



CLINICAL PHARMACY AND PHARMACY MANAGEMENT

Investigation on the clinical use and research hotspot of Lingnan native medicinal materials

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[Abstract] Lingnan native medicinal materials refer to the drugs which are widely used by the people of Lingnan, China and nearby regions, have definite medicinal effects, and are produced locally. Based on the data provided by Guangzhou Kangmei Smart Pharmacy, the authors of this study cross-analyzed the actual amount of use and the research hotspot of the drugs from the collected data and found and studied the drugs with high research value. The purpose of this study was to clarify the relationship between the research hotspot and the actual amount of use of the drugs, reveal the deviation between the using status of Lingnan native medicinal materials and the experience of famous Traditional Chinese Medicine (TCM) doctors, and to provide supporting data and explore possible directions for the development and utilization of Lingnan native medicinal materials.

[Key words] Lingnan native medicinal materials; Kangmei Smart Pharmacy; Clinical use; Research hotspot

1 Introduction

Lingnan native medicinal materials refer to the drugs which are widely used by the people of Lingnan, China and nearby regions, have definite medicinal effects, and are produced locally. In a broad sense, Lingnan native medicinal materials include the Lingnan genuine drugs, such as the "Four Major Southern Medicines," "Top Ten General Medicines," and Lingnan folk medicines. In a narrow sense, the Lingnan native medicinal materials only refer to the unknown folk medicines

except for Lingnan genuine drugs which are locally produced and used in Lingnan, have definite medicinal effects, and are widely used, such as *Ficus hirta*, *Thin Evodia Twig and Leaf*, *Ovateleaf Holly Bark*, *Herba Nervilia Plicatae*, *Chinese knotweed herb*, *Canton Love-pea Vine*, and *Spatulateleaved Sauropus*^{[1] 2-3}. The environmental changes and genetic changes over thousands of years have built these drugs into what they are today. All of the Lingnan native medicinal materials mentioned in this article are being referred to in a broad sense.

China has vigorously promoted the development of the Internet Plus Chinese medicine industry in recent years. Grasping at this opportunity, Kangmei Pharmacy has rapidly developed into China's first

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smart pharmacy of Chinese medicine. Based on the data provided by Guangzhou Kangmei Smart Pharmacy, a cross-analysis was conducted on the actual amount of use, research degree, effects, and other information of drugs obtained from collected data, the drugs with high research value were identified and analyzed, and the development direction of Lingnan native medicinal materials was explored.

2 Table of use of drugs

Through collection and analysis of the actual amount of clinical use of all medicinal materials in the Guangzhou Kangmei Smart Pharmacy in December 2017, April 2018, and August 2018, the application of Lingnan native medicinal materials supported by actual data was outlined, as shown in

Table 1.

The use of drugs was selected in 3 different months of a year, which not only eliminates the medication errors caused by the change in susceptibility of different diseases and syndromes throughout the 4 seasons, effectively reduce the number of samples, simplify the complexity and improve the efficiency, but also guarantees that the selected data represents the drug usage of the whole year. Due to limitations on space, only the use and research of some drugs were listed.

3 Brief description for the use of drugs

In this study, a total of 140 drugs were included in the category of Lingnan native medicinal materials. The data on drug varieties came from

Table 1 Use and research of some drugs

No.	Drug name	Percentage of this drug prescriptions in total*	Number of related articles in CNKI	Use rank	Research rank
01	Tangerine Peel	17.881 4	358	1	46
02	Tomentose Pummelo Peel	2.627 8	366	2	43
03	Microcos paniculata	2.450 9	183	3	61
04	Radix Serratulae Chinensis	2.106 0	10	4	125
05	Fructus Citri Sarcodactylis	1.140 5	1407	5	17
06	Glabrous Sarcandra	0.837 4	658	6	31
07	Roughhaired Holly Root	0.789 0	86	7	84
08	Caulis Tinosporae Sinensis	0.747 1	103	8	75
09	Ovateleaf Holly Bark	0.697 3	177	9	63
10	Snowbell-leaf Tickclover Herb	0.633 7	256	10	50
11	Semen Mangiferae Indicae	0.570 4	53	11	103
12	Chinese knotweed herb	0.559 6	100	12	77
13	Eaglewood	0.487 6	2279	13	11
14	Rose Myrtle	0.474 7	22	14	119
15	Black Nightshade	0.464 1	877	15	23
16	Herba Centellae	0.423 2	1107	16	19
17	Kadsura coccinea	0.404 9	77	17	88
18	Herba Selaginellae Doederleinii	0.391 2	132	18	67
19	Bombacis Cortex	0.384 2	442	19	38
20	Shiny-leaved Prickly Ash	0.343 6	474	20	35

