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UNITED NATIONS INDUSTRIAL DEVELOPMENT ORGANIZATION
Vienna International Centre, P.O. Box 300, 1400 Vienna, Austria
Tel: (+43-1) 26026-0 · www.unido.org · unido@unido.org

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BETTER UTILIZATION OF MEDICINAL PLANTS: THE PHYTOPHARMACEUTICAL SUPPLY SYSTEM IN CHINA

Sectoral Studies Series
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Janos Pogany

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Main results of the study work on industrial sectors are presented in the Sectoral Studies Series. In addition a series of Sectoral Working Papers is issued.

This document presents major results of work under the element Pharmaceutical Industries in UNIDO's programme of Studies and Research 1986/87.

Preface

This study advocates the cultivation and industrial processing of carefully selected medicinal plants under controlled conditions in developing countries as the only alternative to provide crude drugs and phytopharmaceutical preparations that meet all basic criteria for essential drugs.

The establishment or expansion of a phytopharmaceutical industry has economic advantages, in addition to the social benefits, through the better utilization of domestic resources and potential reduction of imports. It contributes also to the evolution of domestic R+D capability in agronomic, agrotechnical, chemical, medical and pharmaceutical sciences.

Medicinal plants represent also an under-utilized reservoir of new and novel drugs that could be used in the treatment of diseases prevailing in developing countries.

This study has been carried out in the Sectoral Studies Branch by Mr. János Pogány. The Branch wishes to acknowledge the contribution of Mr. Ren Dequan, Vice General Manager, China National Corporation of Traditional and Herbal Medicine, State Pharmaceutical Administration of China, for the provision of essential technical, economic and market data on the phytopharmaceutical industry in the People's Republic of China as well as for the consultations on the Chinese experience in the course of this work.

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EXPLANATORY NOTES

References to dollars ($) are to United States dollars, unless otherwise stated.

A comma (,) is used to distinguish thousands and millions.

A full stop (.) is used to indicate decimals.

A slash between dates (e.g., 1980/81) indicates a crop year, financial year or academic year.

Use of a hyphen between dates (e.g., 1960-1965) indicates the full period involved, including the beginning and end years.

Metric tons have been used throughout.

The following forms have been used in tables:

Three dots (...) indicate that data are not available or are not separately reported.

A dash (-) indicates that the amount is nil or negligible.

A blank indicates that the item is not applicable.

Totals may not add up precisely because of rounding.

Besides the common abbreviations, symbols and terms and those accepted by the International System of Units (SI), the following abbreviations and contractions have been used in this report:

PRC	People's Republic of China
SPAC	State Pharmaceutical Administration of China
Rmb	Renminbi
EEC	European Economic Community
R+D	Research and development
GMP	Good manufacturing practices
WHO	World Health Organization of the United Nations
FAO	Food and Agriculture Organization of the United Nations

KEY WORDS

For the purpose of this study, certain repeatedly used terms are defined as follows:

CRUDE DRUG is a fresh or dried medicinal plant, or parts thereof.

ESSENTIAL OILS are flavouring agents, a sub-group of pharmaceutical necessities, obtained from natural source materials mainly of botanical origin.

HERBS are flowering plants containing chemical substances which may have a therapeutic action.

HERBAL REMEDIES (herbal preparations) are finished or partially finished herbal products manufactured on an industrial scale and marketed without regulatory evidence of efficacy and safety.

MEDICINAL PLANTS are higher plants (unicellular plants, e.g., yeasts, green algae, etc. excluded) containing chemical substances which have a proven and established medicinal action.

MEDICINE is the science and art of restoring and preserving health.

MODERN MEDICINE is the system of medicine practised by physicians.

PHARMACEUTICAL NECESSITIES (pharmaceutical aids, auxiliary substances, inert materials, additives, added substances, excipients) are substances that are of little or no therapeutic value but which are useful in the manufacture and compounding of various pharmaceutical preparations. The subgroups of pharmaceutical necessities are (i) antioxidants and preservatives, (ii) colouring, flavouring and diluting agents, (iii) emulsifying and suspending agents, (iv) ointment bases, (v) pharmaceutical solvents, and (vi) miscellaneous pharmaceutical necessities.

PHYTOPHARMACEUTICAL PREPARATION (phytopharmaceutical product, phytotherapeutic specialty, herbal pharmaceuticals) is the safe and effective finished, or partially finished (e.g. yingpian) product licenced by health authorities for use on or for humans to modify physiological systems or pathological states for the benefit of the patient.

PHYTOPHARMACEUTICALS is a collective name for the total extracts and phyto-pharmaceutical preparations.

TOTAL EXTRACTS are prepared from crude drugs for use, as active components, in the manufacture of phytopharmaceutical preparations. Total extracts may conveniently be subdivided into crude extracts and standardized extracts.

TRADITIONAL SYSTEMS OF MEDICINE are ancient and/or culture-bound approaches of medicine practised mainly by registered paramedical personnel but also by physicians.

YINGPIAN is a semi-finished phytopharmaceutical preparation, basically a tea, made from a crude drug or mixtures thereof, which will be decocted, filtered and taken by the patient.

1. INTRODUCTION

Many essential drugs have been discovered through applied research into ethnomedical claims of the therapeutic effects of medicinal plants. Phytopharmaceuticals also play an eminent role in the primary health care system of several developing countries.

This study reviews the current interest in botanical drugs and describes the phytopharmaceutical supply system of the PRC, in particular the provision of essential drugs through strict quality control and industrial manufacture.

The study has been organized so that the technical details of product registration, the list of medicinal plants included in the official Chinese primary health care manual and the description of a small-scale phytopharmaceutical factory are given in the annexes, whereas a global review of the present situation and various aspects of the phytopharmaceutical supply system in China are discussed in chapters 4 and 5.

The literature review indicated continued interest in phytopharmaceutical production and research mainly in developing countries. There is a worldwide emphasis on clinically proven efficacy and safety as well as on modern quality control standards both in production and sales. The main issue is the standardization of regulatory requirements in industrialized countries whereas developing countries aim at supplying essential phytopharmaceuticals for their health care systems to complement the spectrum of chemical drugs.

Detailed statistics permitted an overview of the historical development and present status of the phytopharmaceutical supply system in China. The key elements of success of the Chinese phytopharmaceutical industry were identified and criteria were established for the establishment and/or modernization of a phytopharmaceutical industry in developing countries. The creation of a network of research centers was recommended in order to foster better industrial utilization of medicinal plants in developing countries.

Methodological problems encountered during the study included the use of terms such as "drugs of plant origin", or "herbal industry", etc., with different connotations in the literature. The Chinese industrial and market statistics refer sometimes to traditional "medicine" prepared from natural substances and the figures could not be disaggregated into plant-derived, animal and mineral groups. Nonetheless, both the therapeutic and industrial importance of phytopharmaceuticals could be substantiated. Pharmaceutical necessities of botanical origin such as cocoa butter, acacia, essential oils, etc. have been given low priority. Borderline cases, e.g. castor oil used as a laxative and an emollient have also been disregarded, in particular when such products are traditionally processed outside the pharmaceutical industry. The study does not deal with traditional drugs of animal and mineral origin. Plants used as source materials of building blocks for the synthesis of pharmaceutical chemicals are discussed in another UNIDO study under publication.

2. BACKGROUND

A genuine interest in the many traditional systems of medicine exists among physicians and growing numbers of practitioners of traditional, indigenous and alternative systems are beginning to accept and use modern technology.[1/] The contribution of the WHO's traditional medicine programme to "Health for all by the year 2000" is potentially great. The WHO main objectives are to pursue action at national level on the regulatory evaluation of phytopharmaceuticals, their integration in the health-care system and the training of traditional medicine practitioners. Twenty-one WHO collaborating centers for traditional medicine have been established worldwide and strengthen national efforts in R+D. The network also serves to collect and disseminate information on both useful and harmful traditional practices.

FAO has compiled an initial list of 22 medicinal plants, used as raw materials for drug production in the early 1980s and publishes a newsletter on the activities of a global network of botanists. This work is coordinated by the FAO collaborating centre, the Research Institute for Medicinal Plants Budakalász, Hungary.

The Second Consultation on the Pharmaceutical Industry recommended that UNIDO should "develop guidelines to assist developing countries to accomplish the improved supply of medicinal plants as raw materials or as processed products" and "continue to encourage and promote active collaboration among developing countries and between developed and developing countries in all areas concerning the better industrial utilization of medicinal plants and the development of the pharmaceutical industry for medicinal plants."[2/] The Government of the People's Republic of China and UNIDO jointly organized a Workshop on the Pharmaceutical Industry where Chinese experts presented seven papers on the various aspects of Chinese traditional medicine.[3/] National experts from Bangladesh, Burundi, Kenya, Malaysia, Nepal, Romania, Sri Lanka, Tanzania, Turkey and Zambia presented papers on some technical, health and government policy aspects of traditional medicine in their countries. UNIDO programmes on the industrial utilization of medicinal and aromatic plants were also outlined at the meeting.

1/ Traditional medicine and health care coverage, WHO, Geneva (1983)

2/ Report, Second Consultation on the Pharmaceutical Industry, Budapest, Hungary, 21-25 November 1983, p. 10.

3/ UNIDO/IO.121 and IO.6'5: Proceedings of the workshop on the pharmaceutical industry (combined modern-traditional pharmacy) for promoting technical co-operation among the developing countries, 1-14 November 1982, Beijing and Hangzhou, China, Parts I (1984) and II (1985).

3. OBJECTIVES

The immediate objectives of the report are: (i) to provide basic information for industrial decision-makers involved in the development of a pharmaceutical industry based on medicinal plants; (ii) to provide a source of information on the development of the phytopharmaceutical industry in the PRC; and (iii) to promote the use of modern technology and management in the industrial production of phytopharmaceutical preparations in developing countries.

The long-term objectives are: (i) to foster active collaboration among developing countries and between developing and industrialized countries in mutually beneficial areas of the phytopharmaceutical industry; and (ii) to assist developing countries in the establishment, expansion and modernization of their pharmaceutical industry.

The study also intends to support the Traditional Medicine Programme of WHO by describing a supply system which provides safe and effective phyto-pharmaceutical preparations of good quality at the lowest possible cost for the health care of large segments of the population in developing countries. "First-class medicine for all" would also contribute, in the long run, to the improved economic performance of many people.

Another and broader objective is the stimulation of new thoughts and attitudes among researchers and industrial managers involved in the development and operation of the phytopharmaceutical industry.

4. LITERATURE REVIEW OF THE HERBAL PHARMACEUTICAL INDUSTRY WORLDWIDE

4.1 Medicinal plants

Medicinal plants had been much the same for about 4,000 years. In the 19th century, the apothecary collected many of the vegetable drugs and, from them, made simple mixtures and preparations prescribed by the physician. Chemical and pharmaceutical manufacturing had become well established in industrialized countries by about 1830 when pharmacists started to rely upon commercial sources of standardized phytopharmaceuticals. Although the first 32 synthetic drugs including acetylsalicylic acid, phenacetine and barbitone were developed in Germany at the end of the 19th century, phytopharmaceutical drugs played an eminent role in medicine worldwide until the late 1930s. The active ingredients of some medicinal plants were unknown until the 1960s because the available methods of separation, structure elucidation and quantitative analysis had not permitted the identification of complex chemical structures and the quality control of phytopharmaceutical production. The accuracy of the dosage and, therefore, the consistent therapeutic effect could not be measured and/or scientifically documented. Major advances have been made in research methodology and quality control of phytopharmaceuticals over the last 20 to 30 years. Improved techniques of isolation, coupled with new levels of precision and sensitivity of chemical analysis, provided means for the qualitative and quantitative determination of drug principles for the first time or served to replace more costly and time-consuming biological assays. From 1960 on, still further advances in the techniques of drug standardization continued to revolutionize the various emphases on and approaches to tests and standards. These advances permit that scientific criteria are used for the evaluation of product quality and process reliability which form the basis of all pharmacological investigations. Hence, the major technical barrier of development has been removed and phytopharmaceuticals represent just a class of over-the-counter or prescription drugs.

Rural populations in Bolivia, China, Egypt, India, Mexico, Nigeria, Pakistan, etc. continue to rely on phytopharmaceuticals for specific illnesses and conditions. This situation is expected to continue in the forthcoming decade because the physicians trained in modern medicine have not reached even small-size towns yet. It has logically been assumed that the health and economic importance of the current and future domestic market for phytopharmaceuticals is significant in these countries and that their experience might be relevant and transferrable to other developing countries. Comparable international statistics and technical records on the demand and supply of herbal pharmaceuticals are not available. Secondary sources contained qualitative and descriptive information on the following developing countries: Bangladesh, China, Egypt, Ghana, India, Indonesia, Kenya, Republic of Korea, Mexico, Nigeria, Paraguay, the Philippines, Senegal and Tanzania.

In Bangladesh, the National Drug Policy entered into force in June 1982. The new legislation introduced government control, among others, for phytopharmaceuticals. A number of phytotherapeutic preparations were banned. Identification of active ingredients, standardization of both the manufacturing process and quality control were included among the industrial

objectives. At present, however, the Drug Administration authority does not have enough resources for the effective monitoring of this segment of the pharmaceutical market.[4/]

In Egypt, details of a three-year joint quality control study of the Cairo and Texas Southern universities were recently published. Microbial contaminations were found in some herbal preparations on sale in Egypt and traditionally used in many parts of the Middle East. Other products contained toxic substances caused by faulty storage. Inaccurate labelling of ingredients was found to be another problem.[5/]

In Ghana, the roots of a Ghanaian plant, Cryptolepis sanguinolenta, are studied for their antimalarial effect. The isolated active ingredient is cryptolepine, an alkaloid with a strong antimicrobial activity.[6/]

In India, the Ayurveda, Siddha and Unani systems of medicine are widely practised. There were more than 200,000 registered practitioners, more than 23,000 dispensaries, 441 hospitals and 116 colleges of Indian systems of medicine in 1982. 3,349 units were licenced to manufacture herbal pharmaceuticals but their contribution to the total production was only marginal. The machinery for the collection, production and marketing of these drugs was not centrally regulated. A legal quality control mechanism existed but was found only partially implementable due to the absence of pharmacopoeial quality and industrial manufacturing standards. Important steps towards future development included the publication of the Ayurvedic Formulary of India (Part 1), the list of drugs of vegetable origin currently imported and suggested for experimentation on domestic cultivation and the list of medicinal plants for export. A sub-group on indigenous systems of medicine was established within the Working Group of the National Drugs and Pharmaceutical Development Council to consider comprehensively the evolution of herbal pharmaceuticals used in India.[7/] The Indian Central Drug Research Institute has applied for the marketing approval of a new drug derived from the Indian guggul which has been found effective in reducing the level of cholesterol and other fatty acids during multi-centre clinical trials.[8/] An extract of Phyllanthus niruri reduced the deposition of lipids in the liver, brain, kidneys and heart of rats given alcohol in their diet and may, therefore, be a lead for a hepatoprotective agent.[9/] The leaf extract of Eucalyptus lanceolatus inhibited the growth and sporulation of five fungal species and extracts of Eucalyptus globulus were found more effective than nystatin against Microascus cinerens and Phialophora bubaki.[10/] Exports of medicinal plants were valued at Rs 791.7 million ($US 63 million) in 1984-85,

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4/ Tiranti, D.J.: Essential drugs. The Bangladesh example - four years on 1982-1986, pp. 10-11 (1986).

