Status and Trends of GAP Base Construction of Chinese Materia Medica in Guangdong Province

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Abstract: It is one of the key points for modernization and internationalization of traditional Chinese medicines to construct the Good Agricultural Practice (GAP) base of Chinese materia medica (CMM). GAP helps to minimize contamination and improve the quality of CMM during the plantation and the production of Chinese crude drugs. In this article, the status and development of CMM production bases of GAP in Guangdong Province, China, are presented. The suggestions upon the problems during the development of GAP for Chinese crude drugs are also provided.

Key words: Chinese materia medica; Good Agricultural Practice base; Guangdong; modernization and internationalization; traditional Chinese medicines

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Introduction

The work of the Good Agricultural Practice (GAP) for the production of Chinese crude drugs had made a great progress through planning and drafting, examination, promulgation, and enforcement since 1999. Guangdong, one of the economically advanced provinces in South China, has made considerable achievements in the development of GAP for Chinese crude drugs. Guangdong is an area warm and rainy, all the year round with the average temperature of 19 — 26 °C and the average annual rainfall of more than 1500 mm. As a result, this area is quite rich in medicinal plant resources with the 20% of Chinese materia medica (CMM) production in China, especially including tropical plants or southern Chinese herbal medicines (CHM) such as Amomum villosum Lour., Morinda officinalis How, Pogostemon cablin (Blanco) Benth., Ficus hirta Vahl, Isodon lophanthoides Hara, Polygonum multiflorum Thunb., Aquilaria sinensis (Lour.) Gilg, Nervilia fordii (Hance) Schltr., and Dendrobium nobile Lindl. etc. Nowadays, the production bases of GAP for those herbs, nearly 20 000 hm² in total area, have been established in Guangdong Province based upon the Guidelines for GAP of Medicinal Plants and Animals. The government of Guangdong Province has been actively exploring the cooperative type of “enterprises, scientific institutes, bases, and farmers” for the development of production bases of GAP to make full use of southern CHM. The implement of GAP helps to ensure the quality of CMM and improve the safety and efficacy of finished herbal products and maintain a sustainable development of CMM. This paper summarized the progresses of CMM production bases of GAP in Guangdong Province since 1999.

Process of establishment of GAP bases in Guangdong

According to a WHO’s estimate, most of the world’s population relies chiefly on traditional medicines, a major part of which involves the use of plant extracts or their active ingredients (Akerele, 1992). With the popularization of herbal medicine and the rapid growth in population, traditional medicines, particularly herbal medicines, have been increasingly used worldwide during the last few decades as evidenced by rapidly growing global and national market herbal drugs. The expanding herbal product
market could drive over-harvesting of plants and threaten biodiversity. Poorly managed collection and cultivation practices could lead to the extinction of endangered plant species and the destruction of natural resources. These problems are directly linked to the poor quality of herbal medicines, including raw medicinal plant materials. In order to meet the increasing needs and improve the quality for herbal medicines, efforts in every country to preserve both plant production and knowledge on how to scientifically use them for medicinal purposes are needed to sustain traditional medicine. Ministry of Health in Japan worked out the *Cultivation of Medicinal Plants and Quality Control* in 1992, which provides a detailed description of the techniques and measurements required for the appropriate cultivation. European Herb Growers Association (Europam) drafted *The Guidelines for Good Agricultural Practices of Medicinal and Aromatic Plants* (Europam, 1998; 2006). WHO has made a series of technical guidelines relating to the quality control of herbal medicines, such as *WHO Guidelines in Good Agricultural and Collection Practices (GACP)* for medicinal plants in 2003, in which some principles about cultivation and collection were set out. China State Food Drug Administration (SFDA) began to draft the GAP in 1999, and then issued the *Guidelines for Good Agricultural Practice (GAP) of Medicinal Plants and Animals* in 2002. Related cultivation base began to be authorized with GAP quality system certification in November, 2003. Since then, CMM has been produced and administered in standardization and scientification under the guidance of GAP. The government of Guangdong Province effectively supports and develops the production and cultivation of “Lingnan” herbal medicines which were documented in the outline of Guangdong’s the 11th Five-year Plan in CMM. Meanwhile, the government encourages scientific and technological innovation and promotes the cooperation model of Industry-University-Research Institute. Thus GAP bases construction are increasingly industrialized and popularized in Guangdong. Over the decade, Guangzhou University of Chinese Medicine (GUCM) and related pharmaceutical enterprises have contracted many GAP bases of CMM under the supports of the 10th Five Years Key Programs for Science and Technology Development of China, Guangdong Provincial and Municipal Major Projects of Science and Technology.

