Chapter 1

Introduction to Traditional Herbal Medicines and Their Study

Willow J.H. Liu

1.1 DEFINITION AND TRENDS OF TRADITIONAL HERBAL MEDICINES

According to the World Health Organization (WHO), traditional medicine refers to health practices, approaches, knowledge, and beliefs incorporating plant, animal, and mineral-based medicines, spiritual therapies, manual techniques, and exercises, applied singularly or in combination to treat, diagnose, and prevent illnesses or to maintain well-being. If the material being used is of plant origin, then it is called traditional herbal medicine.

Different types of traditional medicines are widely applied in Asia, Africa, and Latin America to meet primary health-care needs. Traditional medicine has maintained its popularity in most regions of the developing world. The application is also rapidly spreading in industrialized countries, where adaptations of traditional medicines are often termed “complementary” or “alternative.” In the United States, the National Institutes of Health (NIH) uses the name complementary and alternative medicine (CAM) to cover health systems, practices, and products that are not considered part of conventional medicine. Worldwide, among all the different traditional medicine systems, traditional Chinese medicine (TCM) is currently the most popular, followed by Indian medicine. In Western terminology, the name “Oriental medicine” covers Chinese, Japanese, and Korean medicines preferred by immigrants from Korea, while “Asian medicine” is often used to include TCM, Indian (Ayurveda), and Tibetan medicine. Among all treatment methods in traditional medicine systems, medicinal herbs are the most widely applied.
Medicine has been revolutionized in Europe by advances in chemistry, laboratory techniques, and equipment since Robert Koch discovered the transmission of disease by bacteria, followed by the discovery of antibiotics in the early 1900s. Thus, modern medicine is commonly called Western medicine even though there are also traditional medicines in Western countries. It is also called conventional medicine.

Webster’s medical dictionary defines conventional medicine as medicine practiced by holders of medical doctor (M.D.) or doctor of osteopathy (D.O.) degrees and by their allied health professionals, such as physical therapists, psychologists, and registered nurses. Other terms for Western medicine or conventional medicine include allopathy and allopathic medicine, mainstream medicine, orthodox medicine, regular medicine, and biomedicine.

Although conventional medicine is the mainstream medicine in Western countries, application of traditional medicine, including herbal medicines, is growing worldwide for many reasons, in particular, the side effects or inefficacy of modern drugs. The following data are provided by the WHO.

- In Africa, up to 80% of the population uses traditional medicine for primary health care.
- In China, traditional herbal preparations account for 30–50% of the total medicinal consumption.
- In Europe, North America, and other industrialized regions, over 50% of the population has used complementary or alternative medicine at least once.
- In Germany, 90% of the population has used a natural remedy at some point in their lives.
- The global market for herbal medicines currently stands at over USD$60 billion annually, and is growing steadily.

Since the last century, scientists all over the world have studied herbal medicines from the fields of chemistry, biology, pharmacology, toxicology, and clinical trials. Recently, in addition to screening out new drug candidates, investigators also expect to explore the preventative and therapeutic mechanism of herbal medicines that play very important roles in most of the traditional medicine systems, such as TCM and Ayurveda medicine.

1.2 RESEARCH AND DEVELOPMENT OF HERBAL MEDICINES

The use of herbal medicines for treatment of diseases was documented several thousand years ago. As seen from journals, studies on herbal medicines have been encompassed under several different names, such as plant medicine, phytomedicine, pharmacognosy, and natural products. “Natural products” usually refer to products processed or derived from living organisms, including plants, animals, insects, microorganisms, and marine organisms.
Data from the WHO show that 25% of modern medicines are made from plants that were first used traditionally. Examples include atropine, morphine, quinine, ephedrine, warfarin, aspirin, digoxin, vincristine, taxol, and hyoscine.

Traditional medicine needs to be modernized in the twenty-first century. However, modernization of traditional medicine should not be simply Westernization. For herbal medicines, the purpose of a study is not only to screen out bioactive compounds from herbal extracts for new drug development, but also to standardize and control the quality of raw herbal materials and their products to ensure the safety and efficacy; and more importantly, to reveal their preventative and therapeutic mechanisms. So far, only a relatively small number of herbal medicines have been well studied from all of these aspects; these herbs include Echinacea, ginkgo, ginseng, and licorice.