5/ IMS Marketletter, 9 February 1987, p. 27.

6/ IMS Marketletter, 7 May 1984, p. 13

7/ Indigenous systems of medicine, The Eastern Pharmacist, August 1984.

8/ SCRIP No. 936, 1 October 1984, p. 23.

9/ SCRIP No. 1031, 4 September 1985, p. 18.

10/ SCRIP No. 1073, 3 February 1986, p. 21.

an increase of 80.5 per cent over the 1983-84 figure of Rs 438.7 million. Exports of Rs 213.6 million were reported in 1982-83.[11] A compound isolated from the plant Plumbago zeylanica can reduce tumor growth by 70 per cent. United States studies also reported tumor regression and prolonged life of rats with induced lymphocytic leukaemia.[12]

In Indonesia, herbs and phytopharmaceutical preparations should comply with Ministry of Health regulations. Blue or green circles with the registration numbers must be displayed on the label.[13]

In Kenya, the Medical Research Institute is about to begin clinical trials on various medicinal plants widely used in African traditional systems of medicine.[14]

In the Republic of Korea, the 1986 exports of ginseng and ginseng preparations from amounted to $US 96.3 million.[15] About 15 pharmaceutical companies manufacture 68 different kinds of extracts to herbal clinics and hospitals. Phytopharmaceuticals are reimburseable under the medical insurance system.[16]

In Mexico, historical, biological, ethnobotanical, clinical and chemical publications from 1529 to 1982 were reviewed on zoapatle, the Montanoa tomentosa (Cerv.) subspecies tomentosa (Funk.), which has been used in the form of a crude aqueous extract in the Mexican ethnomedicine as an interceptive agent for over 500 years. The article could serve as an evolution model of the pharmaceutical industry because it describes the ancient use of the plant in the Aztec medicine; the transfer of knowledge to Europe in the 16th century; the first domestic research programme on the Mexican flora from 1888 to 1914 including five medical communications on zoapatle; the long way to isolate the active principles between 1894 and 1974 when the first patent application on the isolation and chemical characterization of two novel oxepane terpenoids was filed by the Mexican Social Security Institute in the United States; the delay caused by the selection of an unappropriate model for animal pharmacological investigations; the chemical total synthesis of the two new terpenoids; and recent toxicology tests and clinical trials. It is worth mentioning that nine compounds of complex chemical structure were isolated from zoapatle and five of them have not yet been tested for biological activity. An important conclusion of the article is to seriously consider the use of aqueous zoapatle extract, or a preparation thereof, made from plants grown and processed under controlled conditions in order to assure predictable and reproducible clinical effects at minimum cost to the patient.[17]

11/ SCRIP No. 1109, 9 June 1986, p. 21.

12/ SCRIP No. 1139, 22 September 1986, p. 22.

13/ SCRIP No. 1051, 13 November 1985, p. 20.

14/ SCRIP No. 1139, 22 September 1986, p. 22.

15/ IMS Marketletter, 16 February 1987, p. 14.

16/ SCRIP No. 1198/9, 22/24 April 1987, p. 24.

17/ Gallegos, A.J.: A traditional remedy from Mexico emerges to modern times. Contraception, 27, March 1983, pp. 211-225.

In Nigeria, the Federal Ministry of Health encourages research into traditional systems of medicine and sponsors a research project on the efficacy of drugs which have been claimed beneficial in the treatment of diabetes.[18/] Tests are to be carried out in five teaching hospitals with an antisickling agent derived from the root of Fagara tree. The general research programme includes also identification of the Fagara variety that yields the largest quantity of active ingredient as well as extraction and dosage form process R+D, and toxicity testing.[19/] The National Council of Traditional Medicine Practitioners outlined its objectives at a recent conference in Lagos. These include the intensification of efforts to produce various dosage forms of drugs from Nigerian medicinal plants and the establishment of botanical gardens throughout the country to prevent extinction of rare medicinal plants.[20/]

In Paraguay, university researchers identified more than 200 chemical compounds, derived from traditional folk remedies, as potential drug candidates.[21/]

In the Philippines, a programme was initiated in 1977 to provide safe, effective, cheap and readily available phytopharmaceuticals for the rural poor. The folkloric uses of medicinal plants have to be scientifically validated before they are accepted medically. So far ten total extracts of medicinal plants in 21 phytopharmaceutical preparations have completed satisfactory clinical trials (table 1).

Four phytopharmaceutical preparations -derived from Mentha cordifolia, Vitex negundo, Blumea balsamifera and Carmona retusa- have been registered with the Bureau of Food and Drugs and patented by the Philippine Plants Office. Pharmacological and phytochemical investigations began in the Philippines in the 1920s and it has become an academic subject to train students in research methodology.[22/]

In Senegal, university researchers prepared and tested a cough syrup based on the guera plant. A herbal laxative project shows also promising results. These two items could save the country and estimated $US 670,000 in foreign exchange per year.[23/]

18/ SCRIP No. 1143, 6 October 1986, p. 19.

19/ SCRIP No. 1181, 20 February 1987, p. 19.

20/ SCRIP No. 1193, 3 April 1987.

21/ SCRIP No. 1139, 22 September 1986, p. 22.

22/ IMS Marketletter, 27 October 1986, p. 26.

23/ SCRIP No. 1139, 22 September 1986, p. 22.

Table 1. Phytopharmaceutical R+D in the Philippines

Active ingredient	Dosage form	Strength	Indication
Vitex negundo L.	tablet	300 mg	expectorant
Mentha cordifolia Opiz	tablet	250 mg	analgesic
Ocimum basilicum L.	decoction tablet	10% 300 mg	antitussive
Blumea balsamifera L.	tablet	250 mg	diuretic
Psidium guajava L.	decoction decoction	10% 20%	antidiarrheal, antispasmodic for bed sores, as mouth wash
Carmona retusa Vahl	decoction tablet	10% 250 mg	antidiarrheal, antispasmodic
Garcinia mangostana L.	tablet	300 mg	antidiarrheal
Quisqualis indica L.	tablets	500 mg	anthelmintic
Leucaena leucocephala Lam	powder suspension		anthelmintic
Cassia alata L.	fresh juice decoction lotion	 50%	antifungal

In Tanzania, 134 crude extracts of indigenous plants used in traditional medicine were screened for in vitro antibacterial activity. 59 crude extracts were active against Staphylococcus aureus and eleven inhibited the growth of Escherichia coli. Acacia robusta Burch and Harrisonia abyssinica Oliv. showed the highest activity.[24/]

The West African Pharmaceutical Federation has compiled a sub-regional phytopharmacopoeia in an attempt to encourage research in the use of herbal drugs in the geographical area and help to ensure a high level of safety for phytotherapeutic agents.[25/]

24/ Journal of Medicinal Plant Research, Supplement, pp. 91-97 (1980).

25/ SCRIP No. 848, 21 November 1983, p. 13.

Government policies toward the phytopharmaceutical industry are being reviewed also in industrialized countries. The general tendency is that manufacturers of herbal and chemical drugs should be treated in the same way. As an illustrative example to support this statement, EEC directive #75-319 stipulates that review dossiers for licencing the sales of phytotherapeutic specialities (for which marketing approval was granted before 30 June 1976) must be submitted before 30 June 1988. Preparations will be classified according to their indications. In the case of over-the-counter preparations, efficacy and safety data from the literature are normally accepted, but the chemical and pharmaceutical documentation should reveal the manufacturer's own research findings, quality control methods and process technology. Complete registration documentation including toxicological, pharmacological and clinical investigations is required for prescription drugs. Such documentation outlined in annex 2 is also the scientific evidence that the production system is under sufficient control to assure consistent quality and accurate dosage of phytopharmaceutical preparations. The overall objective of the international registration programme is to remove all non-tariff trade barriers, therefore, to create a single integrated EEC market.

In Germany, the administration of 3 x 40 mg/day of Ginkgo biloba extract for 12 weeks, produced a significant improvement, in double-blind clinical trials, in reaction times and related parameters in geriatric patients suffering from deterioration of mental performance and vigilance. In contrast, hardly any improvement could be achieved in healthy subjects with a good initial condition.[26/]

In Japan, the Ministry of Health and Welfare published an Approval Standard of 210 Prescriptions of Chinese traditional drugs and remedies in 1972. 164 crude drugs of botanical origin are official in the Japanese pharmacopoeia and about 60 others such as liquorice, rhubarb, angelica, ephedra, etc. are also used frequently. The market value of some 164 compositions of traditional Chinese drugs and herbal remedies was 74.8 billion yen ($US 32.2 million) in 1984 which represented 12 to 13 per cent of the non-prescription market.[27/]

The U.S. National Academy of Sciences concluded that nearly half the herbal claims from China are supported by some scientific rationale. Catharanthus, Heliotropium, Maytenus, Podophyllum and Tripterygium are major sources of anticancer drugs in China. It is safe to predict that more modern anti-cancer drugs will be developed from these plants.[28/] The NAPRALERT (NAtural PRoducts ALERT) database, maintained in the University of Illinois, represents an effort to survey, collect and computerize world literature on natural products beginning with the year 1975. Currently the database contains more than 800 million bytes of information taken from more than 70,000 scientific reports. More than 23,000 species of higher plants are listed. Information on specific plants includes ethnomedical (folkloric, traditional) uses, cultivation techniques, genetic improvement, experimental pharmacology of plant extracts, chemical active ingredients, abstracts of

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26/ Arzneimittel Forschung, 35 (II), p. 1459 (1985).

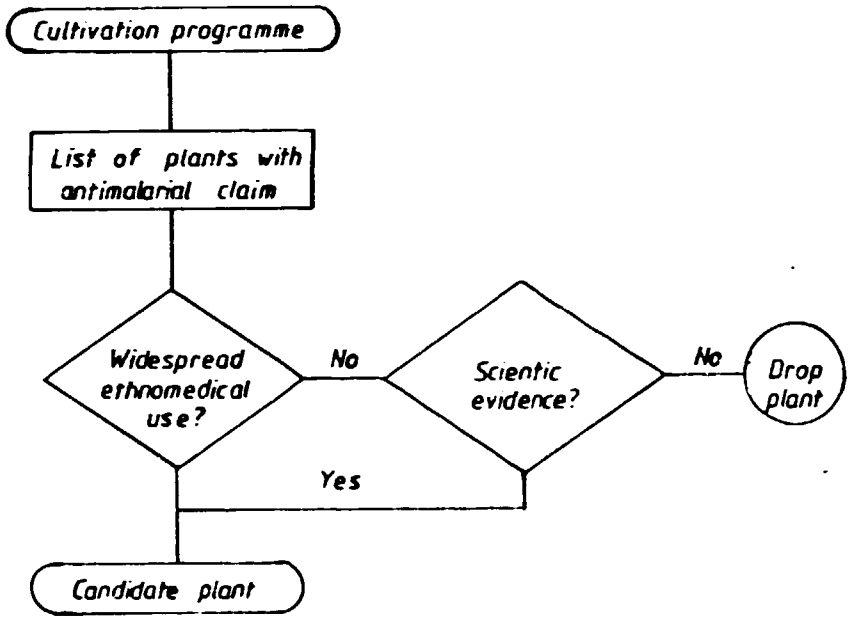
27/ IMS Marketletter, 27 October 1986, p. 25.

28/ Parallels in Chinese and Amerindian Phytotherapy, p. 45.

industrial processes such as cell/tissue culture and so on. Through an agreement with WHO, NAPRALERT data are provided free of charge to developing countries.[29]

Figure 1 shows a possible use of the NAPRALERT system for the selection of medicinal plants with antimalarial effect for domestic cultivation. The database lists all ethnomedical claims. Each member of this population should individually be investigated. Multiregional ethnomedical use or scientific evidence of the effect are the main criteria for the first selection of a medicinal plant for further study.

Figure 1. Computerized selection of medicinal plants for domestic cultivation



29/ IMS Marketletter, 27 October 1986, p. 27.

In the United Kingdom, an investigation into the antidiabetic effects of herbal folk remedies from China, Europa, Pakistan and the West Indies -sponsored by the Medical Research Council and carried out at Aston University- has revealed that some extracts lower blood glucose concentrations without stimulating insulin secretion. This suggests that the extracts may either potentiate insulin's action or act independently of insulin.[30/]

Frequently recurring views on phytotherapy include that: (i) natural products are generally considered as safe when some of them are toxic (carcinogenic, mutagenic, teratogenic, etc.); (ii) unreliable claims are imprudent without intimate knowledge of the agent used; (iii) part of the medical usefulness of phytopharmaceuticals lies in their placebo effect which, in turn, assumes limited use under professional control; and (iv) pharmaceutical preparations should be manufactured from the chemical active ingredient(s) once the pharmacon(s) is/are isolated from the extract. In a little modified form, statements (i), (ii) and (iii) could apply also to chemical drugs, therefore, these views are not particular to phytotherapeutic agents.

4.2 Essential oils and pharmacopoeial phytopharmaceuticals

Essential oils are obtained from natural source materials, mainly plants, by distillation, usually with water and steam or, less frequently, by compression, e.g., in the case of citrus fruits. Essential oil concentrates such as concretes, absolutes, spice oleoresins, etc. are manufactured by extraction with water or non-aqueous solvents.

4.2.1 Essential oils

Lawrence, B.M. reviewed the world production 1984 of essential oils, listed major suppliers and gave production quantities for 168 essential oils. Suppliers of additional 61 essential oils of unknown production quantities were also listed.[31/]

A recent study[32/] describes the current supply position of selected major producers in 18 developing countries and the market trends in the United States, Canada, Western Europe and Japan. The main conclusions of the study are quoted below.

The natural essential oils industry is declining as a result of competition from synthetic substitutes. Besides being cheaper, synthetics have several advantages and the tendency is to use them when they exist. As a result, the prices of natural essential oils are very depressed. Many developing country producers are unable to recover their production costs and are shifting to alternative crops, largely food crops whose prices are tending to rise.