**Status of Guangdong GAP bases**

Herbal medicines have been used in China for thousands of years and are increasingly been used worldwide during the last two decades. According to WHO estimates, the present demand for medicinal plants is about 14 billion US dollars a year and it would be about five trillion US dollars by the year 2050. However, the people experiencing negative effects of herbal medicines have been increasingly reported probably due to their poor quality. This is a reflection that insufficient attentions had been paid to the quality assurance and control of these products, which is directly or indirectly related to the production and plantation of herbal medicines. Most of CMM have long been collected from wild resources in China. As the ecological environment is deteriorating and over-exploited, many wild resources have been reduced and even in extinction which are unable to meet the growing demand of industry, such as wild *Notoginseng Radix*, *Gastrodiae Rhizoma*, *Glycyrrhizae Radix*, and several ‘Lingnan’ medicines in south China, such as *P. cablin*, *M. officinalis*, *A. villosum*, and so on. In addition, improper farming contributes to the germplasm mixture and fertilizer-contaminated CMM, which affected CMM quality together with harvesting at unappropriate time. Therefore, it is urgent to fulfill the guidelines of the CAP to ensure good quality of raw herbal medicines.

**Construction of GAP bases for plantation of CMM**

Twenty-eight national GAP bases have been set up in Guangdong Province, most of which are located in the districts of Yangchun, Deqing, Pingyuan, Heyuan, Xuwen, Zhanjiang, and Xinhui mainly planted with *A. villosum*, *M. officinalis*, *Citrus medica* L. var. *sarcodactylis* (Noot.) Swingle, *P. cablin*, *Andrographis paniculata* (Burn. f.) Nees, *I. lophanthoides*, *E. hirta*, *Alpinia officinarum* Hance, *Lonicera confusa* DC., *C. grandis* “Tomentosa”, *A. sinensis*, *C. reticulata*, *Pheretima aspergillum* (E. Perrier), and so on (Fig. 1). In order to cooperate with the national GAP bases construction, Guangzhou University of Chinese Medicine and many pharmaceutical enterprises supported by Department of Science and Technology of Guangdong
Province have established 12 GAP bases at the provincial level in the area of Pingyuan, Longmen, Deqing, Zhuhai, and so on, including CMM with “Lingnan” characters, such as *Mesona chinensis* Benth., *Spatholobus suberectus* Dunn, *Desmodium styracifolium* (Osb.) Merr., *N. fordii* (Hance) Schlecht, *Ilex asprella* (Hook. f. et Am.) Champ. ex Benth., *Gardenia jasminoides* Ellis, *Baphicacanthus cusia* (Nees) Bremek., *I. pubescens* Hook. et Am., *D. officinale* Kimura et Migo, *Aloe barbadensis* Miller, *Cinnamomum cassia* Presl, and *Ganoderma lucidum* (Leyss. ex Fr.) Karst. Guangzhou Municipal Bureau of Science & Technology also funded the programs about the cultivation of herbal medicines with characteristics of south China, such as *Sarcandra glabra* (Thunb.) Nakai, *Eriobotrya japonica* (Thunb.) Lindl., and *Abrus cantoniensis* Hance. Now the total of the bases is nearly 15,000 hm² in Guangdong Province (Table 1).