To a large extent, the depth and progress of research on herbal medicines depend on the development of related technology and equipment, as well as the in-depth understanding of the human body and diseases. Mechanism study and functional evaluation of herbal medicine involve the fields of chemistry, biochemistry, biology, pharmacology, toxicology, and clinical study. Thus, organized and consistent teamwork is absolutely vital.

Researchers from different labs need to work closely together, discuss problems frequently, and analyze the results instantly. A scientist for extraction and isolation of herbal medicines in the chemistry lab should have enough knowledge of biology and pharmacology to provide an appropriate sample because an improperly extracted or isolated sample provided from his or her lab for biological and pharmacological study could lead to wrong results in the bioassay or animal test. The scientist in the bioassay or animal lab for screening or mechanism study of herbal medicines should make sure that the sample to be tested is correctly extracted, that the concentrations of tested samples are within a proper range, and that the design of the experiment is scientific enough to provide a true result. And to reach such a goal, an adequate understanding of the research target, the functions and indications, as well as clinic applications of the study herb is necessary. The following are several main aspects of herbal medicine research.

1.2.1 Extraction, Isolation, and Identification of Compounds in Herbal Medicines

All the substances in the universe, including plants, are composed of chemical compounds. To study herbal medicine, the major bioactive chemical components should be first known. Only after the biological compounds in herbs are correctly extracted, isolated, and identified can biochemical, biological, or pharmacological studies be performed scientifically.

Chemical studies of herbal medicines provide fundamental substances for further studies of biological and pharmacological activity. During the earlier decades of the 1800s, chemical studies in plants could only be performed on active compounds that were highly concentrated and isolated into a relatively pure form by
techniques such as distillation or extraction with water, acid, base, or alcohol. Their structures were mainly determined by chemical degradation and proven by synthesis in an unambiguous manner. Scientists were unable to determine the stereochemistry of compounds.

The well-known example is the story of aspirin. According to records about willow leaves as an antipyretic treatment in Ebers papyrus, and following the same application of teas made from willow bark as an English herb, chemists and pharmacists successfully isolated salicin from the bark of the white willow, *Salix alba*, between 1825 and 1826. The compound responsible for the remedy was subsequently converted to salicylic acid via hydrolysis and oxidation, and proved as such a successful antipyretic (fever reducer) that it was actively manufactured and used worldwide. Due to severe gastrointestinal toxicity, salicylic acid was converted into acetylsalicylic acid via acetylation by scientists at Bayer. It was given its trade name of aspirin in 1899. Today, aspirin is still the most widely used analgesic and antipyretic drug in the world.

Since the 1950s, chromatography, including medium-pressure liquid chromatography (MPLC) and high-performance liquid chromatography (HPLC), and other methods such as supercritical fluid extraction (SFE), droplet countercurrent (DCC), and high-speed countercurrent (HSCC) have been popularly applied for isolation of natural products, while different types of spectral equipment such as infrared (IR), ultraviolet (UV), nuclear magnetic resonance (NMR), circular dichroism (CD), and mass spectrometer (MS), as well as MS coupled with gas chromatography (GC), have been commonly used for structure identification. Later on, LC-MS and LC-NMR also became available and gradually more popular in the last few decades. These advances have made the time for extraction, isolation, and identification of compounds from herbal medicines much shorter than that of a century ago. Modern extraction and isolation techniques, combined with all types of chromatography, are often guided by bioassays to isolate the active compounds. High-throughput screening with robots also dramatically lowers the screening times. Thus, structure-efficacy elucidation of newly isolated bioactive compounds is no longer a time-consuming and difficult process.

However, the process of finding new drug candidates from herbs for drug development is no longer as easy as the story of aspirin. The story of taxol is that of a difficult journey of a trace compound from a plant becoming a powerful new drug. Taxol is one of the most well-known diterpenes with a very complex steroid structure and anticancer activity. The extract of the bark of Pacific yew (*Taxus brevifolia*) was first found to be cytotoxic in a cellular assay in 1964. The active ingredient was isolated in 1966 with a very low amount, and the structure was published in 1971. By 1969, 28 kg of crude extract had been isolated from almost 1200 kg of bark, but yielded only 10 g of pure material. The research result showed that it acts to stabilize the mitotic apparatus in cells, causing them to act as normal cells rather than undergo rapid proliferation as they do in cancer. But it was not until the late 1980s that its value as an anticancer drug was confirmed.1