*Data from Guangzhou Kangmei Smart Pharmacy within 3 months (The "percentage" in the following text is referred to as "frequency of use").

the "Identification and Application of Lingnan Native Medicinal Materials" ^[1] and the "Guangdong Zhongyaozhi" ^[2], including the genuine medicinal materials of Guangdong which are used nationwide. Although the Kangmei Smart Pharmacy provided the use of drugs by weight, it lacked the objectivity to measure the clinical use of drugs with their weight as a basic indicator. The main analysis indicator selected in this article was the percentage of prescriptions containing a specific drug in the total prescriptions, i.e. the frequency of use.

On the whole, the frequency of use of all Lingnan native medicinal materials was 0.61% after equal weighting, which was less than a quarter of conventional medicinal materials. Tangerine Peel was a drug with the highest frequency of use among Lingnan native medicinal materials, at 17.8%. However, the frequency of use of *Rhizoma Atractylodis* among conventional medicinal materials was 40.1%, and that of licorice root was 38.6%. Compared with conventional medicinal materials, Lingnan native medicinal materials had a quite low frequency of clinical use.

Among the 140 kinds of Lingnan native medicinal materials, 61 kinds had not been used at all in the 3 months, including the familiar drugs such as *Spatulateleaved Sauropus*, *Alocasia macrorrhiza* (Linn) Schott, and *Ficus hirta*. Most of the drugs with a large amount of use were genuine drugs of Lingnan, such as Tangerine Peel, Tomentose Pummelo Peel, *Fructus Citri Sarcodactylis*, and East Asian Tree Fern Rhizome, all of which were among the top 10 drugs with the highest amount of use. Meanwhile, it should be noted that some unknown drugs also received a good ranking for their amount of use, such as *Microcos Paniculata* in the third-ranking, and *Radix Serratulae Chinensis* in the fourth-ranking.

A comprehensive search was conducted from the CNKI database for articles related to each of the Lingnan native medicinal materials,

a manual screening was performed to select the articles highly related to the research of medicinal materials, and the "research rank" was made according to the number of related articles. The research hotspot of Lingnan native medicinal materials was obtained after recording and sorting the number of articles on each of the Lingnan native medicinal materials. Surprisingly, few of the top-ranked drugs within the research hotspot were widely known, and the top 3 drugs were *Pteris multifida*, *Dicliptera chinensis*, and Aromatic Ginger. There were more than 16,000 articles on the study of *Pteris multifida* in particular, in no way conceding *Artemisia carvifolia*, which was studied in more than 4,000 articles. In terms of clinical use and research hotspot, our research group agreed that the representative drugs were *Radix Serratulae Chinensis* (4th in use rank, 16th from last in research rank) which was more used but less studied and *Pteris multifida* (first in the research rank, 22nd from last in use rank) which was more studied but less used. In this article, we analyzed the reasons for the mismatch between the amount of use and the degree of research of these drugs, from the perspectives of famous doctors' experience and legal protection.

According to the frequency of use in those 3 months, some drugs recommended by famous Chinese medicine doctors were not widely used in clinical practice. For instance, *Ilex pubescens* recommended by Xian Shaoxiang for removing blood stasis, *Ficus hirta* recommended by Deng Tietao for restoring vital energy, and Root of Cherokee Rose recommended by Shao Jitang for treating spondylolisthesis had not been used at all within those 3 months. However, other drugs recommended by famous experts were used frequently in clinical practice, such as *Atalantia monophylla* recommended by Liu Youzhang for treating cough, and *Cochinchina Cudrania Root* recommended by Zhen Mengchu for treating

arthralgia.