30/ SCRIP No. 912, 10 July 1984, p. 20.

31/ Perfumer and Flavorist, Vol. 10, October/November 1985, pp. 2-16.

32/ Essential oils and oleoresins. A study of selected producers and major markets, International Trade Center UNCTAD/GATT, Palais des Nations, 1211 Geneva 10, Switzerland (1986).

The existence of favourable soil and climatic conditions is therefore not sufficient for considering entry into the export trade in essential oils. It is the opportunity cost of producing these oils that is the chief determining factor.

The above notwithstanding, several developing countries have in recent years been highly successful in producing and exporting essential oils and in penetrating new markets.

The other implications for existing and potential producers of the current state of the world market for essential oils are as follows:

(a) More strenuous efforts are required to minimize unnecessary year-to-year variations in the supply of natural essential oils in view of the steady availability of most synthetic substitutes. This would reduce the price fluctuations which have done so much to dampen trade confidence in the products under review.

(b) There is a need for a more regular flow of information down the marketing chain from producer to end-user on anticipated supply outturns, in order to facilitate cushioning against unavoidable supply fluctuations.

(c) Submitted samples must not differ measurably or subjectively in quality and character from the consignments from which they are said to be drawn. This aspect has been the subject of numerous complaints.

(d) For many oils increased pre-shipment quality inspection is required to minimize the use of damaged or otherwise unsuitable drums, reduce adulteration practices, and prevent excessive contamination with foreign matter resulting from poor distillation procecures, inadequate filtering, etc.

(e) In some cases there is a need for greater adherence to recognized trading and documentation procedures, and in particular, strict observance of delivery dates.

(f) Prospective producers should co-ordinate their plans with potential buyers from an early stage rather than attempt to launch new products or traditional products from unfamiliar producing regions entirely on their own. Early submission of samples with a view to obtaining comments from buyers before commencing commercial production is vital, as is detailed negotiation of price levels and schedules.

(g) The practice of withholding supplies for a time in order to drive prices up cannot be deprecated too strongly. It has had the reverse effect to that intended, with permanent loss of part of the market.

The above conclusions also generally apply to spice oleoresins. The main emphasis will, however, need to be on the achievement and maintenance of a high, consistent level of product quality in close and constant liaison with overseas buyers. At present there are few problems concerning trading and marketing procedures, or packaging, but it cannot be over-emphasized that a new producer cannot expect successfully to market spice oleoresins on the open market if there have been no prior consultations with prospective buyers. Such consultations are even more indispensable for spice oleoresins than for essential oils.

Appendices of the same study give time series of annual average prices 1975-1985, price ranges for the same period, and tariffs from publicly available sources; list of importers, dealers, merchants and processing/compounding houses in industrialized countries; and a list of standards issued by ISO[33] on essential oils and oleoresins.

4.2.2 Pharmacopoeial phytopharmaceuticals

There are three main differences between phytopharmaceuticals and essential oils. First, the source materials for the manufacture of essential oils are plants with little or no therapeutic value. Secondly, the dominant end-users of flavoring agents are the cosmetic and the food processing industry. Thirdly, major producers of flavoring agents in developing countries depend mainly on exports to industrialized countries.

A group of phytopharmaceuticals, the crude drugs and total extracts official in the pharmacopoeias worldwide behaves in a way very similar to that of essential oils. Their use is declining due to competition from synthetic drugs. Non-pharmaceutical uses have a strong impact on demand, e.g., liquorice is chiefly used and its price is set by the confectionary industry. The prices are depressed on the world market also as a result of intense competition among suppliers from both developing and industrialized countries. In fact, the trend pattern is basically the same as that for any commodity goods in a market situation when supply is regularly higher than demand. The main barriers to entry are, therefore, competitive price and established good business image that can come only from other kind of business with the same buyers.

4.3 Conclusions

Herbal drugs represent a historical stage, from about 1880 to the late 1930s, in the evolution of the pharmaceutical industry in the industrialized countries. The active ingredients isolated from many of the phyto-pharmaceuticals of that stage are essential drugs today. The know-how acquired from the development and operation of medicinal plant processing factories has contributed to the general evolution of research methodology in the pharmaceutical industry.

Phytopharmaceutical preparations and herbal remedies play an important role also in current day's human therapy and represent a steady, mature market worldwide. Publicly available statistical data on demand and supply of phytopharmaceuticals do not permit quantitative assessment of the world market in general, and on specific plant level in particular.

The reviewed literature references indicate continued interest in phytopharmaceutical production and research mainly in developing countries. There is a worldwide emphasis on clinically proven efficacy and safety. Modern quality control standards in the production and sales are also generally emphasized.

33/ International Organization for Standardization, 1-3, rue de Varembé, 1211 Geneva 20, Switzerland.

A large part of the rural population depends on traditional systems of medicine in developing countries where physicians are scarcely or not accessible and the purchasing power of the people is low.

Plants used in traditional systems of medicine offer therapeutic alternatives for the treatment of diseases prevailing or important also in developing countries, e.g., microbial infections, malaria, cancer, etc. They play an important role also in population control.

Manufacturers from developing and industrialized countries could co-operate in the harmonization of industrial quality standards and methodology with the view of saving time and cutting costs of preparing registration dossiers (annex 1) acceptable worldwide or at regional levels.

Developing countries should co-operate in the improvement of the specification of phytopharmaceutical preparations used in the treatment of diseases prevailing in the Third World.

Active international co-operation takes place between developing and industrialized countries to investigate scientifically leads from ethnomedicine.

Producers of pharmacopoeial dried medicinal plants, crude drugs and extracts should establish themselves first in the domestic drug market because this does not require much additional investment from those who cultivate medicinal plants and manufacture phytopharmaceuticals.

The economic importance of essential oils is small in the pharmaceutical industry. Domestic production of essential oils and oleoresins should only be considered if the results of a techno-economic feasibility study offer good returns on investment from current and future domestic sales of these products to the local cosmetic and food-processing industry.

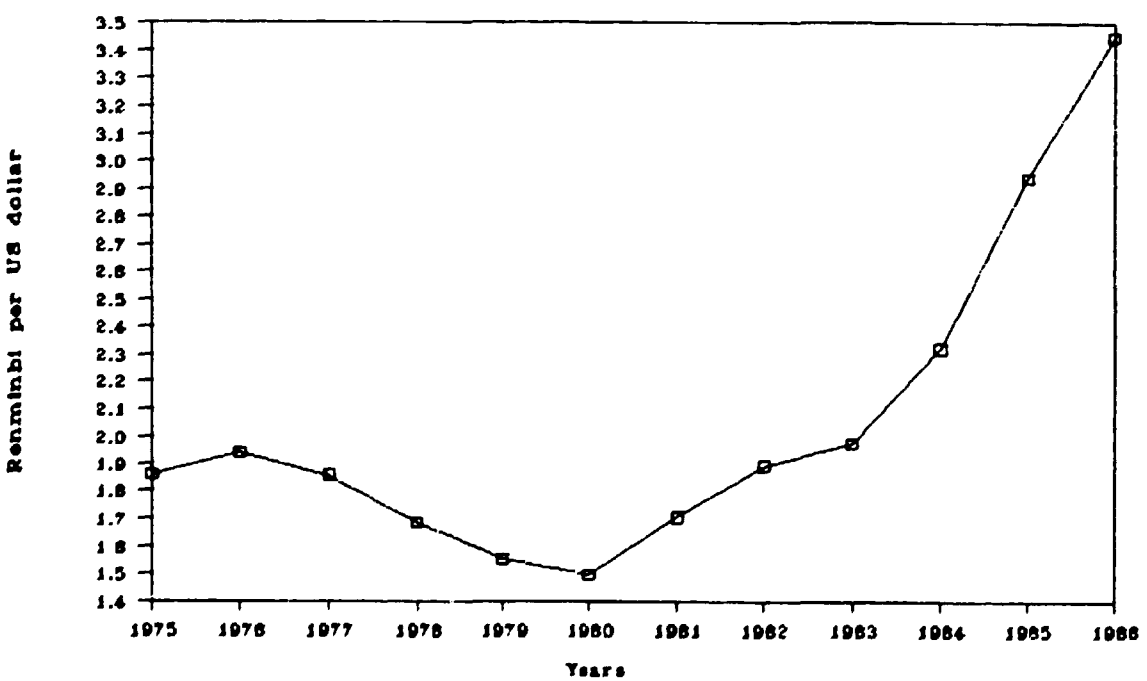
5. THE PHYTOPHARMACEUTICAL INDUSTRY IN CHINA

The documented historical basis of phytotherapy in China dates back to about 2,000 years. Today's official policy recognizes traditional, modern and integrated systems of medicine. The current Drug Administration Law of PRC was published in 1984. Crude drugs and yingpian are discussed in separate chapters. Phytopharmaceuticals are treated together with chemical drugs as regards new product R+D, registration, production, distribution and independent quality control of all activities by the Ministry of Health. Manufacturing premises are licenced and inspected by the Drug Administrations of the 21 provinces, 5 autonomous regions or 3 municipalities, respectively. Current GMP regulations have been drawn up also for phytopharmaceuticals and are gradually implemented. Ex-factory, wholesale and retail prices, in some cases only price ranges, of drugs including phytopharmaceuticals are fixed by the central government and regularly checked by the Price Control Administration. Premises for the wholesale and retail distribution of drugs are approved and inspected by the local government. There are both modern and traditional schools of pharmacy in China. Pharmacognosy remains an important part of pharmacy education in both colleges. The Institute of Materia Medica in Shanghai is devoted to research on the chemistry of natural products. Results of experimental and clinical pharmacological investigations are published in the Acta Pharmacologica Sinica.

5.1 General statistical considerations

The monetary unit in China is the Renminbi (Rmb) denominated in yuan. The Rmb exchange rate is adjusted according to the movements in the value of a basket of internationally traded currencies. The official exchange rate has applied to all foreign transactions since the 1 January 1985. The annual arithmetic average Rmb exchange rates (figure 2) are useful and necessary for international sectoral comparison but current $US values should be handled with care because they distort the Rmb trends since the national currency has continuously been devaluaed against the $US in recent years.

Figure 2. Historical trend in the exchange rate of the Chinese national currency



The Rmb values of total pharmaceutical sales are undervalued because the prices of drugs were reduced thrice between 1975 and 1985, whereas the consumer price index increased from 88 to 111.7 during the same period. Therefore, the current Rmb pharmaceutical statistics represent an unusual case because they should be inflated rather than deflated to arrive at constant value figures.

5.2 Industrial and market statistics

The China National Corporation of Traditional and Herbal Medicine - as an integral part of the State Pharmaceutical Administration of China, the central organization in charge of the administration, production and domestic distribution of drugs - was established in the early 1950s and is responsible for the cultivation, collection and distribution of medicinal substances of natural origin as well as for the industrial production of phytopharmaceutical preparations. One of its first activities was to turn the small processing workshops attached to drugstores into pharmaceutical factories using modern equipment, technology and management methods. As a result, a new branch of modern industry was reborn about three decades ago.

Altogether, 300,000 persons are working in the factories and traditional medicine drugstores all over the country. The annual output of traditional drugs is 700,000 tons. About 5,700 kinds of natural substances, mainly medicinal plants, are processed into 3,000 yingpians and registered preparations. The share of factory-made traditional drugs has continuously increased in the total pharmaceutical consumption from 1978 to 1985 (table 2). In remote mountain districts of the country, yingpian and phytopharmaceutical preparations account for as high as 90 per cent of the drug consumption.

Table 2. Sales 1975-1986 of pharmaceuticals and traditional drugs in China

Year	Total sales		Traditional drugs		Percent share
	Rmb (million)	$ (million)	Rmb (million)	$ (million)	
1975	5,942	3,195	650	350	10.9
1976	6,230	3,209	677	350	10.9
1977	6,770	3,644	743	400	11.0
1978	7,072	4,200	768	456	10.9
1979	7,432	4,779	900	579	12.1
1980	7,809	5,211	1,043	696	13.4
1981	8,377	4,914	1,276	749	15.2
1982	9,359	4,945	1,531	809	16.4
1983	10,579	5,354	1,817	920	17.2
1984	11,423	4,923	2,016	869	17.6
1985	12,061	4,107	2,170	739	18.0
1986	13,600	3,930	2,450	710	18.0

Source: SPAC; 1986 figures are UNIDO estimates.

Table 3 shows some important data of the factory-made traditional drug industry. Of the 519 establishments in 1985, about 10 employed more than 1,000 persons. The highest value of shipments in a single factory was $US 20 million per year. The price structure in 1982 was as given below:

Manufacturer's selling price	100
Wholesaler's selling price	119
Retailer's selling price	137

Table 3. Production statistics 1957-1986 of Chinese traditional pharmaceutical factories (ex-factory price)

Year	Number of establish-ments	Number of employees	Gross output Rmb (million)	Gross output $ (million)	Gross output tons (thousand)	Value added Rmb (million)	Value added $ (million)
1957	...	...	30	12	...	...	...
1958-75	...	...	...	...	...	...	...
1976	...	...	541	279	...	...	...
1977	...	...	571	307	...	...	...
1978	...	...	632	375	...	...	...
1979	269	...	696	448	78	158	102
1980	352	...	871	581	84	219	146
1981	402	86,885	1,095	642	103	297	174
1982	409	98,584	1,352	714	130	409	216
1983	427	104,429	1,600	810	141	478	242
1984	476	110,303	1,780	767	137	569	245
1985	519	118,842	2,094	713	156	715	243
1986	535	125,000	2,360	680	160	810	234

Source: SPAC; 1986 figures are UNIDO estimates.

About 6,000 phytopharmaceutical preparations are distributed in about 40 dosage forms containing 3,800 natural components, mainly medicinal plants. Traditional Chinese medicine is a subject in the curriculum of schools of medicine. There are special colleges for the university education of traditional doctors and are special hospitals for traditional medicine. Each hospital has at least one department for such therapy. More than one million part-time primary health care workers -chijiao yisheng- are trained to treat the commonest and recurrent diseases. The medicinal plants included in their pharmacological manual are listed in annex 2. Table 4 shows the active ingredients and therapeutic use of the market leader products. Table 4 illustrates that the typical phytopharmaceutical preparations are sold mainly in oral dosage forms. The solid dosage forms dominate the sample population. The majority of the crude drugs are medicinal plants but substances of animal origin are also listed in three preparations and a synthetic chemical in one preparation, respectively. The indications are usually well defined and have a therapeutical importance in many developing countries.

