1 History and Manufacture

1.1 Introduction

Due in part to the rapidity with which traditional Chinese medicine has been transposed to this country, many of the early, awkward, first efforts at translation, of both medical terminology and medical practice, have settled quietly and unchallenged into common usage. Such has been the case with the so-called "patent" medicines, a misnomer that has become vernacular when referring to any of the traditional ready-to-take medical formulations developed in China. Although the processes used in the preparation of Chinese herbal pills, powders, plasters, tinctures and wines have been codified and formalized, there is little of the sense of proprietary exclusivity, in either product or process, that we usually associate with the term "patent." To be sure, secret family recipes still exist, as is the case with the small, red "emergency pill" that accompanies **Yunnan Baiyao [12.10]**, for example. Yet most so-called "patent" medicines belong entirely to the public domain, and as long as they are made according to now formally established standards of quality, they may be produced and marketed by anyone, without exclusive license, permission, or rights.

Considerably more than mere proprietary advantage alone directed the development of pills, powders, plasters, wines, and liniments from raw natural substances. Assurance of uniform and controlled dosage, retention of potency, control of such variables as rate of metabolic absorption, efficient distribution and lower cost through large-scale production, have all contributed to the development of a sophisticated pharmaceutical science and industry.

We would not be far wrong in speculating, too, that the overtaxed Sung-dynasty merchant, as well as the frazzled Ming mother, appreciated the simple convenience and economy of a well-prepared herbal pill, powder, or syrup as much as does his or her modern counterpart. *Yan Bian Lian*, the phrase commonly used when referring to these *Zhong Cheng Yao* ("Chinese Ready-to-be-Taken Medicines"), may best express the fundamental reason-for-being of ready-to-take medicaments in any tradition: "Effectiveness, Convenience, Economy."

Yet this most conspicuous advantage of mass-produced traditional Chinese formulae is also its most apparent flaw: standardization makes

•Chapter 10 includes the legal responsibilities of the manufactory.

One year after the Drug Control Regulations Act went into effect, the June 19, 1986 edition of the *China Daily* reported that in the latest round of inspections (March, 1986), 1,763 of China's 1,950 pharmaceutical factories were certified as being up to the law's standards, as were 19,095 out of 24,944 sales and distribution companies. Under the law, uncertified factories must bring all products up to standard to continue production and uncertified sales and distribution centers are denied access to products from factories. During this first year after the law became effective, the Chinese government destroyed poor quality or expired medicines (both modern medicine and Traditional Chinese Medicines) worth over 180 million R.M.B. Yuan. In September, 1986, as a result of this law, several people who were involved in the production and sales of fake medicines in Jinjiang Province were given prison sentences up to 11 years (*People's Daily,* September 12, 1986). Liu Yonggang, Deputy Director of the State Pharmaceutical Administration, stated in the June 19, 1986 *China Daily* that the law guarantees the safety and effectiveness of medicine in China. According to Liu, "control of the quality of medicine will be our top priority for the rest of the decade."

1.3.2 Drug Advertisement Regulations Act, September 17, 1985

The Drug Advertisement Regulations Act, which was issued by the Chinese National Industrial and Commercial Administration and the Health Ministry in 1985, regulates all advertisement of medicines in all media, including advertisements in medical journals, general and medical newspapers, television and radio, and even billboards along the sidewalks and streets.

The law states that if the advertiser is also the drug manufacturer, a permit must be obtained to produce the medicine. If the advertiser is only in sales and distribution, and not involved in the manufacturing, a proper license to sell the medicines, as well as any appropriate business licenses, must be on file. Anyone advertising the sale of medicines must have the approval of the local Public Health Administration. Anyone advertising the sale of a specific medicine must present to the local Provincial Public Health Administration and the local Provincial Industrial and Commercial Administration the permit number of the manufactory that is producing that particular medicine. In addition, they must show

the system less interactive. An overwhelming majority of cases seen by traditional physicians in China are treated with individualized prescriptions, prepared by combining medicinal substances for each disorder on a case-by-case basis. Although most such prescriptions are based on classical formulations (as are most prepared formulae), it is in the ability to *modify* those formulae that the true potential of this modality lies, and by which the herbalist's skill is measured. The necessarily generalized therapeutic targets of pre-manufactured formulae address only the most common symptoms of specific syndromes, and in most cases precludes such customization.

Thus, while prepared formulae are indeed recommended by physicians practicing in China, they are usually intended as supplemental therapy, or for specialized or emergency cases (portal-opening formulae, for example, are almost exclusively prescribed in the prepared format). In general, they are infrequently prescribed alone, and, more often than not, are chosen by patients themselves for self or family care, as many Westerners now employ vitamin therapy and nutritional supplements.[1] The use of Chinese prepared formulae in their country of origin may be more accurately described as doctor-assisted self-prescription than as herbal medicine in its truest sense.