“Cool Tea” is a favorite tea composed of CMM for modern people in recent years. Global and national markets for “Cool Tea” have been rapidly growing and need a lot of crude materials such as “Liangfencao” or “Xiancao” (*M. chinensis*), which is the key material of “Cool Tea”. In order to meet the present needs, we specially established the GAP bases of herbal plants for “Cool Tea” in collaboration with the company of Guangdong Naitai Pharmaceutical Co., Ltd. (Fig. 2). Now there are nearly 4000 hm² of *M. chinensis* in Pingyuan county, all of which may account for 60% of its raw materials. So the county is awarded “the Xiancao County in China” in 2009 by Chinese National Food Industry Association. On the basis of building GAP bases, we draw up the Standard Operation Procedure (SOP) which is a technical guideline on the production of CMM as starting materials for crude drugs, and finished products. The SOP manual is used to train farmers, producers, handlers, and processors to follow good agricultural and collection practices for medicinal plants in order to obtain high quality of herbal medicines. At the same time, the GAP areas are popularized and enlarged in order to realize the standardization, scale, and industrialization. While constructing the cultivation of CMM, some scientific studies about many quality-affecting factors have also been made which include intrinsic (genetic) or extrinsic (environment) such as germplasm, harvesting, processing, fertilizers, pesticides, and storage (Xu, Liang, and Ding, 2005). DNA fingerprinting and chemoprofiling techniques have been employed in various aspects such as selection of the correct germplasm (Pan et al., 2006), the best harvesting time, quality assessment (Liu et al., 2005; Ding et al., 2009; Lin, Den, and Zhu, 2011), and the control of the contents of heavy metals and pesticides (Jia, Jiang, and Zeng, 2009). Now the 28 GAP bases of CMM in Guangdong Province have been established, and the related quality standard was designated according to the Guidelines for Good Agricultural Practice of Medicinal Plants and Animals. In addition, several planting modes have been developed, e.g., “company + base”, “company + farmers”, “cooperative society of CMM production”, and so on. The role of local leading enterprises and professional association should be fully utilized so as to accelerate the process of CMM planting. Further great efforts have been made to develop the above models and promote the cooperation between farmers and companies.
<table>
<thead>
<tr>
<th>No.</th>
<th>Fund Support</th>
<th>Latin name</th>
<th>Place of GAP bases</th>
<th>Area of testing field / m²</th>
<th>Radioactive area / hm²</th>
<th>Cultivative area / hm²</th>
<th>Acceptance and authentication</th>
<th>Cooperated company</th>
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<td>10</td>
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Breeding and establishment of propagation bases

The seeds of genotype or ecotype are adopted for cultivation of CMM. Among various genes, some genes govern excellent hereditary characters such as high production, disease and stress resistance, and some govern the metabolic pathways and rate of active ingredients. Usually, active constituents vary in different ecotypes or genotypes of the same plant species. These differences may be related to physical appearance or efficacy. Besides cultivars identification, we should screen out useful genotype or ecotype by means of modern technology so as to acquire better quality and higher yield with the same consumption as those if not, which is the most important part of implementation GAP for CMM. Now the main methods of systematic, hybrid, mutation, and molecular breeding have been used in the implement of GAP. Guangzhou University of Chinese Medicine and other institutes have made great progress in this area with the sponsorship of national and provincial Natural Science Foundation. At present, by tissue culture, we have obtained disease-resistant plants of *M. officinalis* (Figs. 3 and 4), the plantlets of new variety of *P. cablin* (Fig. 5), test-tube plantlets of *N. fordii* (Du et al., 2005), plantlets of new variety of *P. cablin*, and other seedlings of *F. hirta*, *I. lophanthoides*, *P. multiflorum*, *A. sinensis*, *D. nobile*, etc, which are all the material basis of fine varieties breeding (Lin et al., 2007; Zhang, He, and Xu, 2009) (Fig. 6). We have also carried out studies on induced mutation breeding of *A. villosum* by radiation and molecular breeding of *P. cablin*. Moreover, we have established test-tube propagation base of 15 hm² in cooperation with Guangdong Nantai Pharmaceutical Co., Ltd. (Fig. 7).

