

## THE ROLE OF AGRO PRACTICES SUCH AS BREEDING, PRODUCTION, PROCESSING AND MARKETING OF NEUTRACEUTICALS

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### ABSTRACT

Lately in Japan, the supply of most of crude drugs depends on the imports from China. However, from the standpoint of securing resources and risk diversification in the long term perspective, the resumption of domestic production has been attracting much attention. Recently, a local government and a pharmaceutical company presented their own policies on promotion and revival of the domestic production of medicinal plants. However, in Japan facing with the problem of aging society with a falling birthrate, the farming population is dwindling and the seeds and seedlings as well as the techniques for growing medicinal plants in formerly established production areas have mostly disappeared.

Since the uses of these crops are deeply associated with pharmaceutical products and human health, the safety and the quality of products need to be treated as the priority issues. On the other hand, from the viewpoint of business management, the production cost needs to be reduced to a low level. Consequently, what is at stake is to produce safe medicinal plants of high quality at a low cost. The efforts of research and development in this sector have to address such issues as the facilitation of acquisition of seeds and seedlings, the training of manpower, the development of mechanisation and labor saving technologies suited for large-scale cultivation. Furthermore, it is needed to develop the cultivars suitable for medicinal purposes as well as the methods of processing to produce products with high quality which are safe.

Our centre is committed to carry out the research on production, evaluation of product quality, and collection and preservation of resources of medicinal plants in Japan. We also offer, in response to the requests from local governments, the services of supplying seeds and seedling and of provision of technical assistance. Moreover, we carry out research programs in collaboration with pharmaceutical companies in order to develop labour saving techniques for large-scale mechanised cultivation aiming at cost reduction. The present report shall examine the relevant issues of the sector and the roles of agricultural sciences, through the presentation of research programs implemented by the Hokkaido Division of the Center, concerning the technologies for producing medicinal plants.

## **1.0 PROBLEMS NEEDING SOLUTION FOR SECURING ‘SAFETY’ AND ‘QUALITY’**

Regarding medicinal plants used for preparation of medicines and health supplements, taking account of the particularity of their use, the most important problems concern their “safety” and “quality” in the sources of seeds and seedlings, cultural methods, processing methods and distribution processes. In order to secure the “safety” and the “quality”, it is needed that the government or a certain public institution concerned of each country enacts a necessary law and formulates the criteria to determine safety and quality. The expected role of institutions of higher education including universities and that of research institutions are the generation of basic information to define the aforementioned criteria on safety and quality as well as the development of methods for assessing safety and quality.

Regarding the criteria of quality of medicinal plants and the methods to assess it, the World Health Organisation (WHO) has already published the guidelines<sup>1-6)</sup>. They present the procedures for certifying the safety and the quality of medicinal plants and products derived from them and specify the rules that producers and business operators have to adhere to.

In Japan, regarding the crude drugs used for deriving pharmaceutical products, the standard of quality and the procedures to assess it are defined rigorously by the Japanese Pharmacopoeia<sup>7)</sup>. Concerning the cultivation of medicinal plants, our Centre is taking the initiative in publishing the guidelines for cultural practices and for methods of processing products<sup>8)</sup>.

## **2.0 PRODUCTION OF MEDICINAL PLANTS AND PROBLEMS NEEDING SOLUTION**

Although medicinal plants used to be cultivated widely all over the country in Japan, currently Japan depends on the imports from foreign countries including China for most part of supply of raw materials of crude drugs. Lately in China the population of those who engage in agriculture in rural areas is on the decrease due to the remarkable economic development, and there is a fear that the reduction of resources is taking place as a result of development of natural lands. Those who are associated with market in Japan forecast that the procurement of low-priced crude drugs of high quality will become difficult in the future. Under such social circumstances, Japanese pharmaceutical manufacturers have proposed the policy to acquire again a part of their requirements of raw materials of crude drugs from domestically grown products, and some local governments are trying to revive the production areas.

Key factors in the development of production of medicinal plants in Japan are: provision of seeds and seedlings to growing areas; dissemination of production techniques; creation of human resources of leaders and technical experts. Furthermore, in response to the reduction and the aging of agricultural workers, it is needed to develop cost effective technologies which assure the production of safe products of high quality. The following sections present some cases of efforts made in such context.

