

Industrial Development of Medicinal Plants in China

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중국에 있어서 약용식물의 산업적 발달

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ABSTRACT : In China, medicinal plants play almost the same important role in the general health service as the western medicine. In this paper, we present a brief review about the industrial development of medicinal plants in China. A nation-wide survey shows that there are 11,118 species of medicinal plants in China. The total annual output value of natural products is about \$6,000. The output value of preparations is 3 billion US dollars. Over 100 new drugs have been developed from the medicinal plants. As the trend worldwide today that human-being favors the way of life back to nature, medicinal plants will play a very important role, and their industrial exploitation will certainly be keeping a key position for human health.

Key words : medicinal plant, industrial development, new drug, China.

Introduction

In China, traditional Chinese medicine (TCM) and traditional Chinese drugs play a very important role in the general health service. Traditional Chinese drugs are by no means inferior to the drugs of the western medicine. Most of the traditional Chinese drugs are produced from medicinal plants. Medicinal plants constitute a great social and economic value for China. The annual output value of medicine in

China is around 15 billion US dollars; 6 billion are from natural products (mostly from medicinal plants), and 9 billions are from western medicine. In general, medicinal plants play nearly the same important role in comparison with western medicine (Chang and Xiao, 1993; Cheng et al., 1998).

Traditional Chinese medicine, as practiced today, is still largely based on its unique system of theories, including the concept of Yin and Yang; the concept of Wu-xing (the five elements); the theory of influence imparted from nature; and the

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idea of comprehensive reasoning resulting from direct observations of the patient. Traditional Chinese medicine is in a legal medical system, and many hospitals and clinics in China offer both traditional and western-style treatment, depending on the patient's choice. In Chinese medicine, feeling the pulse of the patient with the doctor's fingers is considered standard procedure, but other routine western diagnostic methods are often also applied. A compound prescription of herbal medicine is usually prescribed by the Chinese doctor following diagnosis (Feng and Zhang, 1997).

Since the founding of the People's Republic of China, a series of principles and policies have been formulated by the government to protect and promote traditional Chinese medicine. The policy of "Developing modern medicine and traditional Chinese medicine" was officially put down in the Constitution. To meet the needs of developing traditional Chinese medicine, the State Council established the State Administration of Traditional Chinese Medicine (SATCM) in 1987 (Li et al., 1997). China is a developing country with 80% of its more than one billion population living in rural areas. Consequently, strengthening primary health care is an important aspect of the State health policy in general. In carrying out this task China places special emphasis on giving full play to the role of traditional Chinese medicine and traditional Chinese drugs, especially in rural areas. In this paper, we presented a brief review about the industrial development of medicinal plants in China (Shen and Lu, 1997).

General Status

There are altogether 1,059 enterprises dealing with traditional Chinese drugs in China with yearly output value about 7,000 million Chinese yuan. Among the 39 large and 114

medium-sized enterprises manufacturing and dealing traditional Chinese drugs, only 14 enterprises surpass 20 million Chinese yuan in whole year sale. Although traditional Chinese drug enterprises in China have made great improvement, they are in a relatively low level; on the whole, 843 of 1,059 enterprises are small in size, most of which still deal predominantly with traditional pill, powder, plaster and pellet, manufacturing products low in science and technology, and about 400 are running at a loss. Some of them are technically deficient so that the quality of the products from some small enterprises can not be guaranteed (Cui and Chen, 1991; Huang and Chao, 1998). More than 800 traditional Chinese drug materials are frequently applied in China, and 300 of them are mainly cultivated. So far, there are more than 600 manufacturing bases, 13,000 cultivation stations and 340,000 cultivation families specialized in production of traditional Chinese drug material in China, with cultivating areas more than 950,000 acres and output about 3,500,000 tons (Xiao, 1997; Yuan, 1997).

The total export amount of traditional Chinese drugs in China in 1996 as an example are 655 million dollars, in which 521 million are from traditional Chinese drug materials while only 134 million are from finished traditional Chinese drug products, nearly equal to 3-5% of the total volume of trade of plant medicine, 15,000 million dollars, in the whole world (Xiao, 1998; Shan and Zhuang, 1998).

Resources of Medicinal Plants

On the basis of the general survey report on Chinese herbal medicine, animals, plants and minerals that are medicinally available have totally amounted to 12,807 kinds. 11,146 kinds of them are medicinal plants (Table 1), subordinate to 383

families and 2,309 genera. 1,581 kinds are medicinal animals, subordinate to 415 families and 861 genera. The other 80 kinds are medicinal minerals. Among them, 800 kinds of traditional Chinese medicines are often clinically used, with traditional prescriptions almost 100,000 kinds and single and efficacious formulas more than 6,000 kinds (Chang and Xiao, 1993). The major Chinese medicinal plants are listed in Table 2 (Xiao and Peng, 1997).