It's worth noting that the 8 medicinal materials selected as the first batch of protected varieties in the "Regulations of the Protection of Medicinal Herbs in the South China" had a good ranking in clinical use, such as Tangerine Peel and Tomentose Pummelo Peel. Even Eaglewood, which is the least used in the 8 medicinal materials, ranked within the top 20. This not only shows that legal protection does have a certain incentive effect on the application of drugs but also shows that the government's selection meets the needs of the drug market.

4 Representative drugs

4.1 *Pteris multifida*

After comparing the data on clinical use and research hotspot, we selected *Pteris multifida* for analysis and discussion, which is used as an antipyretic in Lingnan, with more research hotspots but less clinical applications. We hope to obtain the practical application value and the possibility of clinical application and promotion of these drugs, based on their effects and applications, the experience of famous doctors, and a comparison of the research scope with other related projects.

Formerly known as *Pteris cretica*, *Pteris multifida* often grows on wells, and it was firstly recorded in "Bencao Shiyi"^[3]. *Halymenia Dentata*, Spider Brake, Well Brake, Well Grass, *Pteris nervosa*, and Huguenot Fern are alternative names for *Pteris multifida*. *Pteris multifida* was recorded in the "Records of Picking Herbs in Lingnan"^[1]⁶⁵⁻⁶⁶, which says, "*Pteris multifida* is bitter, slightly cold and poisonous, and specializes in relieving the pathogenic heat and various poisons in the abdomen, destroying parasites, and treating nosebleed and hemafecia, metrorrhagia, bloody flux, bubo swelling, and pain. It can treat stomachache by oral administration." *Pteris multifida* has the effects of clearing heat and

removing dampness, cooling blood for hemostasis, and removing toxicity for detumescence. It is mainly used for the treatment of damp-heat diarrhea, dysentery, damp-heat jaundice, heat strangury, blood strangury, sore throat, as well as the treatment of carbuncle and swelling toxin, and eczema by external application.

Pteris multifida was studied most in these aspects: quality standards, chemical components such as pterisin and flavonoid or extraction method, pharmacological actions such as antibacterial and anti-tumor effects^[4], and effects on other traditional Chinese medicines, such as the toxicity-reducing effect on triptolide^[5]. However, there was a small proportion of highly relevant articles on the study of *Pteris multifida*. The focus of the research was on the comparison of the two drugs, *Pteris multifida* and *Artemisia carvifolia*. We found that there were far fewer articles on artemisinin in the CNKI than those on *Pteris multifida*. However, there were few articles on the use and effect of the Chinese medicinal material in *Pteris multifida*. For instance, there were many foreign articles related to a specific component in the articles on *Pteris multifida*, which did not match our original intention of discussing and promoting the native and genuine medicinal materials of Lingnan.

In addition, *Pteris multifida* is mainly used to treat human dysentery, hepatitis, cholecystitis, mastitis, pelvic inflammatory disease, urinary tract infection, burns and scalds, tumors, thrush, and dermatitis in clinical practice. *Pteris multifida* is mainly used by veterinarians to treat dysentery in pigs, chickens, rabbits, cattle, edema of pigs, and chicken coccidiosis^[6] in clinical practice. *Pteris multifida* is one of the medicinal materials with a good heat-clearing effect in clinical practice for both human and animal, so it should have been widely used. However, the data showed that there were few clinical applications for *Pteris multifida*. The possible reasons for this are as follows. First,

there are many varieties of antipyretics with various effects. From the perspective of heat-clearing and dampness removing, there is a quite large range of suitable drugs available for clinical use with these properties. *Pteris multifida* has no outstanding advantages, compared with the common heat-clearing medicinal materials, such as Indigowoad Root, Roughhaired Holly Root, and *Herba Centellae*. Second, targeted Western medicine is a more common clinical choice for bacillary dysentery and hepatitis, the indications of *Pteris multifida*. Third, *Pteris multifida* is widely unknown. Although there are many studies on it, most clinicians do not know or have used it, nor do they know how to use it in combination with other drugs to achieve better efficacy.