Clearly, such a situation is possible only when a class of primary-care professional herbalists is accessible to a patient population educated in the use of these preparations. The absence of these conditions in the West points to a phenomenon that has had a profound impact on the development of Oriental medicine here: the relative lack of penetration of traditional herbal medicine into the mainstream of Oriental medical education and practice.

Of the important modalities in traditional Chinese medicine (acupuncture, herbal medicine, massage, diet therapy, and exercise therapy), only acupuncture has been allowed, even encouraged, to develop in its entirety, to evolve new applications in its new milieu, to define its scope of education, and to set standards for entry to its professional practice. Traditional Chinese herbal medicine, on the other hand, has developed here much more hesitantly. It has produced fewer comprehensive educational programs, found its way into fewer professional licensing regulations, and has generally attracted less national attention. It has been the acupuncturist, rather than the herbalist, who has defined Oriental medicine for the West, and acupuncture, not herbalism, with which we associate the system and understand its history.

Various factors have contributed to this phenomenon. The significant level of clinical and theoretical skills and primary-source scholarship that are demanded of the practitioner of traditional Chinese herbal medicine have helped postpone its cultural penetration in the West. Certainly the fact that most of the important early teachers, notably Soulie De Morant, Tin Yau So, Nguyen Van Nghi, Van Burren, and J.R. Worsley, were trained principally as acupuncturists, must also be considered.

By whatever premise we choose to understand its evolution, the present stage in the development of the entire modality of Chinese herbal medicine in the West explains much about our understanding and application of the prepared medicines themselves. Without a public conversant in their use, responsible self-prescribing is limited, and access to the medicines therefore becomes dependent on the professionals who provide their health care. Because most providers are themselves not specifically trained as herbal physicians, their use of prepared medicines in patient care represents for many the upper level of their herbal medicine skills. These factors have in many cases combined to elevate prepared medicines, and those health-care providers who use prepared medicines as their sole form of herbal therapy, to a place in the hierarchy of traditional Oriental medicine not enjoyed by their counterparts in China.

Two related axioms should thus be emphasized to help guide the practitioner in the effective use of Chinese prepared medicines.

Prepared formulae are most effective when their prescription is grounded in a thorough understanding of traditional Chinese medical theory and herbal practice. This is not to say that their use should be avoided when such expertise is absent. Yet without comprehensive education and training of the practitioners who choose to use them, the true potential of prepared herbal medicines as effective adjuncts to primary-care therapy, and as valuable additions to the home medicine chest, may not be fully realized.

Finally, the practitioner should be aware that, except in certain acute cases, prepared formulae are best presented in the context of a comprehensive treatment plan, and are rarely intended to stand alone as independent therapeutic entities.[2] Used properly, they are extremely effective, and represent wonderful adjuncts to many therapeutic modalities, providing safe and inexpensive supplemental medicines.

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1.2 History and Manufacture

The history of the manufacture of ready-prepared medicines is a long one, paralleling the history of pharmacology in China. The 1973 unearthing at Ma Huang Dui in Hunan Province of medical manuscripts dating from approximately the second century B.C.E., offers evidence that these preparations were being recommended by physicians for their patients as early as the Warring States period (403—221 B.C.E.). The *Wu Shi Er Bing Fang*, one of the works discovered at Ma Huang Dui, lists not only some 224 individual drugs, but the substances recommended for use as carriers and binders in their processing as medicaments. Though we have developed more sophisticated carriers than the cart-grease, turtle-brains and scalp oil recommended in that work, most forms that are now familiar to us, including pills, powders, syrups, plasters and tinctures, were described there.[3]

It was not until the late Han dynasty, with the publication of the *Shang Han Za Bing Lun (Treatise on Fevers and Miscellaneous Diseases)* in 219 C.E., that the foundations of contemporary Chinese pharmacology were laid. Considered the progenitor of all later works in herbal medicine, the *Shang Han Lun* contains 113 herbal formulae, more than 60 of which are described in prepared medicine format. It is a testament to the scope of that work, and to the modality itself, that such *Shang Han Lun* formulae as **Wu Ling San, Shen Qi Wan [11.2]** and **Zhi Sou Ding Chuan Wan [3.17]**, are, some seventeen centuries later, still considered by practicing physicians to be staples of the modern Chinese pharmacy.