Due to the destruction of forests, overgrazing of meadows, expansion of industry and urbanization, as well as excessive collection in the wild of rare and endangered plants, the natural resources of medicinal plants are being reduced day by day. There has therefore been an urgent need to draw up the necessary plans for medicinal plant resource utilization and conservation (Wang and Gao, 1997). Now, the Chinese government has established the law for development and conservation of medicinal plant resources. The genebank conservation plan was for biodiversity conservation, to store plant germplasm for future uses, to make germplasm available to create new cultivars. Biotechnology such as plant cell culture and hairy root culture was carried out to produce active compounds or for the breeding purpose. Large scale cultivation of medicinal and aromatic plants relies upon strong and continuing research. The contemporary literature in agrotechnology of several medicinal and aromatic plants demonstrates the fact that plant rarities with an abundance of desired constituents can be reproduced, and improved upon under cultivation even in an entirely different area. In addition, non-polluted agrotechnology is rapidly developed in recent years in order to protect the environment, to use the resources continuously, and to get a good quality of crude drugs. Those products are commonly called as "Green crude drugs" (Xiao and Cheng, 1997; Yuan, 1997; Zhang and Xiao, 1993).

Table 1. Medicinal plant resources in China (including 1,208 infraspp. taxa).

Origin	No. Medicinal Plants
Thallophytes	467
Bryophytes	43
Pteridophytes	455
Gymnosperms	126
Angiosperms	
Dicotyledons	8,612
Monocotyledons	1,443
Total	11,146

Table 2. Major medicinal plants cultured in China.

Name of medicinal plants	parts used as drug	Production (tons)
<i>Allium sativum</i>	bulb	10,000-16,000
<i>Dioscorea opposita</i>	rhizome	10,000-16,000
<i>Glycyrrhiza uralensis</i> , <i>G. glabra</i>	root, rhizome	10,000-16,000
<i>Zingiber officinale</i>	rhizome	10,000-16,000
<i>Angelica sinensis</i>	root	3,000-8,000
<i>Astragalus membranaceus</i>	root	3,000-8,000
<i>Atractylodes macrocephala</i>	root	3,000-8,000
<i>Codonopsis pilosula</i>	inflorescence	3,000-8,000
<i>Dendranthema grandiflorum</i>	root	3,000-8,000
<i>Isatis indigotica</i>	root, leaf	3,000-8,000
<i>Lonicera japonica</i>	flower bud	3,000-8,000
<i>Panax ginseng</i>	root	3,000-8,000
<i>Polygonum multiflorum</i>	rhizome	3,000-8,000
<i>Rehmannia glutinosa</i>	rhizome	3,000-8,000
<i>Rheum almatum</i>	root, rhizome	3,000-8,000
<i>Salvia miltiorrhiza</i>	root	3,000-8,000
<i>Aconitum carmichaeli</i>	root	1,000-3,000
<i>Aucklandia lappa</i>	root	1,000-3,000
<i>Coptis chinensis</i>	rhizome	1,000-3,000
<i>Eucommia ulmoides</i>	bark	1,000-3,000
<i>Forsythia suspensa</i>	flower	1,000-3,000
<i>Ligusticum chuansiang</i>	rhizome	1,000-3,000
<i>Lycium barbarum</i>	flower	1,000-3,000
<i>Mentha haplocalyx</i>	total plant	1,000-3,000
<i>Ophiopogon japonicus</i>	root	1,000-3,000
<i>Paeonia lactiflora</i>	root	1,000-3,000
<i>Panax noto-ginseng</i>	root	1,000-3,000
<i>Pogostemon cablin</i>	root	1,000-3,000

Strategy of Industrial Exploitation of Medicinal Plants

(Shen and Lu, 1997; Xiao and Wang, 1997; Shang and Yu, 1997).

1. Multilevels of Development

Primary development is aimed to enlarge the resources and improve the quality of medicinal plants; Secondary development is for the purpose of developing new and improved preparations or products; Tertiary development is focused on the searching of new drugs. The new drugs developed from medicinal plants are divided into 5 categories according to their characteristics (Zhou, 1997; Wu, 1998) :

- I. New crude drug and active ingredient
- II. Injection, new part used and new active fraction
- III. Composite prescription
- IV. Improved dosage form
- V. New usage

2. Multidisciplinary Research

Including botanical, pharmacognostical, chemical, pharmacological and clinical investigations are stressed (Xiao, 1997).