In summary, the drugs with more research hotspots and less clinical applications, such as *Pteris multifida*, have high medicinal value among the antipyretic drugs produced in Lingnan. However, from the perspective of legal protection, such medicinal materials are poorly promoted, since the promotion is more likely to be made from famous doctors' experience and research hotspot.

As an example, Professor Deng Tietao often uses *Hemianthus micranthemoides* Nutt. in combination with *Pteris multifida* Poir to form the drug pair "Zhenfeng" for the treatment of heat strangury, which has a good effect on pure urinary tract infection, present in incipient heat strangury. Also, modification can be made according to symptoms, for instance, Zhenfeng can be used in combination with *Sijunzi* Decoction, *Taxillus chinensis*, and *Stemona japonica* to form Zhenfeng Decoction^[7] for the treatment of strangury that is difficult to recover from. Such experience with these drugs can be summarized and compiled, which can not only promote the use of a specific Lingnan native medicinal material but also help select drugs for clinical treatment.

Research hotspot is also one of the criteria for

judging the clinical value of medicinal materials. The components and pharmacological actions of medicinal materials with more research hotspots are studied more thoroughly, and their effects are definite, so they are easy for doctors to choose and use in clinical practice. In essence, drugs with more research hotspots are studied by more people, the scope of the studies is wider, and they may have more diversified applications, which help develop new Chinese patent medicines.

4.2 *Radix Serratulae Chinensis*

After comparing the data on clinical use and research hotspot, we selected *Radix Serratulae Chinensis* for analysis and discussion, which is a Lingnan native medicinal material with more research hotspots but less clinical applications.

Radix Serratulae Chinensis, also known as Chinese Sawwort Root^[8], is the dried root of feverfew *Serratula chinensis* S. Moore. It has a different origin but similar effects with the common Chinese medicine *Cimicifuga foetida*. It is the conventional variety that is used as medicines of *Cimicifuga foetida* in Guangdong Province. *Radix Serratulae Chinensis* is acrid, slightly sweet, and slightly cold. It acts on the lung, spleen, and stomach via the large intestine, and it has the effects of dispelling wind to promote eruption, clearing heat and detoxication, and ascending spleen-Qi and Yang. It is used to treat a variety of illnesses including anemopyretic cold, fever, headache, measles without adequate eruption, stomach fire toothache, cough and gasp with lung heat, sore throat, chronic diarrhea, rectal prolapse, and uterine prolapse. Compared with genuine *Cimicifuga foetida*, *Radix Serratulae Chinensis* has no antipyretic effect or better effects of promoting eruption and ascending spleen-Qi and Yang. Its main function is to clear away heat and detoxify, so it is primarily used to treat stomach fire toothache, sore throat, cough and gasp with lung heat, and

Yang-toxin macule.

According to famous doctors' experience, *Radix Serratulae Chinensis* has a good analgesic effect and is used to treat lupus erythematosus and syphilis. According to the experience of Professor Zhao Sijing, a famous doctor from Guangdong Province, *Radix Serratulae Chinensis* is mainly used and can be modified in Macule-Dispersing Indigo Beverage (*Indigo Naturalis*, *Guangjiao*, *Gypsum Fibrosum*, *American Ginseng*, *Tree Peony Bark*, *Radix Paeoniae Rubra*, *Radix Serratulae Chinensis*, *Radix Scrophulariae*, and *Glycyrrhiza uralensis*) for the treatment of systemic lupus erythematosus in patients with nutrient-qi injured by pathogenic heat, with deep red tongue, with little or no coated tongue^[9]. In addition, the "Overview of Lingnan Chinese Herbal Medicine" also mentioned that *Radix Serratulae Chinensis* should be mainly used in the treatment of lupus erythematosus^[10]. Such experience shows that *Radix Serratulae Chinensis* has its advantages in clinical application and similar Lingnan native medicinal materials develop their advantages in clinical use through summary and promotion of experience.