Table 4. Typical 25 Chinese traditional drug preparations

Name	Dosage form	Main active ingredients	Indications
Liu Shen Wan	pills	Venenum bufonis Moschus Borneolum syntheticum	Tonsillitis and parotitis
Ganmao Juire Chongji	granules	Fructus forsythiae Folium isatidis Radix isatidis	common cold parainfluenza upper respiratory tract tonsillitis
Annao Niuhuang Pian	tablets	Calculus bovis Rhizoma coptidis Margarita Flos Magnoliae	influenza epidemic encephalitis B. tonsillitis
Donglin Cao Pian	tablets	Herba rabdosiae rubesentis	acute tonsillitis laryngitis pharyngitis
Xinhuang Pian	tablets	Radix pseudoginseng Herba sarcandrae Calculus bovis	cholecystitis acute ictero-hepatitis some sores and inflammations
Xiao Luo Tong Pian	tablets	Rhizoma genkwa	rheumatic arthritis
Shanjin Pian	tablets	Rhizoma smilacis scobinicaulis Spora lygodii	acute and chronic pyelonephritis
Hugan Pian	tablets	Herba artemisiae scopariae Radix bupleuri bile	chronic and persistent hepatitis, hepatocirrhosis
Jigucao Wan	capsules	Herba abri fruticulosi Calculus bovis bile	acute and chronic hepatitis cholecystitis
Biyan Pian	tablets	Fructus xanthii Flos magnoliae Fructus schisandrae	acute and chronic rhinitis
Shexiang Baoxin Wan	pills	Moschus Radix ginseng Storax	Angina pectoralis myocardial infarct chest oppression
Ningxin Bao	capsules	Chinese caterpillar fungus	sinus arrhythmia

(continued)

Table 4. Typical 25 Chinese traditional drug preparations (continued)

Name	Dosage form	Main active ingredients	Indications
Fugang Danshen Pian	tablets	Radix salviae miltiorrhizae Radix notoginseng Borneolum syntheticum	chest oppression angina pectoris
Yuquan Wan	pills	Radix trichosanthis Radix ophiopogonis Radix rehmanniae	diabetes
Lidan Paishi Pian	tablets	Herba lysimachiae Radix curcumae Cortex magnoliae officinalis	cholecystitis cholecystolithiasis
Paishi Chongji	tablets	Herba lysimachiae Caulis akebiae Semen plantaginis	nephrolithiasis
Geng Nian An	capsules	Radix rehmanniae Rhizoma alismatis Cortex moutan radicis	climacteric syndrome
Bai Feng Wan	pills	Radix paeoniae alba Radix codonopsis pilosulae Rhizoma corydalis Fructus amomi	gynesic anemia menoxemia
Qizao Chongji	granules	Radix astragali Fructus jujubae	aleukocytosis
Shuang Bao Su	oral liquid	Radix ginseng Royal jelly	improving appetite and metabolism
Ciwujia Chongji	granules	Radix acanthopanacis senticosi	neurasthenia, insomnia, anorexia
Sanhua Jianfei Cha	tea	Flos rosae rugosae Semen pharbitidis Flos jasmini sambac	exogenous obesity
Jingwan Huong	ointment	Radix sanguisorbae Radix angelicae sinensis	thermal burn
Sports injury	plaster	Herba artemisiae anomalae Flos carthami Myrrh	acute closed injury closed fracture
Zhenggu Shui	liquid + aerosol	Radix angelicae Herba moghaniae macrophyllae Radix pseudoginseng	dislocation of joints and sprains, bone fractures

Source: SPAC.

Factory-made traditional pharmaceutical preparations are exported to markets where the Chinese system of medicine is practised. These are mainly developing countries in the Far East but also Japan and, to a limited extent, the United States. The exports have increased from $US 35 million in 1975, through $US 80 million in 1981, to $US 87 million in 1986. A few components are also imported for the industrial production of phytopharmaceutical preparations but their annual $US volume is negligible.

Table 5 shows the distribution of expenses for the development of a new phytopharmaceutical preparation.

Table 5. Structure of typical R+D expenditures (percentage)

Research area	Expenditure
Quality specifications and formulation	15
Animal pharmacology and toxicology	30
Clinical studies	
phase 1	10
phase 2	30
phase 3	7
Other expenses	3

Source: SPAC.

The central Government established a special fund to promote R+D in new phytopharmaceutical preparations. Local governments also contribute to R+D expenditures but industry spendings represent the lion share of R+D venture capital. Total spendings on new product R+D vary from $US 5.5 million to $US 9.7 million per year. There is also a special government fund to foster the use of new equipment and technology -e.g., modern separation, purification and concentration techniques- in the industrial production of phytopharmaceutical preparations.

5.3 Collection and cultivation of plants

5.3.1 General aspects

Cultivation of medicinal plants is essential (i) to guarantee the continuous supply of starting materials for the pharmaceutical industry, (ii) when given species, varieties or hybrids are known to have the best quality, (iii) when agricultural methods result in a better quality and yield, (iv) if better processing facilities on the collection site help to preserve the therapeutic value of the plant, and (v) in case of drugs subject to government control.

For success in cultivation, the natural conditions of growth should be studied, reproduced and improved upon. Many factors might affect the therapeutic value of cultivated medicinal plants. E.g., Cinchona succirubra grows well at low altitudes but practically does not produce quinine or quinidine. Another point to be taken into account is that different parts of a plant mature at different seasons, therefore, there is an optimum time for harvesting. Herbs are not available throughout the year either. Hence, fresh herbs can only be

used at a specific season and conservation of the therapeutic value in the form of crude drugs and extracts is a prerequisite of the continuous supply of phytotherapeutic agents.

5.3.2 The Chinese achievements

Each year, about 600,000 tons of roughly 600 kinds of natural materials are collected and about 200 medicinal plants are cultivated in China. The quantities made available through collection of feral plants are consistently declining. Collection is continued mainly in those cases when efforts of cultivation have failed or proven uneconomic. One third of this material is processed by the phytopharmaceutical industry, whereas the balance is mainly sold as yingpian. Small amounts of crude drugs are exported and used by other industries, e.g., in the preparation of beverages and tooth pastes.

The agricultural area used for the cultivation of medicinal plants is about 300,000 hectars and produces about 40 per cent of the total output of crude drugs. More than 700 farms produce only good quality medicinal plants in great demand to-day. The China National Corporation of Traditional and Herbal Medicine is also in charge of the collection and cultivation of medicinal plants.

Many important measures have been adopted in order to guarantee the continuous supply of crude drugs both to the industry and the market. Government guidelines were elaborated and decrees entered into force as regards the protection, exploitation and utilization of natural resources. Geographic regions were declared protected areas for the growth of scarcely available medicinal plants. Social consumption and exports of over-collected plants, e.g., Glycyrrhiza glabra, were restricted in order to restore the production basis.

As a result of R+D programmes, previously wild medicinal plants - e.g., Radix platycodi, Radix gentianae, Radix astragali, Radix changii - have successfully been cultivated and plants for the production of previously imported crude drugs - e.g., Stigma croci, Flos caryophylli, etc. - have been domesticated in China.

The Government policy encourages herbalists to see their work as a long-term business. Interest-free credit is given to farmers upon request. The information on demand and supply is widely disseminated. The medium-term industry development plans are reflected in the purchasing prices. Over-supply of demand due to favourable weather conditions is purchased, processed and kept in stock.

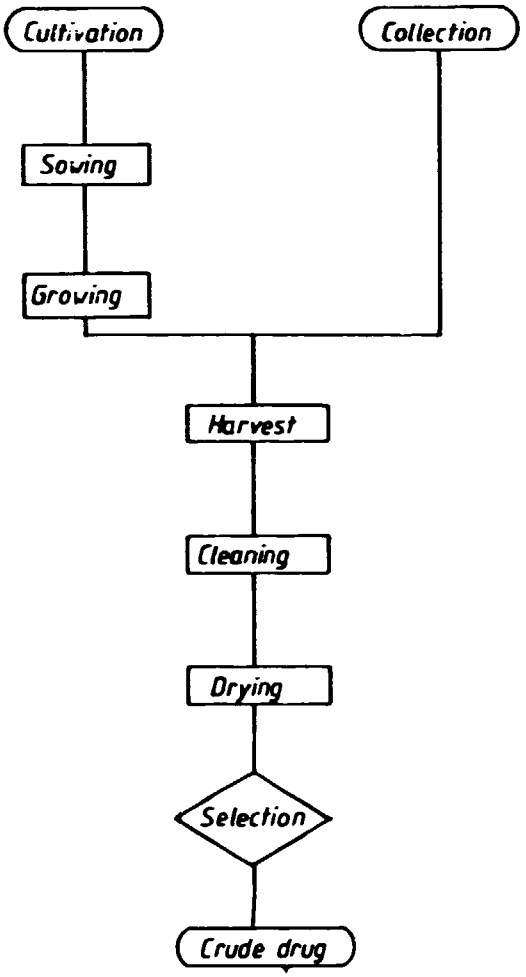
Long-term contracts are encouraged between the industry and medicinal plant farms.

Legislation supports the production of good quality medicinal plants. Certain species should only be grown in specific geographic areas, giving priority to their original place of growth. Medicinal plant farms should be far away from industrial areas. The use of organic fertilizers is encouraged whereas chemical fertilization is restricted. Chemical pesticides must not be used for plant protection. Law stipulates that medicinal plants should be purchased according to established quality standards and different unit prices should be paid for different grades of the same plant species. Sales of inferior quality crude drugs is an infringement of law that must be punished.

The techniques of cultivation and genetic improvement of medicinal plants have continuously been investigated. The best methods are introduced and seeds of selected species are provided to the farmers. There is a recommended sowing time-table. Collection time is determined according to the results of scientific investigations and control methods.

Figure 3 shows the minimum number of steps involved in the collection and/or cultivation of medicinal plants. Particle size reduction, labelling, storage, quality control and extraction of the crude drug may also be done at the site of cultivation.

Figure 3. Schematic illustration of the production of crude drugs



5.4 Industrial technology for the production of phytopharmaceuticals

The collected and dried medicinal plants are processed into phytopharmaceutical preparations in three consecutive steps: treatment of the crude drug, extraction and manufacture of the preparation.

5.4.1 From crude drug to extracts

The crude drugs received in the factory are selected and cleaned to remove undesirable contaminations such as vegetable debris, soil, dust, etc. The particle size is reduced to the specified range. Heat treatment involving chemical changes are also applied in a few cases, e.g., the cardiotoxic aconitine from Aconitum species is hydrolyzed into cardiotonic higenamine (benzoylaconine) and conyneine (aconine) at a temperature of about 100°C

$$C_{34}H_{47}NO_{11} \longrightarrow C_{32}H_{45}NO_{10} \longrightarrow C_{25}H_{41}NO_9$$

aconitine — higenamine — conyneine

to yield the standardized crude drug for the manufacture of phytopharmaceutical preparations. Another example is the steaming of rhubarb with wine to decompose the purgative components but maintain the antibacterial, anti-pyretic and anti-inflammatory properties. The obtained crude drug is called Shu Jun and differs from rhubarb roots and rhizomes, another crude drug used by the industry. Other objectives of pre-processing include destruction of enzymes to improve stability or chemical treatment, e.g., stir-baking with vinegar, to increase water-solubility of active ingredients. Many crude drugs are used in powder form for dosage form manufacture, therefore, grinding is also an import unit operation in the pre-processing stage. The Chinese compendia describe 22 official pre-processing methods.[34/]

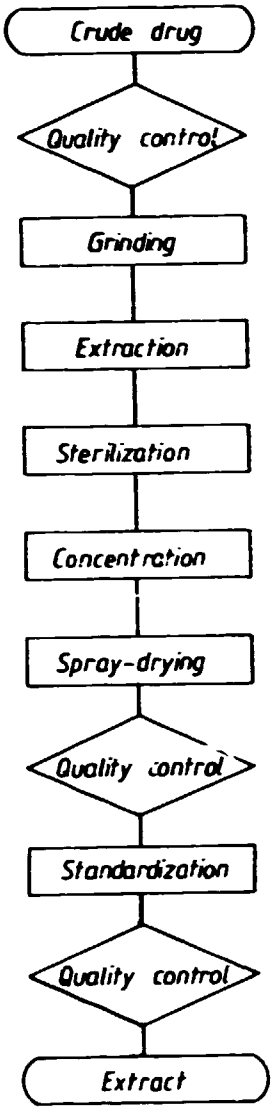
5.4.2 Extraction

Extracts are concentrated preparations of vegetable drugs obtained by the removal of the active constituents of the respective drugs with suitable menstrua, evaporation of all or nearly all of the solvent, and adjustments of the residual masses or powders to the prescribed standards. Most drugs are extracted by percolation. The entire percolates are concentrated, generally by distillation under reduced pressure to diminish the effect of heat on stability as much as possible. Figure 4 shows the unit operations of a modern extraction process. In case of liquid total extracts, the spray-drying operation is omitted. On the other hand, defatting might be involved in the preparatory stage. Basically, the same process is used for the preparation of pharmacopoeial extracts used in the practice of pharmacy worldwide.

Water is the most widely used solvent in the preparation of extracts. Both batch and continuous methods are used usually at a temperature around 100°C and at atmospheric pressure. Therefore, the process costs are low, there is no particular industrial safety risk involved and aqueous effluent treatment is the major environment protection measure to be taken. Alcohol and alcoholic beverages are also used as solvents in the extraction of crude drugs. Several crude drugs are sometimes co-extracted because both the pharmacological action and the toxicity of the compounded extract differ from those of the mixture of the extracts of the individual components. For example, aconite root, when used alone, is a short-acting and toxic cardiotonic agent. Its extraction together with liquorice roots and zingiber rhizomes, which individually have no cardiovascular action, results in Si Ni Tang, a compounded extract with prolonged cardiotonic action and 4-times reduced toxicity.