3. Multilateral Utilization

Medicinal plants are being integrated to the food, cosmetic and agricultural industries as well. They are used as sweetener, bitterness, spices, natural coloring matter, natural insecticides, healthy foods, healthy drinks, cosmetics, etc

New Drugs Derived from Chinese Medicinal Plants

Chinese government issued Drug Approval Law in 1985, which states that new drug application for approval must go through examination of four aspects, safety, activity, stability and controllability. The approval, which is held two times per year, works on traditional Chinese medicine and western medicine respectively with two groups of experts. Applicants should submit an application for the clinical investigation of a particular new drug to the Bureau of Health of province, autonomous regions or municipalities accompanied with requisite information and sample. At the end of the clinical investigation of a new drug, the applicants should submit an application for the production of that drug to the Bureau of Health where the applicant is located, accompanied with the requisite information and sample; no objection is raised, the Bureau of Health should present all the data to the Ministry of Health for trial approval (Zhou, 1997; Fang, 1997). Table 3 showed the new drugs derived from medicinal plants in China (Chang and Xiao, 1993; Xu and Cheng, 1997; Yang, 1997; Zhang and Zhu, 1997; Fang, 1997).

Table 3. New drugs derived from Chinese medicinal plants.

New drugs	Medicinal application
<i>Acanthopanax senticosus</i> (root)	Increasing resistance to Nonspecific stress
d-8-Acetoxy-carvotanacetone	Repellent for mosquito
Agrimorphol	Taeniafuge
Andrographolide	Dysentery
<i>Angelica sinensis</i> (root)	Abnormal menstruation
Anisodamine and Anisodine	Anticholinergic

(Table 3. continued)

New drugs	Medicinal application
Antiepilepsirin	Antiepileptic
Ardisinol I and II and total extract of <i>Ardisia japonica</i> (plant)	Antituberculosis
<i>Armillaria mellea</i> fermentation extract	Sedative
Arteannuin	Antimalaria
Artemether	Antimalaria
<i>Artemisia argyi</i> (leaf) and essential oil	Antiasthmatic
<i>Astragalus mongholicus</i> (root) and polysaccharides	Immunostimulating
Baicalin	Hepatitis
Bao-gong-teng A	Glaucoma
Berberamine	Leucocytes increasing
Bergenin	Antitussive
Biphenyl dimethoxy dicarboxylate (BDD)	Lowering SGPT
<i>Brucea javanica</i> (fruit)	Antitumor
<i>Bupleurum chinensis</i> (root, plant)	Antipyretic
<i>Callicarpa pedunculata</i> (leaf)	Hemostatic
β -Caryophyllene	Chronic bronchitis
Changroline	Antiarrhythmia
Cissampelosine methiodide	Muscle relaxant
<i>Clinopodium polycephalum</i> (plant)	Hemostatic
<i>Cordyceps sinensis</i> fermentation extract	Immunoregulating
<i>Coriolus versicolor</i> (fruit body)	Immunostimulating
<i>Crataegus pinnatifidus</i> (fruit, leaf) and <i>Polygonatum odoratum</i> (rhizome)	Hyperlipidemia
Cucurbitacin B & E	Lowering SGPT (B)
Curcumol, curdione	Early stage of cervix cancer
Cuscohygrine, sedative	Antispasmodic
Cyclovirobuxine D	Angina pectoris and arrhythmia
<i>Cynanchum otophyllum</i> (root)	Antiepilepsy
Daphnetin	Analgesis
dl-Demethylcoclaurine	Antibradyarrhythmia
Dially trisulfide	Hyperlipidemia and various infections
3, 4-Dihydroxyacetophenone	Angina pectoris
Dimer-anthocynidins mixture of <i>Fagopyrum dibotrys</i> (rhizome)	Hyperlipidemia
<i>Epimedium sagittatum</i> (plant) and <i>Ligustrum lucidum</i> (fruit)	Climacteric syndromes
Farrerol	Expectorant
<i>Ganoderma lucidum</i> (fruit body)	Coronary diseases, hyperlipidemia, Neurasthenia
<i>Ganoderma lucidum</i> (spores)	Progressive muscular dystrophy and atrophic myotonia
Gastrodia	Sedative
Gentianine and Gentianidine	Arthritis
Geraniol	Asthnolytic
Total flavonoids and extract of <i>Ginkgo biloba</i> (leaf)	Cronary heart diseases
Gossypol	Antifertility for male
<i>Gynostemma pentaphyllum</i> (plant)	Hyperlipidemia
Harringtonine	Treatment of leukemia
<i>Hedyotis diffusa</i> (plant)	Immunostimulating
Helicid	Sedative, anti-inflammatory
Hemsleyadin	Antimicrobial
Homoharringtonine	Leukemia
Hyperzine A	Improve memory, for myasthenia gravis
10-Hydroxycamptothecine	Stomach and intestinal cancer
Iridubin	Chronic myleocytic leukemia