Current modern methods and techniques such as all kinds of chromatography and spectrometry, and their combined application make the extraction, isolation, and
structure identification of bioactive compounds from herbs dramatically faster than half a century ago. Highly accurate analytical equipment, such as HPLC coupled with UV and/or MS and other detectors, makes the quality control and standardization of herbal products more reliable for pharmacological and clinical studies. Advanced biochemical and biological technologies, such as microarray, allow scientists to easily explore the mechanism study at the enzyme, receptor, and gene levels quantitatively using only small amounts of samples. These advanced technologies and their applications to herbal study will be introduced in the following chapters. With all these available high technologies, time for isolation and identification of compounds from herbs is becoming shorter and trace bioactive compounds are more easily obtained. With the popularity of various spectroscopy methods, identification of isolated compounds is becoming much easier than it was decades ago. Application of hyphenated LC-UV/MS and LC-NMR techniques greatly accelerates the systematic identification of compounds in an herbal extract.

To perform any herbal study, identification of the herbal materials used for study should never be neglected. Morphological, microscopic, physical, or chemical identification can all be applied to identify the raw materials. The availability of HPLC chromatogram or gene fingerprints makes identification of species highly accurate.

1.2.2 Bioassay Screening and Mechanism Study of Herbal Medicines

Scientists have spent over a hundred years trying to screen new drug candidates from herbal medicines. Recently, due to the rapid growth of products of herbal medicine or alternative medicine all over the world, their efficacy and safety have become more and more important. More attention has been drawn to the preventative and therapeutic mechanism study of herbal medicines. For both reasons, bioassay study on herbs is indispensable. Thanks to the advancement of biological technologies, more and more bioassays are available for mechanism study. The mechanism of many effective herbal medicines has been elucidated, such as the well-known ginkgo, Echinacea, red clover, black cohosh, ginseng, and many Chinese and other traditional herbs. Bioassays in vitro are usually followed by in vivo animal tests to further confirm the functional mechanism and understand the absorption, metabolism, and toxicity in living bodies.

Bioassay is commonly performed using enzymes, receptors, genes, cells, and sometimes tissues. In comparison to screening for new drug candidates of single compounds, screening herbal extracts or fractions is relatively difficult due to the solubility or complex composition in herbal samples. Compounds in an extract might interfere with each other, or more specifically, the activity of one compound might be masked by another in the mixture due to the adverse effect or toxicity of the latter. So, the bioassay result of an herbal extract should be carefully evaluated, particularly when a high-throughput method is applied, not only due to the mentioned interference, but also because of the dramatically varied concentrations of bioactive components in different samples prepared under the same conditions.
Mechanism study for herbal medicine does not necessarily use high-technology equipment. The most important thing is to select the right targets. Different enzymes, receptors, or genes should be tested for mechanism of an herbal extract. Assays at different levels should be applied to ensure the positive or negative research results. Evaluation of estrogenic activity of red clover and black cohosh extracts using different bioassays can be used as an example.\(^2\)

In many cases, the corresponding bioactive components for the functional mechanism of herbal medicines are common or universally distributed compounds. Such results may disappoint researchers looking for new drug development, but they are very helpful to scientists who are dedicated to explaining the functions of herbs or willing to understand more about physiological functions of these common compounds in the human body. Examples include linolic acid, a cyclooxygenase (COX) inhibitor in *Angelica pubescens*\(^3\) and an estrogenic agonist in *Vitex agnus-castus* L. (chaste berry),\(^4\) and N\(_{ω}\)-methylserotonin, a serotonin agonist in black cohosh.\(^5\)

### 1.2.3 Pharmacological and Toxicological Study of Herbal Medicines

Similar to modern pharmaceutical study, pharmacological study of herbal medicines include pharmacodynamic (PD) and pharmacokinetic (PK) aspects. Broadly, toxicology is also part of the pharmacology.

PD study of traditional herbal medicines is not always easy. Up to now, only the most popularly used herbs, a very small fraction of the total number used, have been well known with respect to pharmacological effects on animals. One reason is that herbs might treat diseases in a way different from known modern drugs. Black cohosh is one example. This herb has long been used in North America for menopause symptoms in women, but *in vivo* animal study indicated that its extract did not exhibit effects in ovariectomized Sprague–Dawley rats. Further study showed that instead of directly binding to estrogen receptors, extract of black cohosh was reported acting as a mixed competitive ligand and partial agonist of the serotonin and opiate receptor,\(^6\,7\) which indicates that this herb might treat menopause symptoms through regulation of the central nervous system.