34/ Pharmacopoeia I. of the PRC, Appendix, pp. 14-16 (1985)

Figure 4. Flow diagram of the extraction process

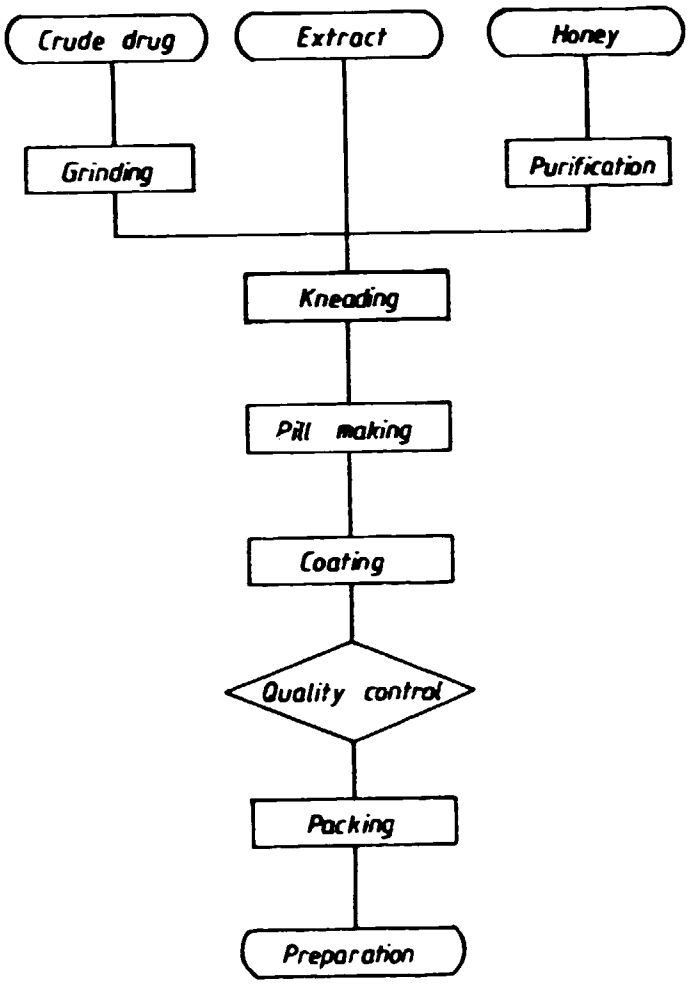


5.4.3 Manufacture of phytopharmaceutical preparations

New preparations, developed to commercial scale during the past five years, represent 90 per cent of the current production volume. Pharmaceutical dosage forms exceed 40 in number and include capsules, granules, tablets, elixirs, suppositories, aerosols, injections, etc. Their manufacturing processes have been reviewed and found to be identical with or very similar to those described in the pharmaceutical literature.[35/] A schematic block diagram of the process for making honey pills is shown in figure 5 to support the former statement.

35/ Remington's Pharmaceutical Sciences, 14th Ed., Mack Publishing Company, Easton, PA, 1970.

Figure 5. Flow diagram of the manufacture of honey-pills



The unit operations in the block diagram are carried out by machinery and equipment generally available in dosage form plants (annex 3).

5.4.4 Quality control

Proper authentication of crude drugs and their source medicinal plants is the basis of both the organized exploitation of domestic resources and regulatory control of the manufacture and sales of phytopharmaceutical preparations.

The minimum quality control objective is to specify macro- and microscopic requirements as well as chromatograms that permit compliance with current regulatory requirements.

Each material used in the production is tested by modern instrumental methods of analysis, e.g., microscopy, separation by electrophoresis of alkaloids with similar chemical structure, spectrophotometry, thin layer chromatography scanning, high-pressure liquid chromatography, etc. The standards are prescribed in the pharmacopoeia or in the registered quality control specifications.

General monographs stipulate the quality standards for each dosage form. The particular aspects of phytopharmaceutical preparations, e.g., impurities, disintegration and dissolution times, labelling requirements, etc. are comprehensively regulated.

5.5 Research and development

5.5.1 Cultivation of plants

The comprehensive research programme includes plant ecological, physiological, biochemical, genetic and pathological studies as well as soil investigations. This programme is the basis of both the legislation for the growth of medicinal plants and continuous training of herbalists in modern agricultural technology.

Selection of species with high yield, good quality and strong adaptability has been achieved by artifical production of mutations.

The seeds of Achyrantheis bidentata were treated with a chemical mutagen. As a result the yield was doubled and roots contained less xylem, therefore, the production of the crude drug became significantly cheaper.

The survival rate of Corydalis seedling and its breeding rate were increased by radioactive irradiation.

Shortage in the supply of wild plants and high price favour cultivation.[36/] Artemisia annua L., known for almost 2,000 years as Qinghaosu is bred in China to increase the production of artemisine, the antimalarial active ingredient of the medicinal plant.

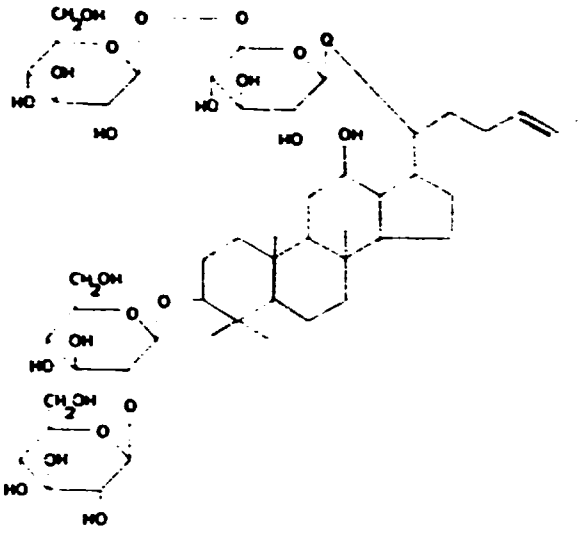
Ganoderma lucidum, Cordyceps and Chinese caterpillar fungus are further examples of the successful cultivation of previously feral plants.

5.5.2 Cell cultures

Rb_1 is one of the main ginsenosides with elucidated chemical structure in ginseng (figure 6).

36/ After three years of experimentation, the Research Institute of Pharmaceutical Sciences, University of Mississipi, harvested Qinghaosu in the USA. About 1 ton of leaves will result first in 100 kg of extract and then in 1 kg of extremely pure crystals of artemisine.

Figure 6. Ginsenoside Rb:



There are 5 other main ginsenosides and 5 secondary ginsenosides with a similar structure in the crude drug. Problems with the supply of the crude drug have motivated investigations for an industrial solution. Researchers succeeded in the cell-culturing of ginseng. Both the qualitative spectrum and the quantity of ginsenosides of the dried cells were found to be the same as those of the cultivated ginseng.[37] The pharmacological activity was also the same.[38]

Plant cell culture, generally used for the biosynthesis of complex chemical structures of pharmaceutical interest, has an industrial history of more than 10 years in China. R+D efforts are continued in this area because of the economic advantages of cell culture against cultivation. It should be mentioned, however, that the cell-cultured crude drugs must not be used in yingpian.

It is generally accepted today that cultivation and cell/tissue culture are the modern approaches to adjust supply and demand for medicinal plants in the long term.

5.5.3 Standardization of crude drugs

In ancient times, physicians and pharmacists were primarily engaged in this type of research. E.g., an early Chinese work described 1892 medicinal herbs with more than 1000 drawings.[39] In the recent 30 years, all historically recorded medicinal plants have been carefully identified by botanical, physical and chemical test methods.

37/ Quian Zhiyu, Journal of Nanjing College of Pharmacy, 2, p. 39 (1980).

38/ Ding Jianyi, ibid., 3, p. 61 (1981).

39/ Li Shezhen: Ben Cao Gang Mu (1578).

The Encyclopaedia of Traditional Chinese Crude Drugs, published in Chinese in 1977, described the botanical and analytical standards of 5646 crude drugs. Scanner microscopy, electron impact mass spectrometry, high performance liquid chromatography, ultraviolet spectrophotometry, etc. have been used to define the chemical structure and quantitative determination of the pharmacologically active ingredients of crude drugs.

The latest edition of the Chinese Pharmacopoeia contains monographs for 647 crude drugs of botanical origin. The Ministry of Health has initiated the standardization of the names of all phytopharmaceutical preparations.

5.5.4 Process development

Pharmaceutical engineering aspects of the production of phytopharmaceutical preparations have been investigated. The main results include the current good laboratory, manufacturing and supply practices which are reflected in the design, construction and mechanization of operations of the factories. Generally applicable processes and operations, e.g., preprocessing techniques, machinery and equipment (annex 3), etc. are standardized and disseminated in the whole industry.

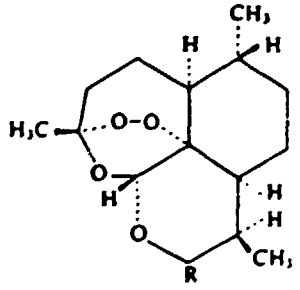
Multifunction extractors with manual or automatic operation, various film evaporators, spray dryers, herb washing machines, stir-heating machines, etc. are examples of capital goods developed and manufactured in China.

5.5.5 New drugs

571 pharmacologically active compounds have been isolated from crude drugs and characterized chemically in China in recent years. 60 new drugs have been developed that originate directly or indirectly from these substances. Illustrative examples are given below.

Qinghaosu and its derivatives (figure 7), a totally new class of antimalarials, are indicated for the treatment of malaria falciparum infections including those caused by chloroquine-resistant strains. Qinghaosu has restored consciousness in patients with the particularly malignant cerebral malaria. Qinghaosu was isolated from Qinghao (Artemisia annua L.) in 1972, as a result of a research programme initiated in 1967 to develop new antimalarial drugs from long established Chinese phytopharmaceutical preparations.

Figure 7. Chemical structure of qinghaosu and its derivatives

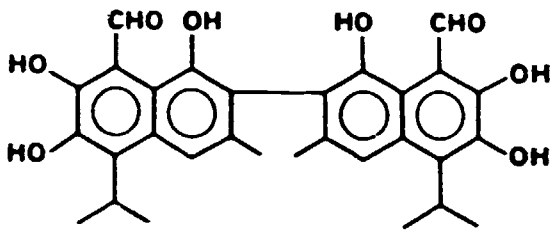


Qinghaosu (R= =O) is practically insoluble in water. Its absorption from the stomach is limited. Qinghaosu suppositories were recently approved for sales in China by the New Drug Evaluation Committee. Its synthetic derivatives, artemeter (R= $-OCH_3$) and sodium artesunate (R= $-OCOC_2H_4COONa$) proved to be outstanding antimalarial agents in clinical trials and the latter is stable as powder for aqueous injection.

The therapeutic importance of qinghaosu drugs lies in the fact that they are effective when other antimalarials fail and they should therefore be reserved for the treatment of such cases.

A loss of fertility was observed among inhabitants of a small isolated village, apparently caused by cottonseed oil used for cooking. Investigations identified gossypol (figure 8) as the most probable causative factor.[40]

Figure 8. Chemical structure of gossypol



Gossypol obtained from Gossypium species is an optically inactive, racemic substance. The dextrorotatory enantiomer can be isolated with good yields from the plant Thespesia populnea.[41] The (+)-optical isomer does not reduce fertility in experimental animals but has some nonspecific weight gain inhibition effects of (+-)-gossypol. (-)-gossypol, if exists separately, can be more potent as a contraceptive and less toxic than the racemic gossypol.

Further research into the efficacy and toxicity of gossypol should be encouraged, because (1) a male contraceptive agent is needed; (2) gossypol is easily available at low cost; (3) it is effective and its antifertility effect is often reversible; (4) its therapeutic index is narrow; and (5) a highly purified substance and a stable dosage form are needed for pharmacological investigations.

40/ Dai et al.: Shih Yen Sheng Wu Hsueh Pao, 11, 1 and 16, 1978.

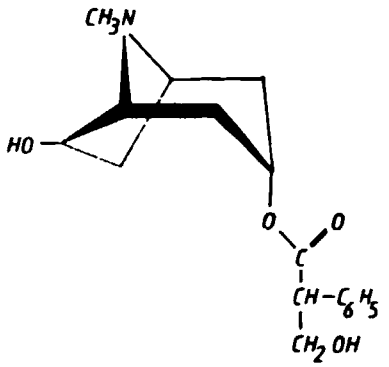
41/ King, T.J. and de Silva, L.B.: Tetrahedron Lett. 3, 261, 1968.

Gossypol has not been used in traditional Chinese medicine, of course, but R+D methodology is basically the same for all plant derived new drugs. Hence, research capacity created for one group of botanical drugs automatically serves others.

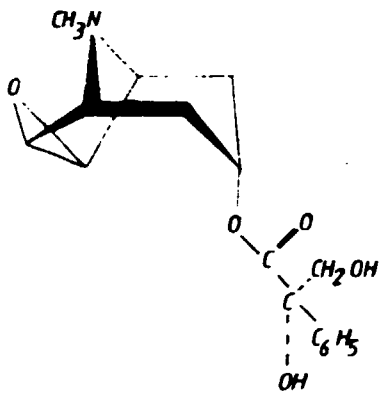
Gossypol exhibits also antiviral and antimalarial activities. Its toxicity however has limited its potential use as a drug. U.S. scientists synthetized gossypol analogues which are less toxic and their antiviral and antimalarial activities are comparable to those of gossypol.[42/]

Chinese scientists have recently isolated anisodine and anisodamine (figure 9) from Anisodus tanguticus which, together with atropine and scopolamine, are called henbane alkaloids. These drugs produce typical parasympatholytic effects but they also have successfully been employed in the treatment of patients suffering from hypovolemic and septic shocks as well as from acute meningitis. Other therapeutic indications include acute poisoning with organic phosphor compounds, severe hepatitis, pancreatitis, renal insufficiency, etc.

Figure 9. Chemical structure of henbane alkaloids



Anisodamine

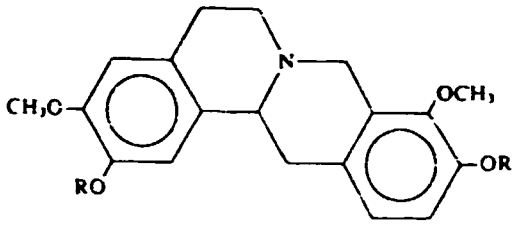


Anisodine

42/ Specification to a U.S. patent application (1985). Dr. Vander Jagt, D.L. and Royer, R.E., University of New Mexico, personal correspondence, 1987.

13 alkaloids were isolated from the Cordialys rhizome, among them tetrahydropalmatine (THP) and stepholidine (figure 10)

Figure 10: Chemical structure of THP and stepholidine



R = $-CH_3$ THP
R = -H stepholidine

THP was first described as a central nervous system depressant and analgesic. Subsequent clinical tests confirmed that THP can advantageously be used as the analgetic ingredient of anaesthesia coctails. THP is also a good sedative with some hypnotic effect.

Yuanhuacine and derivatives were isolated from Yuan-hua (Daphne genkwa) and Wikstroemia chamaedaphne.[43/] The roots of Yuan-hua have been used in ethnomedicine to induce abortus for many centuries. The use of yuanhuacine in humans is discouraged because of the established carcinogenicity for this class of compounds. Veterinary use could be promising.