Promotion of key technologies in GAP cultivation

The Guangdong government pays high attention to industrialization of CMM, and supports the projects approved by the National Ministry of Science and Technology. The government also has positively established the GAP cultivation bases of another ten kinds of herbal medicines...
of “Lingnan” characteristics such as *A. cantoniensis*, *D. styracifolium*, *Cinnamomum cassia* Presl, *I. asprella*, etc, which greatly promote the development of the key knowledge of GAP base and the industrialization of herbal medicines. The past decade has witnessed a tremendous change in GAP (Fig. 8) cultivation by the combination of production, studying and research, the one-stop agricultural industrializing chain of integrating research and development, plantation, manufacture, processing, and marketing has came into being and leads the agriculture of CMM to incline to the intensity, scientization, and modernization. Furthermore, these works became the hot points for mountainous farmers to make money. Now, about 200,000 farmers have involved in CMM cultivation in Guangdong Province. The average income per farmer amounts to 1000—2000 yuan per month. The enterprises also sign plantation and trade contracts with farmers by means of made-to-order farming according to the requests of GAP, which greatly stimulates the production enthusiasm of local farmers. For example, Hutchison Whampoa Guangzhou Baiyunshan Chinese Medicine Co., Ltd. has established the GAP bases of *A. paniculata* and *I. lophanthoides* by contracting with local farmers in Qingyuan and Yingde cities. Now their plantation areas have reached 600 and 100 hm², respectively. The base of *A. paniculata* has passed the quality system certifications of state GAP in 2004. The base of *Citrus grandis* “Tomentosa” was established by the cooperation of Guangzhou University of Chinese Medicine and Guangdong Green Life
Pharmaceutical Co., Ltd. Now the area is up to 800 hm², which is intercropped with other 15 varieties, such as Satalum album L., A. sinensis, Caesalpinia sappan L., and so on. It was accredited by the state GAP experts group in 2010. Guangzhou University of Chinese Medicine and Infinitus (China) Co., Ltd. have co-established the base of M. officinalis How in Deqing country in 2010. Technically, we are actively seeking the integration of production, teaching, and research, and a number of key projects were taken for joint tackling. Now we have solved the problems of low survival rate of tissue culture plantlets of D. officinale and we are improving the technology of “Plastic Film Greenhouse for shading, Flower bed made up of high density” by which the output of D. nobile could be largely increased (Fig. 9). We have improved the trees of A. sinensis in the production of incense materials by making a hole in the stems. At present, more than 800 hm² of A. sinensis trees have began to yield aroma in Dianbai country. All together, great efforts had been made to prepare the quality standards of many CMM (Fig. 10), which laid the groundwork for the quality control of GAP base. Dissemination and application of above key techniques could help large numbers of farmers in poor areas to cultivate the CMM in accordance with SOP. This work not only provided the “true, high-quality, and controlled” raw materials for manufacture enterprises of Chinese patent medicine (CPM), but also played a positive role in improving the ecological environment and speeding up poverty alleviation in poor areas.

**Publication of Study on the Geo-authentic Crude Drug of South China and related achievements**

The monograph, “Study on the Geo-authentic Crude Drug of South China” and the SOP manual for related CHM (Fig. 11) were compiled by joint efforts of team members, which provided the references for the GAP cultivation and study on the geo-authentic crude drug in south China (Chen and Xu, 2007). At the same time, some related research projects achieved the second prize in Scientific and Technological Progress of China Association for CMM in 2008, and the second prize in Guangdong Scientific and Technological Progress in 2007. These studies about GAP have provided a fundamental guarantee for producers to obtain sufficient, good quality of medicinal plant

![Fig. 9  Agricultural integrated cultivation (stereo frame) of D. nobile](image)

![Fig. 10  Fingerprints of some herbal medicines in GAP bases](image)

![Fig. 11  SOP manual for 13 kinds of CHM](image)
materials, and played an important role to assistant farmers richer and structural readjustments in agriculture.