The significant interest in medicine evidenced in the Sung Dynasty, and the revision of the materia medica instituted by T'ai-tsu (927-976), the first emperor of that era, led ultimately to the compilation of the *Tai Ping Hui Min He Ji Jiu Fang (Formularies of the People's Welfare Pharmacies)*, compiled by the physician Chen Shiwen, and published in 1155. Describing some 788 prepared medicines, and introducing the procedures to be used in their preparation, this work is considered the first medical text exclusively devoted to prepared formulae. It was also destined to become the basic manual for the first, formal pharmacological manufacturing facility to be established in Imperial China, the *Shu Yao Suo* (lit., Medicine Processing Facility).[4] Although the *Shu Yao Suo* was precedent setting by virtue of its formalization of procedure and medicinal recipes, its beneficiaries were limited to those fortunate enough to have access to the Imperial Hospital. Citizens in need of medical care depended primarily upon local doctors, who prepared medicines on a custom basis from a repertoire either inherited or collected regionally.

Large-scale production of prepared formulae did not occur until well into the Ming (1368-1644) and Qing (1644-1911) dynasties. In the burgeoning entrepreneurial climate of the times, encouraged in part by governmental decentralization of pharmaceutical production, the growing number of small, privately owned pharmacies began to develop the competitive marketing strategies that would later drive the pharmacological industry in modern China: improved and innovative production methods (through development of new medicinal formats and more efficient manufacturing processes); and product specialization (through advertisement of secret family recipes, and production of new, specialized formulae).

The most successful of these first private enterprises was the Tong Ren Tang Pharmacy, founded in 1669 in Beijing. Located since 1702 on Da Zha Lan Street, a narrow lane wide enough for but a single car in a bustling business section of Beijing, the Tong Ren Tang herbal pharmacy has been run by members of the same family for over 317 years, and is the largest, as well as the oldest Chinese herbal pharmacy still in operation today. Its virtually unrivaled reputation among pharmaceutical firms in China harkens back to Tong Ren Tang's early connections to royalty: the pharmacy's original owner was a pharmacist in the Imperial hospital in Beijing during the seventeenth century, and, during the nineteenth century, the firm was the exclusive purveyor of medicines to the Imperial Palace.

Zhao Congru, current manager of Tong Ren Tang, points to the high standards of production and raw materials to which Tong Ren Tang continues to adhere as the basis for the firm's continued high regard. Herbs are painstakingly sorted and selected by senior pharmacists from those grown in specific geographic areas: *Huang Lian (Rhizoma Coptidis)* from Szechuan Province; *Chen Pi (Pericarpium Citri Reticulatae)* from Xin Hui county in Guandong; *Dang Gui (Angelica Sinensis)* from Min county in Gan Su; *Sheng Di (Radix Rehmanniae Glutinosae)* from He Nan.

Corroborating Tong Ren Tang's assertions of high standards of manufacturing was an article that appeared in the February 14, 1985 issue of the *Jian Kang Bao* (Health News Newspaper). During a routine inventory of medicines in the warehouse on the site of the original pharmacy, *Jian Kang Bao* reported, 130-year old samples of prepared medicines, including **Da Huo Luo Dan [6.2] Su He Xiang Wan [5.4a]** and **Ren Shen Zai Zao Wan [6.3]** were discovered, still fresh and potent in their original wax packages.

Today, some 2000 employees work in four divisions of Tong Ren Tang (three factories, one each for production of medicines, liquors, and extracts, and a retail store), producing 495 varieties of prepared medicines. The most famous prepared medicines produced by Tong Ren Tang include **Niu Huang Qing Xin Wan [6.5]** (of which ten million were produced in 1986), **An Gong Niu Huang Wan [5.2]**, **Ren Shen Zai Zao Wan [6.3]**, **Shen Rong Wei Sheng Wan**, **Su He Xiang Wan [5.4a]**, **Zi Xue Dan [5.1]**, **Da Huo Luo Dan [6.2]**, **Ju Fang Zhi Bao Dan [5.2a]**, **Nu Jin Dan**, and **Hu Gu Jiu**.

Following Tong Ren Tang in size and notoriety is the Hangzhou Second Traditional Chinese Pharmaceutical Works in Zhejiang Province, an outgrowth of one division of Huqing Yutang Pharmacy, first established in Hangzhou in 1874. Known primarily for production of tonic prepared medicines for general health, this modern factory of more than 1000 employees produces over 90 kinds of prepared medicines. Among the best known supplements prepared here are **Ching Chun Bao**, used to maintain health and promote longevity, and **Shuang Bao Su [13.12]**, a general tonic similar to **Ren Shen Feng Wang Jiang [13.1a]**.

Other pharmaceutical companies of note include Shanghai First, Second and Third Traditional Chinese Pharmaceutical Works in Shanghai; Da Ren Tang in Tianjin; and Zhong Lian Traditional Chinese Pharmaceutical Works in Wuhan, Hubei Province.