The chemical structure of trichosanthin, a high molecular weight protein isolated from Trichosanthes kirilowii, was elucidated in 1985. The drug has been used to terminate mid-trimester pregnancies. It should be administered with great precaution on second occasion because of the antigenic nature of trichosanthin.[44/]

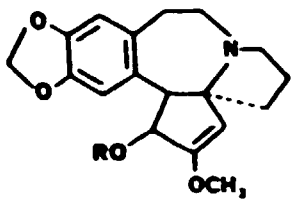
The cephalotaxine derivatives harringtonine and homoharringtonine (figure 11) are the antitumor active ingredients of Cephalotaxus harringtonia variety drupacea.[45/] These compounds have completed phase II of clinical investigations in the United States with very promising results.

43/ Wang et al., Chung-hua Fu Chan Ko Tsa Chih 14, 125-126 (1979); Hua Hsueh Hsueh Pao 39, 421-426 (1981); Chung Ts'ao Yao 12 (8), 1-3 (1981); and Yao Hsueh Tung Pao 16 (6), 51-52 (1981) and 17 (3), 46 (1982).

44/ Bingel and Farnsworth: Botanical sources of fertility regulating agents: chemistry and pharmacology. In: Briggs & Corbin (eds). progress in Hormone Biochemistry and Phamacology, Vol. 1, 149-225, (1980).

45/ Huang, L. and Xue, Z. (1984). In "The Alkaloids, Vol. XXIII", Brossi, A. ed., pp. 157-226, Academic Press, New York, USA.

Figure 11. Antitumor agents of cephalotaxus



R = -H — Cephalotaxine

R = -CO- C(OH)(CH2CO2CH3)-CH2CH2- C(OH)(CH3)-CH3 — Harringtonine

R = -CO- C(OH)(CH2CO2CH3)-CH2CH2CH2- C(OH)(CH3)-CH3 — Homoharringtonine

Hydroxycamptothecin, orginally isolated from Camptotheca acuminala, has been used in China in the treatment of primary liver cancer, leukemia and gastric carcinoma.[46] The compound is now in clinical trials both in the PRC and the United States, in development phase II.

Extracts of two Chinese plants are being tested both in China and the USA as potential drugs for the treatment of hepatitis B, AIDS and aging. The active ingredients of the extracts were first isolated in 1980.

China concluded an agreement with Rhône-Poulenc Santé to develop new cardiovascular, psychiatric and anticancer drugs from 14 Chinese medicinal plants.[47]

46/ Xu Bin and Yang Jin-Song: Hydroxycamptothecin as an antitumor agent. An "Advances in Chinese medicinal research, Chang, H.M/ et al. (eds.), World Scientific Publ. Co., Singapore, 1985.

47/ SCRIP No. 1172, 21 January 1987, p. 19.

5.6 Conclusions and implications

Legal recognition and government patronage granted to traditional medicine is the basis for the development of the phytopharmaceutical industry in China. A systems approach from cultivation of medicinal plants to sales of phytopharmaceutical preparations is the key factor of success.

Feral plants are industrial resources only if they are available in quantities higher than the demand for practically unlimited time or if cultivated in an economically feasible way.

Cultivation, storage, extraction and production are based on scientific methodology and modern technique.

The quality of crude drugs and phytopharmaceutical preparations is measured by chemical criteria in a proven correlation with the efficacy, safety and therapeutic use.

The phytopharmaceutical industry uses mainly domestically grown or cultivated plants, therefore, the convertible currency component of the direct material costs is nil or negligible.

Genetic improvement and other agricultural and agrotechnical aspects to increase the content of the active ingredient in crude drugs have become an important economic issue with the cultivation of medicinal plants.

Dried medicinal plants and standardized extracts of pharmacopoeial monographs such as Belladonna Leaf, Powdered Digitalis, Opium Tincture, Senna Fluid Extract, etc. are prepared by the same industrial technology as described in sections 5.3 and 5.4 of this chapter.

The scientific investigation of ethnomedical claims is a well-established interdisciplinary methodology which starts with the verification of the pharmacological effect in animals.

The second step is the botanical and phytochemical research because a chemical structure might be unique to a plant germs (e.g., cephalotaxus alkaloids) or found in various species (e.g., yuanhuancine and derivatives) sometimes reported under different names.

The majority of plant-derived compounds described in this section have a complex chemical structure difficult to prepare by chemical total synthesis. E.g., both the cephalotaxine nucleus and the esterifying acids of harringtonines are prepared by sophisticated multistep syntheses and their stereoselective coupling is a challenging problem even at laboratory scale. Therefore, isolation by extraction seems to be the preferred techno-economic choice of commercial manufacture, as opposed to organic chemical synthesis.

On the other hand, molecular modification of the parent compound might result in better therapeutic properties. E.g., qinghaosu was found effective in 75 per cent of the cases whereas its derivative, artemether, produced a cure rate of 96 per cent in the treatment of Plasmodium falciparum malaria. Partial synthesis might also be justified by the scarce availability of the biologically active principle and the abundance of a chemically similar building blocks as in the case of harringtonines and cephalotaxine.

Industrial research also includes investigation of tissue culturing, in particular when the medicinal plant is not available in sufficient quantities and/or cannot efficiently be cultivated.

Once the quality of the active ingredient has been standarized formulation R+D is initiated to guarantee the stable, good quality of the phytopharmaceutical preparation.

Detailed pharmacological and clinical trials are needed to substantiate experimental claims in humans.

All these activities require capital intensive and highly organized R+D and good marketing strategies to replenish, or even increase research funds.

6. GENERAL CONCLUSIONS

Herbal drugs had played a decisive role in the therapy of human diseases worldwide until the end of the 19th century when the first group of about 30 pharmaceutical chemicals was synthetized in Germany. Phytopharmaceutical preparations were the main category of drugs until the late 1930s but they have only a limited health importance in industrialized countries to-day. The situation is different in developing countries where a large part of the rural population depends on ethnomedicine because physicians are scarcely accessible and the purchasing power of patients is low.

Most medicinal plants should be collected at the right season and processed into crude drugs and/or crude extracts so that they contain and preserve their optimum therapeutic value. This objective can be best achieved if the medicinal plants are cultivated and processed under quality controlled conditions preferably close to the site of harvesting.

Herbal remedies can rarely be considered essential drugs in developing countries but phytopharmaceutical preparations are used in the treatment of infections, parasitic diseases, cancer and cardiovascular diseases, in population growth control, as analgesics and expectorants, etc. They statisfy therefore not only a perceived demand but also a medical need. Since phytopharmaceuticals should meet the same criteria as other drugs, the risk-benefit considerations should also be the same. This statement does not apply to herbal remedies.

Cost-benefit calculations have not been made. It can nonetheless be stated that the price for the good and consistent quality must be paid because the use of standardized crude drugs and crude extracts is more expensive than that of the herbal remedies prepared from self-collected and preserved crude drugs. The main economic advantages include the use of domestic raw materials, the creation of jobs both in the agriculture and industry, and the regular availability of drugs for primary health care. The development of research experience in related sciences is an additional benefit.

It is unlikely that drastic social, economic and technical changes are going to take place in developing countries during the forthcoming decade. Hence, the establishment and modernization of a phytopharmaceutical industry seems to be a technically feasible and economically acceptable, sometimes attractive proposal also in those countries where the domestic market is not large enough to support a pharmaceutical chemical industry. The investment costs are relatively small, the dosage form and quality control capacities are convertible and the acquired knowledge and experience will prove to be useful at an eventual later diversification stage.

The generalization of the Chinese case study has led to the following main factors affecting the establishment and/or modernization of a domestic market oriented phytopharmaceutical industry:

(a) A socially desired and officially endorsed demand for phyto-pharmaceuticals.

(b) Macro- and microclimatic conditions favourable for the growth of priority medicinal plants.

(c) A developed general level of agriculture.

(d) Continuous availability of feral and/or domesticated medicinal plants.

(e) A developed dosage-form processing industry and/or a developing pharmaceutical chemical industry.

(f) Interest in the preparation of pharmaceutical extracts.

(g) Interest in phytopharmaceutical research.

(h) Continuous education and training of agronomist, medical, pharmaceutical, paramedical and technical professionals.

(i) Availability of low-cost manpower.

(j) Investment and tax preferences in the start-up period.

(k) Industrial safety and environment pollution legislation.

(l) General technical and management level of the existing industry.

Some of these factors are absolute criteria, e.g., climate, others are essential such as the existence of a dosage-form processing industry, whereas the third group, e.g., tax exemption generally favours the development of any industry. It is important to recognize, however, that industry is one of the two key elements and efficient distribution of drugs among the rural population is also required for the smooth functioning of a phytopharmaceutical supply system.

Interest in exports of established phytopharmaceuticals assumes marketing capability in destination countries, whereas negotiation experience in licencing contracts is a prerequisite for the mutually advantageous joint development of new drugs for international sales.

There is mainly an academic interest in investigating ethnomedical claims in industrialized countries. Plants of therapeutic importance are cultivated, patents are granted for modified chemical structures and clinical trials are conducted to study use of the active ingredients in the treatment of diseases of global importance such as cancer. Since the R+D activities on medicinal plants include cultivation, cell/tissue culture, etc. and the new drug development model is the same as that for chemical drugs, applied research is a very capital intensive and long process, in particular when global sales is the strategic objective.

7. RECOMMENDATIONS

7.1 Domestic production

The national health policy should include a policy on phytopharmaceuticals covering continuous supply of source medicinal plants, domestic production, quality control, distribution, new drug R+D and related aspects such as legislation, registration and training. A national list of priority medicinal plants should be developed by using ethnomedical experience and the NAPRALERT database to concentrate initial efforts on established drugs used in the treatment of diseases prevailing in the country. Priority medicinal plants should be cultivated, processed and distributed under quality-controlled conditions.

People should regularly be trained through mass media - mainly radio - what medicinal plants to collect, how to preserve their therapeutic value and how to prepare home remedies used for self treatment. The information service should list those conditions when self-diagnosis is acceptable and encourage patients to consult paramedical staff or a physician in all other cases. Government assistance may be extended to an inspection service of crude drugs at weekly markets, seasonal fairs, etc. and should include control of distribution channels of herbal remedies.

Yingpians should be manufactured under regulatory control for non-prescription drugs in small-scale industrial establishments close to the site of cultivation. Teas for self-medication should generally be made available and promoted. The major part of phytopharmaceutical teas should, however, be dispensed by registered paramedical personnel and/or physicians and pharmacists.

Phytopharmaceutical preparations should be manufactured according to the regulatory requirements for dosage forms. The additional process, extraction, should be carried out at the site of the dosage form factory. These drugs should be registered, produced and sold under the regulatory control of the Ministry of Health. In case of exports, regulatory requirements of the destination country must also be observed.

When socially, technically and economically feasible, active ingredients should be isolated and used in industrial production instead of crude drugs and total extracts.

7.2 International co-operation

R+D activities concerning new drugs derived from medicinal plants should be done from the earliest possible stage together with partners experienced in international sales, in order to access the necessary venture capital and know-how as well as to protect own economic interest to the maximum extent.

Cultivation and industrial process technology with various degrees of sophistication is available for transfer both from developing and industrialized countries. Training should best be given, as part of the technology transfer, both in the donor and recipient countries. Such programmes should closely be linked to the national list of priority medicinal plants.

International co-operation would be useful in the establishment and continuous updating of a statistical database (definitions, disaggregation of national production and trade quantities and values into therapeutic groups and individual products, price structure, price index, number of industrial establishments, work force, etc.) which would permit monitoring the development of the phytopharmaceutical industry and selected issues at national, regional and global levels.

Upon government request, UNIDO can provide technical assistance in the elaboration of a national policy or implementation thereof. UNIDO could also initiate the establishment of collaborating centres for general phytopharmaceutical industry training and as the technical bases for experimental work required in connection with the technical assistance programme.

Annex 1

to the study

BETTER UTILIZATION OF MEDICINAL PLANTS:

The Phytopharmaceutical supply system in China

Illustrative contents of a phytopharmaceutical registration dossier

Part I GENERAL INFORMATION

IA Administrative data
IB Summary of product characteristics
IC Expert reports on - botanical documentation; -chemical/pharmaceutical documentation; - toxicological/pharmacological documentation; - clinical documentation.

Part II BOTANICAL DOCUMENTATION

IIA Cultivation/collection and extraction
IIB Quality control of IIA
IIC Other information

Part III CHEMICAL AND PHARMACEUTICAL DOCUMENTATION

IIIA Composition
IIIB Method of preparation
IIIC Control of starting materials
IIID In-process control
IIIE Control tests on the finished product
IIIF Stability
IIIG Other information

Part IV TOXICOLOGICAL AND PHARMACOLOGICAL INFORMATION

IVA Acute toxicity
IVB Toxicity with repeated administration
IVC Foetal toxicity and fertility studies
IVD Mutagenic potential
IVE Carcinogenic potential
IVF Pharmacodynamics
IVG Pharmacokinetics
IVH Other information

Part V CLINICAL DOCUMENTATION

VA Human pharmacology
VB Clinical documentation
VC Other information

Part VI SPECIAL PARTICULARS

VIA Dosage form
VIB Samples
VIC Manufacturer's authorization(s)
VID Marketing authorization(s)

Annex 2

Medicinal plants in the official Chinese paramedical manual

Medicinal plant	Crude drug
Acalypha australis L.	whole plant
Acanthopanax gracilistylus,	roots and bark of stems
Achillea sibirica Ledeb.	whole plant
Aconitum chinense Pext.	roots
Acorus calamus L.	roots and stems
Acorus gramineus Soland.	roots
Actinidia chinensis Plan ch.	fruits, stems, roots
Adenophora stricta Miq.	roots
Adina rubella Hance	whole inflorescence
Agastache rugosa O. Kuntze	stems and leaves
Agrimonia pilosa	whole plant
Ailanthus altissima Swingle	roots and bark
Ajuga decumbens Thunb.	whole plant
Akebia trifoliata	vine and fruit
Alangium chinense	roots and stems
Aletris spicata (Thunb.) Franch.	roots,chin of whole plant
Aleurites fordii Hemsl.	flowers, fruit and leaves
Alisma plantago L. var. par. viglosum Torr.	---
Alopecurus aequalis Sobol.	whole plant
Amaranthus bidentata Bl	roots
Amaranthus spinosus L.	whole plant
Amomum costatum, Roxb.	---
Amomum xanthioides Wallich	fruit
Ampelopsis brevipedunculata Trautv.	fruit, roots, leaves
Ampelopsis japonica	roots
Andrographis paniculata Nees.	whole plant
Anemarrhena asphodeloides Bunge	---
Anemone vitifolia Buch-Ham.	whole plant
Angelica anomala, Pall.	---
Angelica polymorpha Maxim var. sinensis	---
Angelica pubescens Maxim.	roots and rhizomes
Angelica sylvestris L.	---
Angiopteris fokiensis Hieron	rhizomes or fresh hert
Aquilaria agallocha, Roxb.	---
Aralia chinensis L.	roots and stems
Arctium lappa L.	seeds, roots, leaves
Ardisia crenata Sims.	roots
Ardisia japonica Bl.	whole plant
Arenaria serpyllifolia L.	whole plant
Arisaema consanguineum	stem tuber
Aristolochia debilis S. et Z.	roots, stems and fruits
Aristolochia mollissima Hance	whole plant
Artemesia apiaceae	whole plant
Artemesia vulgaris L.	leaves
Artemisia capillaris Thunb.	whole plant

