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Review

International Trends of Good Agricultural Practice(GAP)

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ABSTRACT

Consumers have been requiring more higher level of food and agricultural products safety. The system of Good Agricultural Practice(GAP) has been spreaded over the world. Korea also introduced the GAP system in agricultural industry. GAP is related to the production side in the whole traceability system. The establishment of GAP system is a prerequisite to secure food safety.

This study reviewed the concept of GAP and necessities and backgrounds of introducing the GAP system. Also, this study analyzed the problems which have been appeared in the GAP program and proposed the policy strategies and directions for the Korean GAP system.

So issues for the GAP system are as follows; computerizing of traceability system, forming the cooperative works among the related governmental departments, establishing a certification system to relate with crop features, efficient management, ensuring distribution channel and the research for estimating GAP consumer surplus is need to analyze GAP program more efficient. In addition, It is necessary to keep the records of the data to analyze the GAP program more accurately.

Key words : Good Agricultural Practice(GAP); Traceability System; Distribution Channel.

Introduction

Medicinal herbs used in Oriental Pharmacy are traditionally gathered from wild resources with the exception of edible, vegetable categories. With the rising demand from users over the ages, more and more popularly used items are grown in agricultural fields. Most of medicinal herbs, of course, are originally obtained from wild sources. Those that are in popular use have already followed the natural course of turning to agricultural production.

The natural force of supply and demand has initiated the agricultural production of commonly

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Table. 1. A summary of the recommendations in China

Chapters	Items	Main Contents
Chap 1	General principles	Purpose and significance.
Chap 2	The environment of the cultivation area	The detail request for the ecological environment such as air, water, and soil conditions in the cultivation area.
Chap 3	The germplasm and breeding material	The plant or animal species should be identified correctly and the quality of the germaplasm resource should be controlled.
Chap 4	The management of cultivation	The cultivation process, such as how to use fertiliser, soil, water and how to control the insect pest and plant diseases, should be controlled by standard operation procedure (SOP) principles.
Chap 5	The harvest and process at the harvest place	The optimal harvest time should be studied and fixed. The specific request for process, drying conditions, etc. is clearly written in this chapter.
Chap 6	Package, transport and storage	It should be clearly recorded for each batch of the drug materials. The request for the transport, such as using clean container, for the storage, such as light, temperature, and humidity, is clearly provided in this chapter.
Chap 7	Quality control	The specific request for quality control, such as the items to bo checked, the request for the characteristic, foreign matter, water, and ash content, is clearly provided in this chapter.
Chap 8	The equipment and operator	This chapter provides the request for the trained operators, the request about the product and process place, and equipment.
Chap 9	The document management	It should be recorded in every detail and particular for the whole process of cultivation, process, transport and storage, etc. The document should be kept properly at least five years.
Chap 10	Supplement	Supplementary explanation.

used medicinal herbs, particularly for the precious, expensive items. The over-harvest of wild medicinal plants is frequently observed and thus threatens the extinction of the species and might lead to the eventual loss of biodiversity of the wild resources. The only way to prevent this process of ecological disaster is to introduce agricultural growth of these wild species (Wang and Xiao, 2000). The botanical and medicinal plant experts are aware of the urgent need for the promotion of agricultural

production of herbal plants and the first national meeting on this issue was held in 1998(Wang and Lin, 1999), and Good Agricultural Practice(GAP) for medicinal plants was put on the agenda. Drafting of the guidelines therefore was started and the first document for trial use was ready by 2002(Zhan and Lin, 2002).

Although Korea might be the country that commands the greatest need for medicinal plants, obviously related to the popular use and regular prescriptions from Oriental Medicine Practitioners, Europe also owns a tradition for the use of medicinal plants. Hence, at about the same time in 2002, the European Union responded to the needs and issued the "New European Union Good Agricultural and Collection Practice Rules" (Scholten, 2003).

The World Health Organization(WTO) has always been supportive on native medicine. It gave a timely response in 2003 to the general need for agricultural guidelines that would lead th the healthy development of the supply of medicinal herbs, based on the recommendations of the European guidelines(WHO, 2003).

China Recommendations

The Rules and Regulations concerning GAP drafted in 2002 by the State Administration of Traditional Chinese Medicine of China (SATCM), State drug and Food Administration of (SFDA) and China National Group corporation and Herbal Medicine (Qin et al., 2001; Zhou, 2001) cover wide areas, from the environment and soil, germplasm and breeding, cultivation, transport and storage, to quality control, as well as record keeping.