## 2.1 Development of Production Techniques for Mechanisation and Labor-saving

In the commercial production of herbal medicines, the greatest problems to be dealt with are the reliable supply of raw materials and the reduction of their cost in cultivation processes. These problems call for solutions by collectivising the production areas to enlarge the scale as well as by improving the efficiency of farming management through adoption of mechanized and laborsaving techniques in the farming processes as a whole.

An example of the achievements is as follows. The root of Mongolian milk vetch [*Astragalus mongolicus*, name of crude drug, *Ogi*, *Huang qi* (Astragalus root)] is used as a crude drug. The shape of root is straight with a diameter of 0.7 to 2 cm and a length of 30 to 100 cm. In the cultivation of *A. mongolicus*, the challenge is how to harvest efficiently the long slender root without damaging it.

In Japan a vegetable plant, great burdock, *Arctium lappa*, the edible root of which very much resembles that of *A. mongolicus*, is cultivated all over the country. For harvesting the vegetable crop, a specialised implement mounted on a tractor and called burdock harvester has been developed and is being used by most of growers of great burdock.

We have tried the burdock harvester for digging the roots of Mongolian milk vetch and demonstrated that they can be harvested continuously without the need for modifying the machine. We concluded that the machine can be utilised satisfactorily by growers themselves. Furthermore, we have studied the possibility of mechanisation of sowing operation and demonstrated that it is conveniently mechanised by applying the machine for sowing wheat and soybean, if the shape of plates for feeding seeds is improved to conform to milk vetch seeds.

As a consequence of the success of trials for mechanising seeding and harvesting operations, currently the commercial production of the crop has been started.

## 2.2 Development of Processing Techniques for Securing Safety and Quality

As an example of research efforts for improving safety and quality, I would like to present the study on methods for processing Green Dragons [*Pinellia ternate*, name of crude drug, *hange*, *Ban xia* (Pinellia Tuber)]. Dried tubers (0.2 to 2 cm in diameter) of *Pinellia ternate* are used as a crude drug. In the Japanese market, buyers prefer to acquire the merchandise in which processed tubers have white surface and powdery appearance. Incidentally, when the tubers are dried by a heated air drier, tuber surfaces turn to brownish tinge, and the products consequently losing commercial value. The principal production areas of *Ban xia* (Pinella tuber) are in China where the fumigation with sulfur (sulphuring) is reportedly practiced in order to give white appearance to the tuber.

The fumigation by sulfur of food and pharmaceutical products is restricted in Japan, because residual sulfuric substances may cause harmful effect on human health.

Therefore, we have studied the method to dry Pinella tubers in a safe and reliable manner and devised a process which excludes the uses of chemicals and special machines<sup>9)</sup>. The method enables the drying of Pinella tuber while preserving white color through the regulation of temperature and humidity of aeration, with an advantage that the process is able to be expanded to that of an industrial scale by applying multi-purpose equipment used by manufacturing industries.

### **3.0 IMPROVEMENT OF VARIETIES SUITED FOR MEDICINAL USES**

Our centre has developed one variety of Job's tears (*Coix lacryma-jobi* var. *ma-yuen*) and two varieties of peony (*Paeonia lactiflora*). In the breeding of medicinal plants and nutraceuticals, objectives include, in addition to traits such as higher yield and resistance to diseases which are the objectives in breeding of ordinary crops, also the content of marker compound or the advantages in operations of cultural management and harvesting. The following sections present the cases of the 3 varieties developed by our Center.

#### **3.1 Breeding of An Ultra-early Variety of Job's Tears**

"*Kitano-hato*", a variety of Job's tears, is an ultra-early strain of this crop species. This variety was registered according to UPOV protocols in 2005 in Korea (Registration No. Job's tears 5), and in 2007 in Japan (Plant Variety Protection Registration No. 15003, Japan). In 2008, commercial production was started in Hokkaido, Japan, and 3 parties, our Center, private enterprises, and growers, have been cooperating in the development of production areas.