Medicinal plants in th.
official Chinese
paramedical manual

Medicinal plant	Crude drug
Asarum blumei Duch.	roots
Asarum sieboldi, Mig.	---
Aspidistra elatior Blume.	Roots, stems or leaves
Aster tataricus L.	---
Aster trinervius Roxb.	whole plant
Atractylis ovata	---
Atractylis ovata	---
Auricularia auricula - Judae Schrot.	spores
Bacopa monniera, Hyata	---
Begonia evanstana Andr.	tuberous roots and fruits
Begonia laciniata Roxb.	roots
Belamcanda chinensis (L.) DC	roots
Benincasa hispida Cogn.	---
Berberis chengii Chen.	roots and stems
Bletilla striata	stem tuber
Boehmeria nivea (L.) Gaud.	roots, stems and leaves
Botryopleuron axillare Hemsl.	whole plant
Brucea javanica (Linne) Merri	fruit
Buddlea officinalis, Maxim.	---
Bulbophyllum inconspicuum Maxim.	whole plant
Bupleurum chinense DC.	whole plant
Callicarpa pedunculata R. Br.	whole plant
Campanumaea pilosula, Franch.	roots
Campanumoea javanica Bl.	roots
Campsis chinensis Voss.	flowers or whole plant
Cannabis sativa L.	seeds
Capella bursa pastoris Medic.	whole plant
Carpesium abratanoides L.	whole plant
Carpesium divaricatum Sieb. et Zucc.	roots or whole plant
Carthamus tinctorius L.	flowers
Caryophyllus aromaticus, Linne	---
Cassia tora L.	---
Castanea mollisima Bl.	furry globe or root bark
Cedrela chinensis Juss.	buds, flowers, legumes
Celastrus articulatus Thunb.	roots,stems,leaves
Celosia cristate L.	flowers
Centella asiatica (L.) Urb.	whole plant
Centipeda minima L. A. Braun et Aschers	whole plant
Ch'en P'i (dried tangerine/orange)	peel
Ch'ing p'i (Dried tangerine peel)	---
Ch'ing-kuo (Olive, Canarium album)	---
Ch'ing-tai (Indigo flower)	---
Ch'uan Pei (Szechuan fritillary)	---
Ch'uan Wu (Szechuan monkshood)	---
Chaenomeles lagenaria	fruits

Medicinal plants in the official Chinese paramedical manual

Medicinal plant	Crude drug
Chenopodium ambrosicides L.	whole plant
Chi-nei-chin (Gold-in-chicken)	---
Chiang (ginger)	---
Chiang-t'i (ginger)	sprouts
Chrysanthemum cinerariaefolium Vis.	flowers or whole plant
Chrysanthemum indicum L.	whole plant
Chrysanthemum morifolium Ramat.	flowers
Chu Sha (cinnabar, vermillion)	---
Chung Ju-Shih	---
Cibotium barometz (L.) J. Sm.	roots, stems, downy hairs
Cimicifuga foetida (skunk bugbane)	---
Cinnamomum camphora (L.) Neeset Ebern.	roots and leaves
Cirsium japonicum Dc	dried roots
Clematis chinensis Osb.	roots
Clerodendron bungei Steud.	roots, leaves, stems
Clerodendron cyrtophyllum Turcz.	leaves and roots
Clerodendron trichotomum Thunb.	roots and leaves
Cnicus segetum (Bunge)	whole plant
Cnidium monnieri (L.)	fruits or whole plants
Cocculus trilobus DC	vine
Codonopsis lanceolata Benth. et Hook.	root tuber
Coix lachryma jobi L.	seeds
Commelina communis L.	whole plant
Coniogramme japonica	rhizomes or whole plant
Conioselinum univattum	---
Coptis chinensis	---
Coriandrum sativum L.	whole plant
Coriaria sinica Maxim..	leaves
Cornus officinalis S et Z.	fruits
Corydalis ternata, Makino	---
Crataegus cuneata Sieb et Zucc.	roots and fruits
Crotalaria sessiliflora L.	whole plant
Cucurbita moschata Duch. var. toonas Makino	seeds
Curculigo orchioides Gaertn.	roots
Curcuma longa L.	---
Cuscuta japonica Choisy	fruit or whole plant
Cyclea hypoglauca (Schauer) Diels	roots
Cynanchum caudatum Maxim.	rhizomes
Cynanchum japonicum variation	---
Cynanchum stauntoni	roots and rhizomes
Cynanchum stratum Bunge	roots and stems
Cyperus rotundus, L.	rhizomes
Cyrtomium fortunei J. Sm.	rhizomes
Dalbergia hupeana Hance	leaves
Daphne genkwa Si. et Z.	flowers and roots

Medicinal plants in the official Chinese paramedical manual

Medicinal plant	Crude drug
Daphne odora Thunb.	stem and flowers
Datura metel L. f. alba	roots, leaves, flowers
Dendrobium nobile Lindl.	stems
Desmodium caudatum DC.	whole plant
Desmodium styracifolium (Osbeck.) Merr.	whole plant
Dianthus superbus Linn.	whole plant
Dichondra repens, Forst.	whole plant
Dichroa febrifuga Lour.	roots and leaves
Dicliptera japonica Makino	whole plant
Dioscorea babatas Decne.	stem tubers
Dioscorea bulbifera L.	root tubers and bulbils
Dioscorea tokoro Makino	rhizomes
Dipsacus japonicus Miq.	roots
Dolichos lablab L.	---
Drosera peltata Sm. var. lunata Clarke	roots or whole plant
Drynaria fortunei (kze.) J. Sm.	rhizomes
Dryobalanops camphora Coleb (Camphor)	---
Duchesnea indica (Andr.) Focke	whole plant
Dysosma auranticocaulis	rhizomes
Eclipta prostrata L.	whole plant
Elaeagnus pungens Thunb.	stem and leaves
Elephantopus scaber L.	whole plant
Emilia sonchifolia DC	whole plant
Ephedra	---
Epidemium sagittatum (S. et Z.) Maxim.	leaves
Equisetum hiemale L.	whole plant
Eriobotrya japonica Lindl.	leaves
Eriocaulon sieboldianum S. et Z.	whole plant
Eucalyptus robusta Sm.	leaves
Euchresta japonica	---
Eucommia ulmoides, Oliv.	---
Euonymus alata (Thunb.) Regel	stems and branches
Eupatorium fortunei Turcz.	stems and leaves
Eupatorium odoratum L.	whole plant
Euphorbia hirta L.	whole plant
Euphorbia humifusa Willd.	whole plant
Euphorbia sieboldiana	roots
Euryale ferox Salisb.	seeds,stems, roots,leaves
Evodia lepta	roots and leaves
Evodia rutaecarpa	fruits
Fagopyrum cymosum Meisn.	roots or whole plant
Fan Hsieh-hsieh (Senna)	leaves
Fei Huang (Flying locust)	---
Ficus pumila L.	stem or fruit peel
Foeniculum vulgare Mill	fruits

Medicinal plants in the official Chinese paramedical manual

Medicinal plant	Crude drug
Forsythia suspensa Vahl.	fruits
Fritillaria callicola	---
Galium gracile Bunge	whole plant
Gardenia jasminoides Ellis	roots and fruits
Gastrodia elata	---
Gaultheria cumingiana	rhizomes
Gentiana scabra Bunge.	whole plant
Ginkgo biloba L.	seeds, seedcoat or leaves
Glechoma hederaceae L.	whole plant
Gleditsia sinensis Lam.	legumes/thorns from stem
Glochidion eriocarpum	roots and leaves
Glochidion puberum (L.)	roots,stems,leaves,fruits
Gnaphalium multiceps Wall	whole plant
Grifola umbellata (Pers.) Pilat.	basidiocarp
Gynura segetum	whole plant
Hai Tsao (seaweed)	---
Hei Chih-ma (Black sesame)	seeds
Heleocharis plantaginea R. Br.	---
Hibiscus mutabilis L.	flowers and leaves
Hibiscus syriacus L.	root bark and blossoms
Ho Hsieh (waterlily)	leaves
Horenia dulcies Thunb.	fruit and peel
Houttuynia cordata Thunb.	whole plant
Hsing-jen (Almond)	---
Hsueh-chih (Resin from Calamus draco, Willd)	---
Hu-chiao (pepper)	---
Hu-lu (gourd)	---
Huang-ch'i (locoweed, yellow vetch)	---
Huang-pai (Phellodendron)	---
Hydrilla verticillata	whole plant
Hydrocolyte rotundifolia Roxb.	whole plant
Hypericum ascyron L.	whole plant
Hypericum japonicum	whole plant
Hypericum sampsonii	whole plant
Ilex asprolla Champ.	roots
Ilex cornuta Lindl.	whole plant
Imperata cylindrica var. major (Nees) C.E.Hub	roots and flowers
Indigofera tinctoria	roots and leaves
Inula cappa DC	roots or whole plant
Inula japonica Thunb.	flowers
Ju-hsiang (Pistachio)	---
Ju-ku'ei (Cinnamon)	---
Juglans regia L.	seeds and seedcoats
Juncus effusus L.	whole plant
Jussiaea repens L.	whole plant

Medicinal plants in the official Chinese paramedical manual

Medicinal plant	Crude drug
Justicia gendarussa, L.	---
Justicia procumbens L.	whole plant
Kadsura peltigera Rehd. et Wils.	fruits,roots,stems,leaves
Kan Ts'ao (Licorice, Glycyrrhiza species)	---
Kao-li Shen (Korean ginseng)	---
Kochia scoparia Schrad.	whole
Ku-ya (rice grain)	sprouts
Kuei Chih (Cinnamon sticks)	---
Lagerstroemia indica L.	roots
Laminaria	---
Land isopoda	---
Lantana camara L.	roots
Leonurus heterophyllus Sweet.	whole plant and fruits
Lepidogrammitis drymoglossoides (Bak.)	whole plant
Lepisorus thunbergianus	whole plant
Lespedeza cuneata (Dum. Cours) G. Don.	whole plant
Lien-tzu (Lotus)	seeds
Ligustrum lucidum Ait.	seeds
Lilium brownii var. Colchesteri Wils.	whole
Lilium concolor Salisb.	bulb or whole plant
Lindera strychnifolia	roots
Lithospermum erythrorhizon Sieb et Zucc	whole plant
Litsea cubeba Pers.	whole herb
Lobelia radicans Thunb.	whole plant
Lonicera japonica Thunb.	flowers and vine
Lophatherum gracile Brongn.	roots and leaves
Loropetalum chinense, Oliv.	whole plant
Lycium chinense Mill.	fruits, root bark
Lycoperdon gemmatum	---
Lycopodium cernuum L.	whole plant
Lycopus lucidus Turcz. var. hirtus Regel	whole plant
Lygodium japonicum (Thunb.) Sw.	whole plant, sporangium
Lysimachia christinae Hance	whole herb
Lysimachia paridiformis Franch.	whole plant
Macleaya cordata (Willd) R. Br.	roots, stems and leaves
Magnolia liliflora Desr.	buds
Magnolia officinalis Rehd & Wils.	dried bark and flowers
Mahonia bealei Carr.	roots and stems
Mahonia japonica DC.	roots and stems
Mai-ya (Malt)	---
Mallotus apelta	roots and leaves
Malva verticilata L.	whole plant
Marsilea quadrifolia L.	whole plant
Melastoma dodecandrum Lour.	whole plant
Melia azedarach L.	fruit and bark of root

Medicinal plants in the official Chinese paramedical manual

Medicinal plant	Crude drug
Mentha arvensis L.	whole plant
Millettia dielsiana Harms. et Diels.	roots and vine portions
Millettia reticulata Benth.	roots and vines
Miscanthus sinensis	---
Mo-yao (Myrrh)	---
Momordica cochinchinesis	seeds
Mongrialis hirta Wedd.	roots, leaves,whole plant
Morus Bombycis, Koidz	root bark
Musa basjoo Sieb. et Zucc.	roots
Nandina domestica Thunb.	roots and stems
Nelumbo nucifera	fruit, floral receptable
Nepeta japonica Maxim.	---
Nephelium longana Camb.	---
Nephilium litchi Camb.	seed
Nerium indicum Mill.	leaves
No-tao Ken (rice plant)	roots
Nothosmyrnium japonicum Miq.	---
Oenanthe stolonifera DC	whole herb
Olaenlandia diffusa	whole plant
Omphalia lapidecens	---
Ophiopogon japonivcus ker-gaw	root tubers
Orthodon fordu Maxim.	whole plant
Osbeckia chinensis L.	whole plant
Ostrea cucullata, Born.	---
Ou-chieh (nalumbo)	rootstock
Oxalis Corniculata L.	whole plant
P'i-ma (castor bean)	seeds, roots and leaves
Pa-tou (Croton)	bean
Paederia species	whole plant
Paeoma albiflora Pallas var. tricocarpa Bunga	---
Pai-hsien P'i (Leucobrya species)	---
Pai-t'ou Weng (White Anemone)	---
Pan-ta-hai	---
Panax quinquefolium	---
Parabarium micranthus (Wall.) Pierre.	roots and mature vine
Paris cocos Wolf.	---
Paris polyphylla S..	roots
Patrinia scabiosaefolia Fisch.	roots, whole plant
Perilla frutescens (L) Brit.var.crispa Decne	whole plant
Petasites japonicus, Mig.	---
Peucedanum pracruptorum Dunn.	roots
Pharbitis nil Choisy	seeds
Phaseolus angularis Wight.	seeds
Pholidota chinensis Lindl.	whole plant
Phragmites communis Trin.	roots