Radix Serratulae Chinensis has been exported over the years. Although it's largely used in clinical practice, there is little research about the drug. The existing researches focus on its quality standards, chemical components, and effective components, especially ecdysterone.

The authors believe that there is still substantial room for the study of *Radix Serratulae Chinensis*. Studies^[11-14] have shown that both *Cimicifuga foetida* and *Radix Serratulae Chinensis* contain high mass fractions of palmitic acid and linoleic acid, and have significant differences in other components. *Cimicifuga foetida* contains 4-vinylguaiaicol, paeonol, and indole alkaloids which have anti-inflammatory activity, while *Radix Serratulae Chinensis* does not contain such components. Ecdysterone, volatile oil, ceramide,

and cerebroside are the main chemical components of *Radix Serratulae Chinensis*^[15-16]. Ecdysterone is a natural steroid with insect molting activity. It can promote the synthesis of nucleic acid and protein, regulate sugar metabolism, lipid metabolism, and gene expression, as well as improve immune function. It can also have an antioxidant effect, and promote the proliferation of multiple cells, the formation of blood vessels in the ischemic area, and the development of collateral circulation^[17-18]. *Radix Serratulae Chinensis* has the effects of lowering cholesterol and treating cerebrovascular diseases and is particularly effective in treating brain hypoxia and brain ischemia. Modern pharmacological studies have shown that such effects are associated with the component ecdysterone. In summary, the similar and different effects of *Radix Serratulae Chinensis* and *Cimicifuga foetida* need to be studied further, and most of the studies on ecdysterone are not based on *Radix Serratulae Chinensis*. Compared with other Chinese medicines containing ecdysterone, the different effects, shortcomings, and advantages of *Radix Serratulae Chinensis* remain to be studied.

In conclusion, there is much room for studies on the native medicinal materials with fewer research hotspots but more clinical applications, such as *Radix Serratulae Chinensis*. The authors' aimed to explore the medicinal value of such drugs based on their advantages in clinical use through research, promote such research and clinical use, and make full use of such drugs.

5 Recommendations for promotion of Lingnan native medicinal materials

After interviews with multiple clinicians, we found that clinical TCM doctors do not have a comprehensive understanding of Lingnan native medicinal materials but different doctors have mastered the clinical use of different native medicinal materials. After long-term use, doctors have mastered the medicinal properties of

these drugs, and modification of these drugs in prescriptions can often achieve good results. For instance, Herb of Ghostplant Wormwood is often used by Director Hua Rong of Traditional Chinese Medicine Hospital of Guangdong Province. Why not use native medicinal materials in large quantities? The reason is very simple. Compared with the common medicinal materials, there is little information about Lingnan native medicinal materials, and their effects remain to be proven, which inhibits forming prescriptions with them.

Compared with traditional medicinal materials, little experience has been inherited in the application of native medicinal materials, which is indeed a vital deficiency directly creating problems such as low popularity and small application scope, which in turn leads to fewer research hotspots, causing a Matthew Effect. In order to protect these medicinal materials, we should examine existing articles to learn from the valuable experience of our predecessors. Moreover, we should carry out modern pharmacological studies to select drugs that have real curative effects. We also recommend that the country expands the scope of the legislation to protect drugs. The influence from the national level should not be underestimated. Lastly, the task of informing clinicians about native drugs that have curative effects cannot be overlooked.

6 Conclusion

Native medicinal materials are the essence of Traditional Chinese Medicine, an important carrier for the inheritance of excellent Chinese culture, and a vital resource for innovation. The inheritance and innovation of native medicinal materials is a scientific issue for us to explore. Due to the specific climate and geographical environment, a natural medicinal plant germplasm bank with diverse germplasm and an excellent ecological environment has formed in the Lingnan region, where medicinal materials are produced to treat multiple specific

diseases in South China. This bank has unique and distinctive regional characteristics and advantages in China. More varieties of native medicinal materials are produced in Lingnan than in other regions, so Lingnan native medicinal materials are worth researching.

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