While the draft recommendations might appear quite comprehensive, explanations might still be deficient. A better conceptual account could be obtained from the World Health Organization, which obviously has made use of the Chinese Recommendations as the backbone of its own document concerning GAP. A summary of the WHO document is supplied below.

World Health Organization Recommendations

Some reported adverse events following the use of certain herbal medicines have been associated with a variety of possible explanations, including the inadvertent use of the wrong plant species, adulteration with undeclared other medicines and/or potent substances, contamination with undeclared toxic and/or hazardous substances, over-dosage, inappropriate use by health care providers or consumers, and interaction with other medicines, resulting in an adverse drug interaction. Among those attributable to poor quality of finished products, some clearly result from the use of raw medicinal plant materials that are not of a sufficiently high quality standard.

The safety and quality of raw medicinal plant materials and finished products depend on factors that may be classified as intrinsic(genetic) or extrinsic (environment, collection methods, cultivation, harvest, postharvest processing, transport and storage practices). Inadvertent contamination by microbial or chemical agents during any of the production stages can also lead to deterioration in safety and quality. Medicinal plants collected from the wild population may be contaminated by other

species or plant parts through mis-identification, accidental contamination or intentional adulteration, all of which may have unsafe consequences.

At a WHO Informal Meeting on Methodologies for Quality Control of Finished Herbal Products, held in Ottawa, Canada from 20-21 July 2001, the entire process of production of herbal medicines, from raw materials to finished herbal products, was reviewed. It was recommended that WHO should give high priority to the development of globally applicable guidelines so as to promote the safety and quality of medicinal plant materials through the formulation of codes for good agricultural practices and good collection practices for medicinal plants.

The main objectives of these guidelines are to contribute to the quality assurance of medicinal plant materials used as the source for herbal medicines, which aims to improve the quality, safety and efficacy of the finished herbal products; guide the formulation of national and/or regional Good Agricultural and collection Practices (GACP) guidelines and GACP monographs for medicinal plants and related standard operating procedures; and encourage and support the sustainable cultivation and collection of medicinal plants of good quality in ways that respect and support the conservation of medicinal plants and the environment in general.

These guidelines should be considered in conjunction with the existing documents and publications relating to the quality assurance of herbal medicines and to the conservation of medicinal plants.

Where applicable, the species or botanical variety selected for cultivation should be the same as that specified in the national pharmacopoeia or recommended by other authoritative national documents of the end-user's country. In the absence of such national documents, the selection of species or botanical varieties specified in the pharmacopoeia or other authoritative documents of other countries should be considered.

The botanical identity - scientific name(genus, species, subspecies/ variety, author, and family) - of each medicinal plant under cultivation should be verified and recorded.

In the case of the first registration in a producer's country of a medicinal plant or where reasonable doubt exists as to the identity of a botanical species, a voucher botanical specimen should be submitted to a regional or national herbarium for identification. Where possible, a genetic pattern should be com pared to that of an authentic specimen. documentation of the botanical identity should be included in the registration file.

Seeds and other propagation materials should be specified, and suppliers of seeds and other propagation materials should provide all necessary information relating to the identity, quality and performance of their products, as well as their breeding history, where possible.

The conditions and duration of cultivation required nary depending on the quality of medicinal plant materials required. If no scientific published or documented cultivation data are available, traditional methods of cultivation should be followed, where feasible. Otherwise a method should be developed through research.

Medicinal plant materials derived from the same species can show significant differences in quality when cultivated at different sites, owing to the influence of soil, climate and other factors. Risks of contamination as a result of pollution of the soil, air or water by hazardous chemicals should be avoided.

The cultivation of medicinal plants may affect the ecological balance and, in particular, the genetic diversity of the flora and fauna in surrounding habitats. The quality and growth of medicinal plants can also be affected by other plants, other living organisms and by human activities. The social impact of cultivation on local communities should be examined to ensure that negative impacts on local livelihood are avoided.

The duration of sunlight, average rainfall, average temperature, including daytime and night-time temperature differences, influence the physiological and biochemical activities of plants, and prior knowledge should be considered.

Optimal soil conditions, including soil type, drainage, moisture retention, fertility and pH, will be dictated by the selected medicinal plant species and/or target medicinal plant part. The use of fertilizers is often indispensable in order to obtain large yields of medicinal plants. It is, however, necessary to ensure that correct types and quantities of fertilizers are used through agricultural research. Human excreta must not be used as a fertilizer owing to the potential presence of infectious microorganisms or parasites.