Technical training of SOP of CMM
The training of personnel should be conducted regularly in the light of the regulations of GAP guidelines. The responsibilities of all those involved in GAP cultivation should be clearly set out in a written document. The actual producer of medicinal plant materials should understand the general principles and bear in mind the issues associated with the cultivation of medicinal plants as well as post-harvest processing of medicinal plants. The researchers from Guangzhou University of Chinese Medicine regularly give farmers training courses at the bases and strengthen the key knowledge of GAP cultivation. These courses include botanical identification, cultivation characteristics, and environmental requirements (germplasm, soil type, light, fertilizer, pesticide, and requirement), as well as the means of harvesting, processing, storage, and so on.

Implementary models of GAP
The workgroups for coordinating GAP base construction and panel of experts have been established under the direction of the Guangdong Provincial Department for Science and Technology. Through field survey and regular meetings, experts panel of GAP gave suggestions and help farmer and enterprise to solve problems. In order to implement GAP of CMM, we must adhere to the principles of “science and technology as the forerunner, quality as the center, industrialization as the objective”. During the course of GAP bases construction, creative enterprises system as mainstay, market as guidance, and agricultural planting as base have been explored. At the same time, diversified planting models were also set up according to the combination of production, teaching and research.

Model of Chinese patent drug industry + scientific research + bases + farmers
The GAP production base and its seedling base of A. paniculata, a main raw material of Xiaoyan Lidan Tablets, were jointly set up by Guangzhou University of Chinese Medicine with Whampoa Guangzhou Baiyunshan Chinese Medicine Co., Ltd. in Qingyuan. At the same time, we have established the GAP base of P. cablin, the main material of antiviral oral liquid, cooperated with Guangzhou Xiangxue Pharmaceutical Co., Ltd. Energetic efforts were made to extend “enterprises plus households”, “production on orders” and other methods of industrialized agricultural production of CMM strongly supported by Guangdong government. In this way, the farmers’ enthusiasm was greatly enhanced. A great quantity of good materials were produced which could meet the needs of enterprises at home and abroad.

Way of the government guidance, company undertaking, scientific research supervision, and farmer participation
With the support of provincial and local governments, Guangzhou University of Chinese Medicine and Guangdong Pingyuan Nantai Pharmaceutical Co., Ltd. co-established the GAP plantation bases of south China in Pingyuan county, Meizhou city. The workgroups of Guangzhou University of Chinese Medicine guided local farmers to engage in CMM plantation in a planned way. Now, the GAP demonstration base of CMM planting, raw material production base for “Cool Tea” of Guangdong Province, and seedling propagation base had been established. CMM germplasm resources nursery has been also built in order to preserve the wild resources of south China with the collection of near 100 species. Over 30 kinds of south China CMM have been cultivated in this base with plantation areas of 10 000 hm². The only one species of M. chinensis, which acreage was up to 800 hm², and brought extra income nearly 30 million yuan for local farmers in 2008. At present, they have also signed a contract with Guangdong Jiaduobao Drink & Food Co., Ltd. for the supply of 3.5 × 10⁶ kg raw materials of M. chinensis. On the basis of GAP base construction, we jointly exploited a series of high value-added products by means of raw CMM cultivated in bases, in order to stimulate the enthusiasm of company for cultivation, such as, preparing slice and spore powder of G. lucidum, the powder for foot sauna, the granules for clearing and nourishing throat, etc.