Medicinal plants in the
official Chinese
paramedical manual

Medicinal plant	Crude drug
Phryma leptastachya L.	whole plant
Phyllanthus urinaria L.	whole plant
Phyllostachys nigra Munro	whip-like roots
Physalis alkekengi L.	roots, leaves, fruits
Physalis pubescens Linn.	whole plant
Phytolacca esculenta Van Houtt	roots
Pin-lang (Betelnut Areca catechu Linne)	---
Pinellia ternata (Thunb.) Breit.	tuberous stems
Pinus massoniaca	---
Piper betle L.	leaves and stems
Plantago major Lin.	whole plant
Platycodon grandiflorum A. DC.	roots
Pogonatherum crinitum (Thunb.) Kunth.	whole plant
Polygala japonica Houtt.	whole plant
Polygala tenuifolia Willd.	roots
Polygonatum officinale All.	rhizomes
Polygonum aviculare L.	whole plant
Polygonum bistorta L.	roots and stems
Polygonum chinense L.	whole plant
Polygonum cuspidatum Sieb. et Zucc.	roots and leaves
Polygonum hydropiper Linn.	whole plant
Polygonum multiflorum Thunb.,	root tubers, stems,leaves
Polygonum perfoliatum L.	whole plant
Poncircus trifoliata	peels, fruit
Portulaca oleracea L.	whole plant
Potentilla discolor Bunge.	roots
Potentilla kleiniana Wight et Arn.	whole plant
Poulzolzia zeylanica (L.) Benn.	whole plant
Prunus japonica, Thuno.	seeds
Prunus mume Sieb et Zucc	---
Psorales corylifolia L.	---
Pteris multifida	whole plant
Pueraria pseydohirsuta Tang et Wang	roots and flowers
Pycnostelma paniculatum (Bunge.) K. Schum.	roots or whole plants
Pyracantha fortuneana	fruit or leaves
Pyrrosia lingua (Thunb.) Farw.	whole plant
Quisqualis indica L.	---
Ranunculus japonicus	whole plant
Ranunculus succarinii Mig.	whole plant
Raphanus sativus L. var. macropodus Makino	---
Rehmannia glutinosa	whole
Rheum officinale	---
Rhododendron molle G. Don.	flowers and roots
Rhodomyrtus tomentosa Hassk.	roots and leaves
Rhus semilata Murr.	roots and leaves

Medicinal plants in the
official Chinese
paramedical manual

Medicinal plant	Crude drug
Rohdea japonica Roth.	roots and leaves
Rosa chinensis Jacq.	flowers, roots and leaves
Rosa cymosa Tratt.	Roots, leaves and fruits
Rosa laevigata Michx.	roots, fruits and leaves
Rubia cordifolia L.	roots
Rubus roseafolius Smith.	---
Rubus tephrodes Hance	roots and leaves
Rumex daiwoo Makino	roots
Sagina maxima A. Gray	whole plant
Salvia miltiorrhiza L.	roots
Sambucus javanica Reinw.	whole plant
Sambucus racemosa L.	leaves, stems, roots
Sang (Mulberry)	twigs,leaves,achenes
Sanguisorba officinalis L.	roots
Sapium sebiferum Roxb.	roots and leaves
Sargentodoxa cuneata	stems
Saururus chinensis	whole plant
Saussurea lappa Clarke (Inula)	---
Saxifraga sarmentosa L.	whole plant
Scheffera arboricola Hyata	stems and leaves
Schizophragma integrifolia Oliv.	roots and vine
Scopolia japonica	---
Scrophularia ningpoensis Hemsl.	roots
Scutellaria baicalensis, Georg.	---
Scutellaria barbata	whole plant
Sedum kamtschaticum Fisch.	whole plant
Sedum makinoi Maxim.	whole plant
Sedum spectabile Boreau	whole plant
Selaginella tamariscina	whole plant
Semiaquilegia adoxoides	stem tuber
Senecio palmatus Pall	---
Senecio scandens Buch-Ham.	whole plant
Shan (Fir)	roots
Shen-ch'u	---
Shih Suan (Garlic)	corm - fresh whole produc
Siegesbeckia orientalis Linn var.pubescens	whole plant
Siler divaricatum, Benth et Hook	---
Sinomenium acutum Rhed. et Wils.	roots
Smilax Glabra Roxb	stem tubers
Smilax china L.	roots
Smilax nipponica Mig.	roots
So-yang (Orobanche)	---
Soerissa fetida	whole plant
Solanum lyratum	whole plant
Solanum nigrum L.	whole plant

Medicinal plants in the official Chinese paramedical manual

Medicinal plant	Crude drug
Solidago virgo-aurea	whole plant
Sophora flavescens Ait.	roots
Sophora japonica	buds,flowers,legumes
Spirodela polyrhizd (L.) Schleid.	whole plant
Stachys baicalensis	whole plant
Stellaria alsine	whole plant
Stemona tuberosa Lour.	root tubers
Stenoloma chusana	whole plant
Stephania hernandifolia Walp.	root tubers
Stephania, sp.	Tuberous roots
Strobilanthes flaccidifolius Nees.	roots and leaves
Su-mu (Logwood)	---
Suan (leek)	---
Sung-hua Fen (Pine cone pollen)	---
T'ing-li-tzu (Draba memorosa subspecies)	seeds
Ta Fu-p'i (Betelnut palm)	---
Ta Hui (Pa-chiao Hui-hsiang)(Common fennel)	---
Ta Tou (Hei Tou)(Black soybean)	---
Ta-Feng-Tzu (common chaulmoogra)	---
Ta-feng Ai	---
Tamarix chinensis Lour.	branches and leaves
Tan P'i (Bark of Root Peony)	bark
Taraxacum mongolicum Hand-Mazt	whole plant
Terminalis chebula Retz.	---
Tetrapanax papyrifera (Hook) koch.	spongy pith
Tetrastigma hemsleyanum Diels et Gilg.	root tuber
Thuja orientalis L.	---
Tinospora capillipes Giagnep.	tuberous roots
Torreya nucifera	---
Tou-ch'ih (Salted black bean)	---
Trachelosperum jasminoides Lem.	vines and stems
Trachycarpus excelsa Wendl.	silky hair of palm, roots
Tribulis terrestris L.	fruit
Trichosanthes cucumeroides	roots or fresh fruits
Trichosanthes kirilowii Maxim.	fruits,peels,seeds,roots
Trigonella foenumgraecum L.	seeds
Tripterygium wilfordii Hook. F.	roots,leaves,flowers,frui
Ts'ao (date)	---
Tulipa edulis	---
Tylophora ovata (Lindl.) Hock	roots
Typha latifolia L.	pollen
Typhonium giganteum	stem tuber
Tzu-shih (lindera species)	nut of fruit
Uncaria rhynchophylla (Mig.) Jacks.	curved thorns on stem
Vaccaria pyramidate	seeds

Medicinal plants in the official Chinese paramedical manual

Medicinal plant	Crude drug
Valeriana officinalis	roots
Verbena officinalis L.	whole plant
Veronica peregrina L.	whole plant
Viola diffusa Ging.	whole plant
Viola japonica Langsd.	whole plant
Vitex cannabifolia Sieb. et Zucc.	roots, leaves and fruits
Vitex negundo L.	fruits,leaves,roots
Wickstroemia indica A.C. Mew	roots
Xanthium strumarium L.	fruits or whole plant
Yeh-ming sha (bat droppings)	---
Zanthoxylum bungeanum Max.	capsule peels or seeds
Zanthoxylum nitidum (Lam) DC.	roots
Zanthoxylum planispinum Sieb. et Zucc.	seeds and roots
Zanthoxylum simulans var. podocarpum Huang	roots, stems, bark
Zingiber nigrum, Garth	fruit
Zizyphus vulgaris, Lamm var. spinosa Bunge	seeds

Annex 3

to the study

BETTER UTILIZATION OF MEDICINAL PLANTS:

The Phytopharmaceutical supply system in China

Technical Description of a Small-Scale Phytopharmaceutical Factory

1. GENERAL DESCRIPTION

The technology and equipment of the small-scale phytopharmaceutical factory outlined in this annex is based on several years of satisfactory operation in the PRC. It has been designed for the extraction of medicinal plants as well as for the production of phytopharmaceutical preparations.

2. DAILY PRODUCTION CAPACITY

Extraction plant

- Pretreatment, 100 kg of crude drug
- Aqueous extraction, 50 kg of crude drugs
- Alcoholic extraction, 50 kg of crude drugs
- Deionized water, 18 tons

Syrup plant

- Preparation of syrup: 600 kg
- Filling: 1,500 bottles of 30 ml
  4,500 bottles of 100 ml
  500 bottles of 500 ml

Eye drops plant

- 500-5,000 plastic bottles of 5 ml
- 500-5,000 plastic bottles of 15 ml

Ointment plant

Ophthalmic ointment: 1,000-5,000 tubes of 2.5 g
1,000-5,000 tubes of 5 g
Skin ointment : 500-2,500 tubes of 10 g
500-2,500 tubes of 25 g

3. WORKING SYSTEM

- 300 days/year
- 1 shift/day
- 6 hours/shift

4. QUALITY STANDARD

Crude drugs, extracts and preparations should meet the requirements of the official compendia and industry specifications, respectively.

5. PRODUCTION PROCESS

The production processes and unit operations are essentially the same as those described for extracts and pharmaceutical dosage forms in textbooks.

6. INDICATIVE DEMAND FOR MATERIALS

The yearly consumption of crude drugs in the model plant was 30 tons but this figure and its specific composition depends on the actual demand for phytopharmaceuticals. Demand for auxiliary and packing materials also depend to a large extent on the production programme.

The annual consumption of selected auxiliary and packing materials is given below:

Ethanol	15 tons
Saccharose	120 tons
Soft paraffin	100 tons
Liquid paraffin	5 tons
Cation exchange resin	200 kg
Anion exchange resin	350 kg
Glass bottles	195,000 pcs
Plastic containers	300,000 pcs
Ointment tubes	525,000 pcs

7. PRODUCTION STAFF

The distribution of direct work force in the plant is as follows:

Extraction plant	11
Syrup plant	14
Eyer drops plant	4
Ointment plant	7
Quality control	4

8. CONSUMPTION OF UTILITIES

Potable water, mainly used for cooling, cleaning and as input for technology water, should have a maximum temperature of 30°C. Its quality should meet the requirements of the pharmacopoeia. The operating pressure should be 10 m higher than the elevation of the building.

Table A.1. Water consumption

Production unit	Maximum tons/hour	Usual tons/day
Extraction	50	150
Syrup	6	24
Eye drops	1	5
Ointment	2	10
Laboratory	1	5
	TOTAL	194

The model plant is operated with a power of 380 V and 50/cycle.

Table A.2. Power supply consumption

Production unit	Usual daily
Extraction	100 kW
Syrup	40 kW
Eye drops	10 kW
Ointment	20 kW
Laboratory	10 kW
TOTAL	180 kW

The maximum pressure of steam is 6 kg/cm^2. The highest load is 1.8 tons/hour, whereas the usual consumption is about 5 tons per day.

Brine of -5°C temperature is required only in the extrative plant for cooling. Maximum load is 40,000 Kcal/hour. Usual daily consumption is 100,000 Kcal/day.

The production area is about 1,500 m^2.

9. MACHINERY AND EQUIPMENT

Table A.2 lists only the production requirements. It does not include equipment for storage and transportation, machinery maintenance, the steam boiler, fittings and pipelines for domestic water supply and sewage system, high voltage transformer, lighting equipment and materials etc.

General analytical and test apparatus for quality control are listed but specific requirements depend on the choice of phytopharmaceutical preparations.

Table A.3. Main process equipment

Item	Quantity
Extraction plant	
Dryer with blower	1
Herb cutter	2
Grinding machine	1
Electric hoist	1
Water extractor	1
Condenser	1
Transfer pump	1
Precipitating tank	1
Pressure filter	1
Overhead tank	2
Preheater	2
Film evaporator	2
Vapor-liquid separator	2
Concentrated solution storage tank	1
Vacuum evaporator	1
Water jet pump	1
Water circulating pump	1
Water tank	1
Alcohol overhead tank	1
Alcohol precipitating tank	2
Clarified liquor overhead tank	1
Alcohol recovery still	1
Condenser	1
Concentrated alcohol receptor	1
Dilute alcohol receptor	1
Extract storage tank	10
Alcohol make-up tank	1
Alcohol transfer pump	1
Alcohol extractor	1
Circulating tank	1
attached with submerged pump	1
Percolation liquor storage tank	1
Hot water tank	1
Hot water pump	1

Table A.3. Main process equipment (continued)

Item	Quantity
Condenser	1
Dilute alcohol receptor	1
Alcohol evaporator	1
Condenser	1
Concentrated alcohol receptor	1
Dilute alcohol receptor	1
Alcohol distillation still	1
Fractionating tower	1
Condenser	1
Cooler	1
Alcohol receptor	2
Transfer pump	1
Hand cart	3
Vacuum pump	2
Buffer vessel	2
Air compressor	1
Lift	1
Refrigerator	1
Hydrochloric acid storage tank	1
Liquid caustic storage tank	1
Cation-exchange column	1
Anion-exchange column	1
Mixed-ion exchange	1
Deionized water storage tank	2
Deionized water transfer pump	1
Syrup plant	
Hand cart	2
Electric hoist	1
Sugar dissolution tank	1
Transfer pump	1
Pressure filter	1
Cooler	1
Syrup storage tank	1
Measuring tank	1
Syrup make-up tank	3
Hot water tank	1
Syrup transfer pump	1
Syrup overhead tank	3
Bottle washing machine	3
Deionized water tank	1
Booster pump	1
Bottle dryer	2
Bottling machine	3
Belt conveyor	1
Storage vessel	10

Table A.3. Main process equipment (continued)

Item	Quantity
Eye drop plant	
Deionized water overhead tank	1
Make-up tank	1
Sterile filter	8
Overhead tank	2
Measuring bottle	2
Filling machine	2
Sealing machine	1
Cabinet dryer	1
Tray for lining up bottle	30
Bottle-washing pit	3
Vessel	10
Ointment plant	
Electric hoist	1
Vaseline melter	2
Autoclave	1
Filter	1
Vaseline storage tank	1
Liquid paraffin storage tank	1
Liquid paraffin overhead tank	1
Vaseline measuring tank	1
Grinding mill	1
Sieving machine	1
Make-up tank	2
Transfer tank	2
Filling and sealing machine	2
Belt conveyor	1
Tube sterilizer	1
Quality control laboratory	
pH meter	1
Spectrophotometer	1
Polarimeter	1
Refractometer	1
Hydrometer	2
Microscope	1
Conductometer	1
Blow-drying thermostat	1
Thermostatic incubator	1
Low-pressure sterilizer	1
Sintered glass filter	2
Vacuum pump	2
Power stabilizer	3
Vacuum dryer	1
Refrigerator	2

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