(Table 3. continued)

New drugs	Medicinal application
Irisquinone	As an enhancing agent for cancer chemo- or radiotherapy
<i>Isatis indigotica</i> (root, leaf)	Antimicrobial
d-Isocorydine	As spasmolytic and analgesic
Isomangiferin	Antitussive, expectorant
d-Kainic acid	Vermifuge for Ascaris
Lappaconitine	Analgesic
Ledol	Antitussive
<i>Leonurus artemisia</i> (plant)	Abnormal menstruation
Linalool	Antimicrobial
Ligustrazine	Occlusive cerebral vessel diseases
Luteolin	Antitussive
Lysinotin	Antituberculosis
Metetradrin iodide	Muscle relaxant
4-Methoxy-5-hydroxycanthin-6-one	Antimicrobial
Oleanolic acid	Hepatitis
Oxymatrine	Antimicrobial
<i>Patrinia scabiosaeifolia</i> (root)	Sedative
<i>Physochlaina infundibularis</i> (root)	Antiasthmatic
Piperitone	Asthmolytic
<i>Polygonum multiflorum</i> (root)	Hyperlipidemia
<i>Polyporus umbellatus</i> (sclertia)	Immunostimulating
<i>Pseudolarix kaempferi</i> (bark)	Scabies and ringworm
Psorlen	Leukoderma
<i>Rhododendron dauricum</i> (leaf)	Antitussive
<i>Rhododendron mariae</i> (leaf)	Bronchitis
Rhynchophylline	Hypotensive, sedative
Rovifon	Expectorant, antitussive
Rotundine	Analgesic, sedative
Rubescensine, Oridonine, Ponicidine	Esophageal and liver cancer
Rubidate	Leukocyte increasing
<i>Rumex patientia</i> (root)	Hemostatic
<i>Salvia miltiorrhiza</i> (root) and <i>Panax notoginseng</i> (root)	Coronary diseases, angina pectoris
Sarmentosine	Lowering SGPT
Schisandrins and total alcoholic extract of <i>Schisandra chinensis</i> (kernels)	Lowering SGPT
Scutellarin	Occlusive cerebral blood Vessel diseases
Securinine	Facial paralysis
Sinomenium	Rheumatoid arthritis
Sodium ferulate	Thromboangiitis, obliterans
Sodium houltuyfonate	Antibacterial
Sodium tanshinone sulfonate	Cardiovascular diseases
<i>Spatholobus suberectus</i> (stigma)	Abnormal menstruation
Tanshinones	Antibacterial
±Tetrahydropalmatine	Analgesic, sedative
Tetrandrin	Analgesic
Thevetosid	Cardiotonic
Toosendanin	Antiascariasis
Trichosanthes protein	Induces premature abortion
<i>Tripterygium wilfordii</i> (root)	Rheumatoid arthritis
Tutin	Schizophrenia
<i>Typha angustata</i> (pollens)	Hyperlipidemia
Yejuhualactone and essential oil of <i>Chrysanthemum indicum</i> (inflorescens)	Prostatitis
Yuanhuacine A & B	Induces premature abortion

In addition to the development of new drugs listed in Table 3, product development in China has involved investigation of plants used for the following purposes (Chang and Xiao, 1993; Xiao and Peng, 1997; Zhou, 1997) :

(1) Sweetener : *Glycyrrhiza uralensis*, *G. glabra* (root, rhizome), *Rubus suavissimus* (leaf), *Siraitia grosvenovii* (fruit), *Stevia rebaudiana* (leaf).

(2) Bitterness agents : *Humulus lupulus*, *Gentiana scabra*, *Swertia japonica*, *Citrus aurantium*, *Taraxacum mongolicum*, *Artemisia absinthium*.