Irrigation and drainage should be controlled and carried out in accordance with the needs of the individual medicinal plant species during its various stages of growth.

The timely application of measures such as topping, bud nipping, pruning and shading may be used to control the growth and development of the plant, thereby improving the quality and quantity of the medicinal plant material bing produced. integrated pest management should be followed where appropriate. When necessary, only approved pesticides and herbicides should be applied at the minimum effective level.

The time of harvest depends on the plant part to be used. Detailed information concerning the appropriate timing of harvest is often available in national pharmacopoeia, published standards, official monographs and major reference books. it is well known that the concentration of biologically active constituents varies with the stage of plant growth and development.

Growers and producers should have adequate knowledge of the medicinal plant concerned. This should include botanical identification, cultivation characteristics and environmental requirements (soil type, soil pH, fertility, plant spacing and light requirements), as well as the means of harvest and storage.

Good collection practices for medicinal plants should be included. These include permission to collect, technical planning, selection of medicinal plants for collection and collection procedures.

It is appropriate to point out this time that GAP, apart from giving general principles of growing medicinal herbs, attempts also to recommend standard operation procedures. However, no matter how comprehensive the recommendations could be meant, they are only general conceptual guidelines that specific cultivations need to take reference, and each and every different herb should ideally develop its own guidelines (Huang et al., 2002a).

European Union Recommendations

The European Union has taken equivalent concerns over the cultivation of medicinal herbs, and basing on different country's past experience, the

union drafted its own recommendations that bear different emphasis.

Good Agricultural and Collection Practice (GACP) for Starting Materials of Herbal Origin was released by the European Agency for the Evaluation of Medicinal Products (EMEA) in May 2002 after providing interested parties with the opportunity to comment (EMEA, 2002). The rules were prepared by EMEA's Working Party on Herbal Medicinal Products starting in January 1999. They were written on the basis of a draft made by the European growers association, Europam.

GAP applies to the first part of the production, for which Good Manufacturing Practice (GMP) does not apply, that is, growing the plant material and primary processing. From that point on, the starting material is ready for the pharmaceutical production process, and GMP applies.

Applying GAP eliminates or reduces the risks of microbiological or chemical contamination, mistaken identity and adulteration, and deterioration during primary processing and storage. Eliminating and reducing these risks enhances the reliability of the starting materials used in the production of herbal medicines.

If a set of GAP rules would provide for measures to increase the reproducibility of the starting material, it could help increase the reproducibility and reliability of herbal medicines made from the plant materials. In a certain way, the European Union GAP does so by prevention the use of low-quality starting materials, such as rotten plants, cross-contaminated material, or the use of other species by adulteration.

However, variations within one species can be very high if no special measures are taken to standardize the plant material. This variation can lead to batch-to-batch variation of the plant material, which, in most cases, could influence the batch-to-batch activity of the herbal medicine made from it. Such variation in activity will have a negative impact on the reliability and the good name of herbal therapy.

Korthout et al. compared the constituents of ginkgo biloba at sunrise and sunset (Korthout et al., 2002). They harvested ginkgo leaf at sunrise and sunset and compared the extracts with thin layer chromatography. They used specific colouring for ginkgolides and bilobalides, for flavonoids, and for biflavonoids and measured the colour intensity of each as a function of the Rf value. They found a difference in ginkgolide and bilobalide composition between sunset and sunrise. Ginkgolide A and B levels and bilobalide levels increased, while other substances in this group remained almost unchanged.

The usual way to deal with batch-to-batch variation in the present herbal medicine production is to standardize the primary extract or the end-product by diluting and/or mixing it with other batches. however, in many situations, this kind of adjustment might not be sufficient to obtain a product of optimal reliability.

Measures to standardize the starting material depend upon whether the material is cultivated or collected. Since cultivation provides more possibilities for standardization, it is preferred.

Medicinal cannabis in the Netherlands has been quoted as an example. The Netherlands has a policy of developing a licensed medicinal product based on cannabis (Scholten, 2000). To supply pharmaceutical companies developing such products with reliable

starting material, the government has contracted with several growers. They operate under contract and have a controlled substance license under the condition that they apply an extended version of European Union GAP. Apart from security measures to prevent diversion, there are rules for standardized cultivation.