Job's tears variety "*Kitano-hato*" is an ultra-early one which makes it possible to harvest seeds even in cold region. In the cold region of Hokkaido, existing varieties have not allowed the harvest of seeds, because snow begins to fall before flowering and ripening take place. In the case of "*Kitano-hato*", it flowers in late July and the seeds mature in October before snow begins to fall.

In many cases, Job's tears is cultivated in temperate regions where the needs for controlling diseases and insect pests have been presenting substantial constraints. In the case of cultivation of Job's tears "*Kitano-hato*" in the cold region of Hokkaido, to the contrary, the cool climate there is favorable for lowering the incidence of diseases and insect pests, enabling the cultivation with reduced or no application of agricultural chemicals, the farming practice preferred by Japanese consumers. Moreover in Hokkaido, the large-scale mechanized farming of food crops such as rice and wheat is very much developed, and such a type of mechanization technology is equally applicable to the cultivation of Job's tears. Consequently, the combination of varietal characteristics of Job's tears "*Kitano-hato*", the cool summer climate in Hokkaido, and the type of agriculture prevailing there has made it possible to grow Job's tears of high quality at a low cost in Japan.

#### **3.2 Breeding of Medicinal Peony Varieties of High Yielding Traits**

The peony variety, "*Kita-saisho*", registered in 1996 in Japan according to UPOV protocols (Plant Variety Protection Registration No. 5005, Japan), is one which yields a large quantity of root used for medicine, having been developed by using the content of marker compound as a criterion of selection.

Existing peony varieties have been developed mainly for the ornamental quality of flowers. While the root of peony is used for medicinal purposes, existing varieties are vulnerable to the occurrence of diseases such as rusts during the summer, which causes the withering of aerial parts, and has constituted the constraint factor limiting root yield.

Peony variety "*Kita-saisho*" shows few signs of withering during the summer and yields a large quantity of root. Moreover, it has the characteristic of a high content of marker compound, paeoniflorin, specified in the Japanese pharmacopoeia and used as a

selection criterion in the breeding process. The variety tends to show reddish tinge in the cross section of roots processed as a crude drug. Since Japanese market rather prefers white products, currently this variety is not grown so widely.

### **3.3 New Peony Variety with a Particular Flowering Trait**

The peony variety, “*Benishizuka*”, of which the procedures for plant variety protection registration are in progress, is a variety that is slightly inferior to “*Kita-saisho*” in respect of root yield, but has overcome the defect of reddening of root cross section. Furthermore, the peony “*Benishizuka*” is a variety which exhibits a particular flowering trait. The rate of flowering is extremely low and plants of the variety flower only at a rate of 5 % of the entire population at flowering time. This trait presents a disadvantage as an ornamental plant. However, in cultivation of peony as a medicinal plant, an operation has to be carried out to eliminate flowers (flower picking), in order to fatten the roots. Consequently, flower picking operation otherwise required for peony grown for medicines is not necessary in the case of cultivation of “*Benishizuka*”, offering a great advantage of realising labor saving in cultural management.

## **4.0 CONCLUSION**

The necessary conditions imposed on medicinal plants and crops as raw materials for pharmaceutical products and nutraceuticals, are that the products with a high level of safety and quality have to be produced at a low cost. We believe that the role to be played by agronomic research and the orientation of policy in this sector can be summarised as follows:

- (i) Compared to the cases of general agricultural crops, the establishment of cultural techniques and the development of suitable cultivars are not well advanced in the medicinal plants used as crude materials for processing medicines or as those for preparing nutraceuticals. Consequently, it is needed to carry out research and technology development focusing on productivity enhancement.
- (ii) Since these medicinal plants are closely associated with medical treatments and human health, it is needed for a public institution to establish the guidelines for cultural practices and processing methods for their production, and to standardise the criteria for assessing product quality.
- (iii) Very few technical experts and scientists are engaged in the production in this sector. However, there exists practically no university or research institution which is devoted to the training of qualified professionals. Since the sector requires the occupation with a wide range of knowledge and skills in agronomy, botany and pharmacy, the creation of human resources would contribute to its development,

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