicine are complex, and there are many varieties with multiple base resources. The same base resource can affect the stability of product quality due to differences in origin, harvesting season, processing, preparation of decoction pieces, and specification levels. Therefore, relevant research should be taken seriously. When conducting research on the pre-treatment of medicinal materials, as these factors have a significant impact on the quality of medicinal materials, the base resources and specification levels of medicinal materials (decoction pieces) should not be arbitrarily changed, but should be relatively fixed to ensure the safety, effectiveness, stability and uniformity of preparations.

Clinical data collection

Under attachment 1 of *Administrative Measures for the Registration of Preparations in Medical Institutions*, "Chinese medicinal preparations, that are prepared by traditional techniques according to theoretical formulation of Chinese medicine (that is, the material basis for treating diseases in original formulas is not changed during the preparation process), and have been used in specific medical institutions for more than 5 years (including 5 years), can be exempted from data items 13 – 17"^[4]. Under attachment 1 of *Detailed Rules for the Administration of Filing Traditional Chinese Medicine Preparations Prepared by Traditional Processes in Medical Institutions in Guizhou Province* (Trial), "If a prescription has been used in a specific medical institution for more than 5 years (including 5 years), its preparation can be exempted from data items (15) to (17)"^[6].

For the varieties that take the path of exempting clinical, pharmacodynamic and toxicological study in registration and the path of exempting pharmacodynamic and toxicological study in filing, it is necessary to provide the usage history of "prescriptions" that they have been used in medical institutions for more than 5 years according to the above management documents. Attention should be paid to the collection of this part of data: ① the essential requirement for a usage history of more than 5 years is also to comprehensively, systematically, and scientifically evaluate the effectiveness and safety of the medicines in the treatment of a specific disease or syndrome under the guidance of traditional Chinese medicine disease theory, combined with modern scientific technology and methods. Therefore, after forming a fixed prescription, a thorough design plan must be considered in advance, including topic positioning, treatment factors, subjects, effect indicators, observation methods, efficacy judgment, statistical analysis, and progress management. The specific contents should be implemented in accordance with the requirements of Good Clinical Practice (GCP). For example, *Administrative Measures for the Registration of Preparations in Medical Institutions* stipulate that the sample size

of experiments should meet statistical requirements. Under the use background item in *Guiding Principles for Research Technology of Traditional Chinese Medicine Preparations Prepared by Traditional Processes in Medical Institutions in Guizhou Province* (Trial) and *Guiding Principles for Preparation Research Technology in Medical Institutions in Guizhou Province* (Trial), "more than 100 relatively complete supporting materials should be provided"^[7]. Therefore, in the collection of clinical data cases, it is necessary to have a representative and a certain number of cases. When the same preparation has multiple indications, clinical studies should be conducted separately. The number of trial cases for each main indication should not be less than 60, and a separate control group should be established. ② A usage history of more than 5 years is within the prescribed period of continuous use in a specific medical institution. There should be no interval between intermediate years, and clinical cases should have a balanced continuity. Original materials such as doctors' prescriptions, inpatient medical orders, research project records, outpatient medical records and clinical dispensing records should be kept intact and well documented.

Conclusions

The characteristic technology of traditional Chinese medicine is a summary of the experience of the Chinese nation through thousands of years of production and life practice in understanding life, maintaining health and overcoming diseases. The characteristic technology of traditional Chinese medicine needs to be inherited, which is the foundation of the development of traditional Chinese medicine. Based on the problems existing in practical work, we should look for a breakthrough in inheritance, innovate and develop it closely with reality, and further study and explain its scientific mechanism with modern methods and means.

The Law of People's Republic of China (PRC) on Traditional Chinese Medicine promulgated on July 1, 2017 stipulates that: "Only varieties of traditional Chinese medicine preparations prepared by traditional techniques can be prepared after being filed with provincial food and drug supervision and administration departments, without the need for preparation approval number"^[8]. In recent years, the research and development of traditional Chinese medicine preparations has become a hot spot in the research and development of preparations by medical institutions. Traditional Chinese medicine preparations prepared by traditional processes and their entrusted preparation matters have changed from the current licensing management to filing management. The registration model of traditional Chinese medicine preparations has undergone significant changes, emphasizing more on real data and evaluation results from the objective world, respecting traditional medication experience, and emphasizing the inheritance and innovative development of traditional technological experience. Under the top-level design of the national policies and regulations on traditional Chinese medicine, Guizhou Province has promulgated

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resolving blood stasis. On this basis, Persicae Semen was added, with a pungent and moist taste. Spicy taste can promote the movement of pungent fragrance, promote qi circulation, eliminate blood stasis, and unblock collaterals; Schizonepetae Herba can nourish blood, replenish liver dryness, and not only unblock collaterals but also harm yin and blood. Drying Rehmannia Root, Codonopsis Radix, Angelicae Sinensis Radix cool blood and moisten dryness; Schizonepetae Herba and Saposhnikovia Radix have effects of wind dissipation; Paeoniae Radix Alba can dispel wind and relieve itching, to realize clinically effective treatment for androgenic alopecia with blood heat and wind dryness syndrome^[11].

In this study, the effect of supplementing Western medicine with Liangxue Xiaofeng Powder on AGA is obvious and suitable for promotion. However, due to the limitations of time, manpower, equipment and other reasons, its use method still stays in the traditional Chinese medicine formulation. Although its compatibility and prescription have been explained and the initial clinical efficacy has been compared, the specific effective ingredients and mechanism of its drug compatibility have not been deeply explored, which needs to be gradually improved in future studies.

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detailed rules for the implementation of traditional preparation filing management, guiding principles of research technology, *etc.* Hospitals should seize the opportunity to continuously develop and advance traditional Chinese medicine preparations in hospitals and lay a solid foundation for the development of new drugs.

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