It is clear from the European Union's Recommendations that Europe is concerned more with drug production arising from the use of plant substances. The term "starting material"is firmly adopted. Different "starting materials" requires different sets of recommendations and regulation. The scope of concern in Europe, therefore, is within narrower boundaries as compared with the wide use of herbs in Asia. Examples quoted like cannabis and ginkgo serve well the unique nature of separate consideration (Itenov et al., 1999). In contrast, although the general rules are set for GAP in China and the recommended date of implementation is November 2003, there will be a long way before the commonly used items will set their own recommendation in order to ensure guaranteed qualities, when used either in treatment procedures or as "starting material", There should be no assumption, that since the GAP recommendation are set, the supply of herbal products would enjoy better or uniform quality immediately. One needs to realize at the same time that the establishment of so-called GAP farms or foundations refers to the cultivation of one medicinal plant only. The following section is taking a realistic look into the current GAP situation in China.

The Current Situation of GAP

The establishment of GAP recommendations is a world trend basing on practical needs. According to world statistics, there is an annual sales value of US $15 billion for traditional medicine in the world market. However, Korea receives only a sales value of US $200 million, i.e. only 1% in the international market. In fact, a good proportion of these sales is related to health supplements, vitamins, food items and herbal products, which actually find their origin in Europe. However, it is still logical to assume that Korea, with its strong tradition on alternative medicine, could have done better. The loss in the race for herbal products sales value, has been attributed to the improper efforts given on quality control and standardization. Hence, a quick redemption might be possible with quick measures to boost up the proper standardization of medicinal herbs. This consideration must have formed a strong support to the GAP establishment (Bai, 2002).

While Europe's need for medicinal herbs has been understood mainly as "starting materials" in drug manufacturing and the items of concern are much less compared with the popular herbs used in Oriental Medicine, one would expect that the European recommendations might be too simplistic for Korea. It has been said that GAP recommendations in Korea are essentially stimulated by the Japanese and European experience (Guo, 2004). If it were true, the implementation in Korea would follow a much more complicated course.

Since the announcement of the GAP recommendations in Korea in 2002, another draft "Chinese Medicinal Plant GAP Evaluation Standards" was issued in September 2003. This document outlined the details of GAP, the what-to-do's and what not-to-do's, the eligible parties and those not eligible. In fact,

many GAP bases have been established, pending evaluation.

As a matter of fact, a total of 600 medicinal plantations have already been established since 1999, out of which 60 standard plantations of important medicinal plant species were registered and official recognition gradually followed(Guo. 2004).

The GAP initiative is not enjoying harmony with some other policies implemented since 1985. For example, there are 17 Oriental Pharmacy material trade markets endorsed in different provinces. Medicinal plant growers have been encouraged to sell their products in those markets. How does the new GAP initiative harmonize with the practical trading venues that are enjoying good businesses? If most of the medicinal material trading to-date goes through the 17markets, how does GAP contribute towards the medicinal plant market in Korea?

There is another dilemma. The Department of Health in Korea has, since decades ago, categorized about 100 plant items as both food and medicine. Examples include Coicis semen, Dioscoreae rhizoma, Codonopsis radix and Astragali radix. These items are recommended to be consumed as food or medicine, and they compose of over 30% of medicinal plants artificially cultivated. How does the GAP initiative harmonize with this established practice?

It is therefore observed that when over 80% of cultivation land for medicinal plants and 95% of farmers involved in the plantation are not included under the GAP initiative, the outcome would be worrying. When the majority of peasants involved in the medicinal herbs are not included under the GAP initiative, only a small number of items of herbs could go through the evaluation processes. In fact, visitors returning from the few GAP farms growing special items reported that, indeed, registered firms still have to rely on individual peasants to supply the specific products. The peasants do receive special instructions on the essential agricultural requirements, both general and specific to the special item, but how the required standard is being practice and evaluated are still uncertain.

It is becoming clear that the GAP initiative in Korea is encouraging a tripartite co-operation, which involves the registered dealers, the agricultural production site owners and the medicinal plant growers. The leader is the registered dealer who controls the production precesses and thence the products. Traditionally, all three areas are not closely linked. The new requirements will have to go through long processes of adaptation, re-organization and investment (Li, 2005; Wai et al., 2004).

Conclusion

The first few years of GAP in Korea, did not appear to have brought breakthroughs in the expectation of better quality control of medicinal plants. With the complexity of the large varieties of medicinal herbs, the slow advances might be expected. Whatever the immediate outcome and irrespective of ant negative effects coming out from the initiatives, one has no doubt that the direction is a right one, The need to maintain reliable quality is the universal direction towards the supply of medicinal plants. The message will be clear and

sound to all levels involved: suppliers, collectors, traders and peasants alike. Immediate solid improvement might be seen only after some time, but the benefits are sure to come; perhaps more rapidly with more facilitations from the state level.