Trends and existing problems of Guangdong GAP base
Nowadays, GAP cultivation of CMM has been carried out vigorously in Guangdong Province. It is not only benefit to the development of CMM by providing the sustainable and good-quality resources of CMM for
the manufacturing enterprise of proprietary CMM, but also plays an important role in adjustment of agricultural structure and the reform of medical system. Therefore, it is important and necessary to greatly develop and support the GAP cultivation of CMM in the future.

Promoting the adjustment of agricultural structure

With the development of rural market economy, Guangdong Provinical government has been adjusting the structure of agricultural production continuously. The plantation structure has been transformed into diversification. The implement of GAP cultivation of CMM has accelerated the step of local agricultural adjustment. During the process of GAP implementation, we have adopted “government guidance, enterprise leader, sci-tech supporting, farmers participation” model according to market demands, encouraged local farmers to engage in the plantation of CMM in a rational and sequential manner. Of course, this method is flexible and more practical, which could be adjusted by the need of market and enterprise. In these years, the fast developing of GAP cultivation of CMM is not only benefit to the adjustment of agricultural structure, but also to farmers’ income and the enthusiasm of growers. Now, many GAP bases adopted these models in Guangdong Province which have made better economic benefit.

Promoting the reform of healthcare in countryside

Healthcare reform is an arduous and complicated task in China. Rural health service is the key point of Chinese medical systems. CMM characterized by simplicity, convenience, efficacy, and lowcost plays an indispensable role in rural medical systems and is very popular with rural residents of Guangdong Province. Therefore, the popularization of the GAP plantation of CMM and impartation of the Chinese medicine knowledge to local farmers will improve the level of using herbal medicine and healthcare. This will in turn arouse their enthusiasm for production and bring about hope for the GAP plantation of CMM.

Supplying the raw materials for the manufacturing enterprise of CPM

It is inevitable and necessary to build the GAP base of CMM for the manufacturing enterprise of CPM. With the rapid growth of the modernization of CMM and large-scale development of the pharmaceutical enterprise of CMM, it is unprecedented to pay more and more attention to the supply of raw materials. Actually it is like this, the confusions of CMM supply is formed a dramatic contrast with the step of modernization, while the quality of CMM could not be guaranteed and some resources of CMM have been exhausted or endangered. This problem has become the bottleneck of the pharmaceutical enterprises of CMM. Therefore, it is very important to develop GAP bases of CMM which would greatly relieve the shortage of material resources in essence. This method could guarantee the quality of CMM from fountainhead so as to realize pollution-free, non-pesticide residue, and satisfying the limit standards for heavy metals. The GAP construction will bring good reputation. There is no doubt that the quality assurance for raw materials will lay foundation for creating the famous trademark of proprietary CMM in the world.

Benefits for CMM resources and ecological environment

The cultivation of CMM could be going back to hundred years ago, such as Ginseng, Notoginseng, and so on. The mode of large-scale plantation could protect the wild resources as well as efficiently protect the local ecological environment. The development of GAP base in south China will make great contributions to CMM resources sustainable development and environmental protection in Guangdong Province.

Existing problem in GAP operation

The GAP of CMM is comprehensive and related to authentification of Chinese medicine, agricultural science, plant protection, plant ecology, medicinal plant cultivation, and so on. The implementation problems are to be expected, such as plant physiology, genetics, thremmatology, and insectology. However, many college or university of Chinese Medicine is deficient in those knowledge which is necessary in the GAP production. The breeding fine varieties and insect pest prevention still need to be improved by means of modern agriculture and biotechnology. Therefore, we should cooperate with agriculture universities or institutes. For the reason given above, intellectual property rights owned by ourselves are still lack, the additional value and availability of CMM resources are low, and there are less appropriate strategy in grand
brand cultivation. Moreover, we should develop broad cooperative relationships with the agriculture and forestry department and draw on their experience so as to promote production efficiency of GAP plantation, also construct information network service platform for CMM fast circulation.

The work of GAP cultivation is a long-term and arduous work, and we still need to make a joint effort to build a sustainable system of GAP management for CMM.

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