Clinical and laboratory research over the past three decades have led to both the development of new formulae and to adaptations of traditional ones. Such formulae as **Shen Jing Suai Ruo Wan [13.9]** and **Jiang Ya Wan [7.15]**, both developed by the famous contemporary physician Shi Jinmo, and **Bi Yan Pian [1.11]** developed through clinical trial, are new members of the pharmacopoeia. **Guan Xin Su He Wan [5.4]**, an important formula for the treatment of heart disease, is a modification of the traditional Song dynasty Chinese prepared medicine **Su He Xiong Wan [5.4a]**, which is still used widely to treat unconsciousness, coma, and stroke.

1.3 Quality Control

The intense pharmaceutical development in China during the past three decades has made evident the need for standardization and quality control mechanisms in the production and distribution of traditional prepared formulae. No longer were the zealously guarded manufacturing

processes and secret family recipes, passed down exclusively through paternal transmission, appropriate for the growing national and international patient populations. In response to the Chinese government's call for standardization, regional manufacturers of prepared medicines were organized early in the 1950's to establish a consensus on production methods, nomenclature, and formulation. Among the outcomes of these meetings were the publications of the first modern Drug Code (in 1953) and, in 1957, of the text *Wan San Gao Dan Ji Cheng (Collection of Prepared Medicines)*, in which 2,782 prepared medicine formulae were codified.

Although the 1953 and the later, 1977, editions of the Drug Code of the People's Republic of China *(Zhong Hua Ren Min Gong He Guo Yao Tian)* established guidelines for correct preparation and administration of prepared medications, until recently, little was done to enforce them at the level of manufacture.[5] The Drug Code Administration Law of 1985 *(Zhong Hua Ren Min Gong He Guo Yao Tian Guan Li Fa)* was structured to address this situation, and represents China's most comprehensive effort thus far in drug quality control. Manufacturers must now obtain a license, based on adherence to acceptable standards of preparation, in order to produce prepared formulae. Certain articles of that law have been highlighted here to offer some insight into the present state of the traditional pharmaceutical industry in China. A related law, the *Drug Advertisement Regulations Act* of 1985, is summarized below in section 1.3.2.

1.3.1 Drug Control Regulations Act, July 1, 1985

The Drug Control Regulations Act (formally the *Administrative Law of Medicine of the People's Republic of China)*, was issued by the Chinese National Administrative Bureau of Drugs on September 20, 1984, and became effective July 1, 1985. Qi Moujia, director of the National Administrative Bureau of Drugs, stated that the purpose of the Drug Control Regulations Act is to guarantee the quality of drugs (*China Daily*, July 3, 1985). At about the time of its enactment, there were 6,499 different prepared medicines produced in China, 1,000 of which were considered to be commonly used.

•Chapter 1, Article 3, of the law states that the People's Republic of China encourages the development of both modern medicine and traditional Chinese medicine, and that the Chinese government will protect

the geographical source of the herbs and encourage the cultivating of Chinese herbal medicines.

•Chapter 2, Article 4, establishes a licensing procedure for drug manufactories, which includes license expiration dates and renewal protocol.

•Chapter 2, Article 5, states that any factory that produces medicines must have specific personnel appropriate for such production, including pharmacists, engineers, and technicians. Further, this section states that such personnel must be provided with proper space, buildings, and equipment suitable for the production of the medicines for which the manufactory is licensed, as well as the equipment and expertise to assess medicinal quality.

•Chapter 2, Article 6, states that the process of producing Chinese herbal medicines must follow the requirements of the Pharmacopoeia of the Peoples Republic of China, or the requirements issued by the local government.

•Chapter 2, Article 7, states that the materials and supplementary materials used to produce the medicine, as well as the container holding the medicine, must conform to certain regulations.

•Chapter 2, Article 8, states that the medicine must be inspected for quality before it leaves the factory. If the medicine fails the inspection, it cannot be released.

•Chapter 5, Article 33, standardizes certain specific medicines, allowing no deviation from established ingredients. It is illegal to use additional ingredients that are not medicinal ingredients, or to substitute ingredients. It is also illegal to *use* medicines that have been produced by factories that do not have the proper license.

•Chapter 5, Article 34, states that certain standards must be met in terms of herbal quality. This means, for example, that if an herbal formula requires 10% ginseng, it is illegal to make the formula with 7% ginseng. In addition, it is illegal to use herbal medicines that have exceeded their expiration date.

•Chapter 5, Article 35, states that the clinical personnel who come into contact with the herbal medicines must have annual health exams to insure protection of the herbal contents from any contamination.