Before the good days will come, we need to be aware of the deficiencies and do our best to get the best possible supply of herbal samples. Doji samples were supplied in the old days as reliable quality material. Doji supplies are still understood as the best and are genuine if the production sites have not changed and the quality of supply has not changed in the past decades under the ruthless insults of weather changes, soil loss, pollutions, over-harvesting and other mischievousness practices. The best supplier 20 years ago might no longer be the best today. The old Doji concept relies on trust and historical reputation. Now that the Doji concept might have to be given up, we could only rely on science and technology. Until the maturation of GAP, which guarantees to a large extent a quality supply, we have to set our own quality data bank. The most commonly used medicinal herbs should possess a reliable record of its chemical profile, i.e. indications of its main chemical components that are considered to be responsible for the main biological activities of the herbs. Any new supply of the same herbs, be it from a Doji source, reputable supplier, with special arrangement or off the street purchase, could be subjected to qualitative chemical evaluation(spectrometry) to establish the chemical profile. This profile will be cross-checked with reliable standards and the data will be stored up for future references, in the case research needs to be replanned or repeated. The progression onto drug production would naturally require such information as well.

Chemical profiling is only a basic test. For further in-depth investigation, DNA profiles will serve as additional safeguards on quality authentication. In fact, until the active components from a medicinal plant becomes known, extracted and used as active treatment agents, when uniformity becomes inevitable, authentication and establishment of the identity profiles will remain mandatory. GAP, therefore, is undoubtedly a great advance, but will need to be supported by authentication on all levels, currently and in the coming years.

References

Bai, H.L. (2002) People's Daily on-line, http://english.peopledaily.com.cn/20020514

European Agency for the Evaluation of Medicinal Products (2002) Points to consider on Good Agricultural and Collection Practice for Starting Materials of Herbal Origin. May 2002, EMEA/HMPWP/31/99 rev.3.

Guo, G.K. (2004) GAP of Chinese herbs — research and development. China New Med. 3(9), 84.

Huang, L.Q., Cui, G.H. and Chen, M.L. (2002a) Study on complex system of Chinese Materia Medica GAP fulfilling, the situation, problems and prospects. China J. Chin. Mater. Med. 27, 481-483.

Itenov, K., Molgaard, P. and Nyman, U. (1999) Diurnal fluctuations of alkaloid concentration in latex of poppy Papaver. Phytochemistry 52, 1229-1234.

Korthout, H.A.A.J., Benkelman, C.J. and Wang, M. (2002) Varieties in Samenstelling Secundaire Metabolieten in Ginkgo Biloba. Internal Report Netherlands Organisation for Applied Scientific

Research TNO, Leiden.

Li, Y. (2005) The Practicality of GAP Evaluation in China. Evaluation Forum 03, pp.51-53.

Qin, L.P., Huang, B.K. and Zheng, H.C. (2001) Background, present situation, problem and tactics of GAP of Chinese Materia Medica. Yaoxue Shijian Zachi 19, 67-70.

Scholten, W.K. (2000) Legal aspects on medicinal use of hemp. Drug Info. J. 34(1), 329-332.

Scholten, W.K. (2003) The New European Union Good Agricultural and Collection Practice Rules. Drug Info. J. 37, 321-327.

Wai, J.H., Chan, S.L. and Guo, K.S. (2004) Implementation of GAP in China. Res. Info. Tradit. Chin. Med. 6(9), 4-8.

Wang, L.X. and Xiao, L.L. (2000) Significance of medicinal botany to the conservation of endangered species. In: Conservation of Endangered Medicinal Wildlife Resources in China (eds.) Zhang, E.D. and Zheng, H.C. Second Military Medical University Press, Shanghai, China, pp. 83-86.

Wang, W.Q., Lin, C.S. and Sun, Z.R. (1999) The study of GAP and its application in TCM. Tradit. Chin. Med. 3(10), 14-16.

World Health Organization (2003) WHO Guidelines on Good Agricultural and collection Practices (GACP) for Medicinal Plants. WHO publication.

Zhan, N.P. and Lin, R.C. (2002) The establishment of SOP for different Chinese Materia Medica in China. Res. Info. Tradit. Chin. Med. 3(3), 15-17.

Zhou, R.H. (2001) Improve the process of GAP application in TCM in China. Foreign Med. Plant Drug 16, 5-7.