(3) Spices : *Foeniculum vulgare* (fruit), *Illicium verum* (fruit), *Cinnamomum cassia* (bark), *Capsicum annum* (fruit), *Piper nigrum* (fruit), *Zingiber officinale* (rhizome), *Zanthoxylum bungeanum* (fruit), *Amomum kravanh* (fruit), *A. villosum* (fruit).

(4) Natural coloring matter : *Curcuma longa* (yellow), *Gardenia jasminoides* (yellow), *Hippophae rhamnoides* (orange), *Lithospermum erythrorrhiza* (violet), *Capsicum annum* (red), *Carthamus thinctorius* (red, orange), *Coreopsis lanceolata* (yellow).

(5) Natural insecticides : *Chrysanthemum roseum*, *Melia azedarach*, *M. toosendan*, *Derris trifoliata*, *Sophora flavescens*, *Millettia pachycarpa*, *Tripterygium wildordii*, *T. hypoglaucom*, *Celastrus angulatus*, *Artemisia apicea*.

(6) Health drinks : *Actinidia chinensis* (fruit), *Chrysanthemum morifolium* (inflorescence), *Crataegus pinnatifidus* (fruit), *Hibiscus sabdariiiffa* (calyx), *Hippophae rhamnoides* (fruit), *Psidium guajava* (fruit), *Ribes nigrum* (fruit), *Rosa roxburgii* (fruit), *Tamarindus indica* (fruit), *Vaccinium uliginosum* (fruit), *Zizyphus jujuba* (fruit).

(7) Health foods or general tonics : *Panax ginseng* (root), *P. quinquefolium* (root),

Astragalus mongholicus (root), *Cordyceps sinensis* (dead caterpillar), *Ganoderma lucidum* (fruit body), *Zizyphus jujuba* var. *inermis* (fruit), *Dioscorea opposita* (rhizome), *Lycium barbarum* (fruit), *Tremella fusiformis* (plant), *Acanthopanax senticosus* (root).

(8) Cosmetics : *Rosa rugosa* (flower), *Polianthes tuberosa* (flower), *Narcissus tazetta* var. *chinensis* (flower), *Lanvandula angustifolia* (inflorescence), *Pogostemon cablin* (plant), *Cymbopogon citratus* (plant), *Panax ginseng* (root, plant), *P. quinquefolium* (root, plant), *P. notoginseng* (root), *Gynostemma pentaphyllum* (plant), *Salvia miltiorrhiza* (root), *Angelica sinensis* (root), *Polygonum multiflorum* (rhizome), *Hippophae rhamnoides* (seed oil).

Conclusion

As a trend worldwide today that human-being favors the way of life back to nature, the transition of the medicare towards disease-free, the prevalence of nature therapy and traditional medicine are becoming more and more predominant. Thus, medicinal plants will play a very important role, and industrial exploitation of medicinal plants will certainly be keeping a key position in this respect. Traditional Chinese Medicine has been used in China for thousands of years, and developing new drugs from traditional drugs is a shortcut. It is necessary to integrate the traditional experiences with modern science and technology. In a drug development program, as the first stage, we could make full use of the collected ethnopharmacologic information by a chemotaxonomic point of view. Selected relevant plant samples for in vitro bioassays include inhibition or stimulation of receptor binding inhibition or stimulation of biochemical reactions and/or inhibition or stimulation of enzyme systems. It is then followed by detailed chemical,

pharmacological and toxicological studies, and eventually clinical trials. On the other hand, many effective prescriptions emerged in practice could also be selected for further detailed multidisciplinary research towards new drug finding. During the process of development of new drugs from medicinal plants, the new pharmacological model for traditional drugs has crucial importance. Moreover, producing active fractions from cell and tissue culture by large - scale bioreactor will become more and more important for supplying the raw materials to pharmaceutical industries.

적 요

중국에서 약용식물은 서양의학과 동등한 수준으로 인간의 건강증진과 유지 및 치료를 위해 매우 중요한 역할을 수행하고 있는데 본 논문에서는 중국에서 약용식물의 산업적 발달에 관해서 간략히 고찰하였다. 현재 중국에서 약용식물로 이용되고 있는 식물은 11,118종에 달한다. 이들 약용식물이 가공되지 않고 천연산물로 이용되는 연간 총 생산액은 60억달러에 달하며 조제형태로 이용되는 총 생산액은 30억달러에 달한다.

지금까지 약용식물로부터 100여종 이상의 신약이 개발되었으며 천연자원에 의존하려는 세계적인 추세를 감안한다면 약용식물의 중요성은 더욱 증대할 것이며 산업적 개발이 인류의 건강을 유지하는데 결정적 역할을 할 것으로 기대된다.

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