Chinese scientists have done numerous pharmacological studies on Chinese herbs. Therapeutic mechanisms of the most commonly used Chinese herbs have been known by systematic PD studies.\(^8\,9\,10\) However, there is another challenge in the pharmacological study of Chinese herbs; that is, in the vast majority of cases, the practitioners prescribe formulas that consist of several (sometimes over 20) herbal ingredients for the treatment. This makes the study difficult not only due to the complex analysis of chemical composition for quality control of the test samples, which is important to keep good reproducibility of the results, but also because of the complex theories of TCM behind the combination of different herbs, which will be mentioned in Chapter 10.

Many people mistakenly believe that herbal products are safe. Although most herbal medicines are relatively safe in comparison with modern drugs, results from
toxicological studies show that this is not always true. To a large extent, the safety of herbs depends on dosage and period of administration. It is necessary to mention that purification of some herbal extracts may increase their toxicity. This is because, while the active components are concentrated, the concentration of toxic compounds may also be increased. Sometimes, the active components are toxic. In this case, while the therapeutic effect is enhanced, the toxicity is also increased. Examples include ephedra extract and herbal extracts from the Aristolochia family. Studies of aristolochic acid found in several herbs in Aristolochia family have shown its significant carcinogenic and mutagenic effects and poisoning of the kidney. In TCM, processing of raw herbal materials with different methods, such as extended heating with steaming or boiling to decompose the chemical bonds of toxic ester or glycoside compounds in herbs, has been long applied to reduce the toxicity of Chinese herbs. Examples include aconitine in radix Aconiti and sennosides in rhubarb.

PK study of herbal medicines is so far mainly applied to herbs with known active compounds. The concentrations of these active index compounds in the blood, urine, and other body liquids or tissues after a certain period of administration are measured and compared by means of UV, MS, GC-MS, HPLC-MS, and other analytical methods to analyze the distribution of the compounds and change of concentrations with time. To herbs with unclear composition or whose concentration could not be monitored with analytical methods, their efficacies are measured and time-efficacy curves are drawn. In addition, PK–PD models are also applied to the study of herbal PK.

This book covers the PD and toxicology studies of herbal medicines, but not the PK. The reason is that the methods of sample collection for PK study of herbal medicine are the same as those for modern drugs. The analytical methods for absorbed and metabolized known compounds in herbs can refer to the qualitative and quantitative analysis of herbal medicines in Chapter 9. Keep in mind that the complex chemical composition of herbal preparations always makes the analysis relatively difficult.

In comparison with so many PD study reports of herbal medicines, only a few systematic PK studies for herbal preparations have been reported; one example is the PK of alkamides in Echinacea purpurea. Progress of the PK study is covered in recent review articles.

### 1.2.4 Chemical Standardization and Quality Control of Herbal Medicines

Substitute or counterfeit herbal materials are often found in the market. Even for the right species, the chemical composition and concentrations of bioactive compounds may vary dramatically with different collection seasons and regions as well as storage. Therefore, it is necessary to chemically standardize the herbal extracts or products for biological, pharmacological, and clinical studies.

The complex composition of herbal medicines makes the quality control of herbal products much more complicated. With the increase in knowledge about the bioactive and main compounds in most of the commonly used herbs and the popular
application of various analytical instruments such as HPLC, equipped with UV, MS, and other detectors, fingerprint chromatograms are becoming powerful qualitative and quantitative methods for standardization of herbal medicines. Such standardization is not only necessary for quality control of final herbal products, but also important to guide the species collection and cultivation, as well as the optimization of the processing procedure.

1.2.5 Clinical Studies of Herbal Medicines

Anything that exists on the earth has a need for survival. Many traditional herbs have been used on human beings to prevent and treat diseases for hundreds or even thousands of years. The fact should be acknowledged that most of the herbs have been used by countless people. Take Chinese herbal medicine as an example. The efficacies, toxicities, therapeutic and toxic dosages, as well as cautions and contraindications of most herbs have been well recorded in many traditional Chinese herbal books. Although the terminologies used for diagnosis and treatment of diseases in traditional and modern medicines are different, researchers are encouraged to figure out the symptoms described in traditional terminologies for the application of traditional medicine and try to match them to that of modern diseases for scientific clinical trial.

A successful clinical trial depends on accurate scientific design. In comparison to the trial for a single chemical drug, that for an herbal product is more complicated due to the complex composition and difficult quality control of the components. The extract method, the concentrations of the main or bioactive compounds in the products (or the purity of the products), the number and criteria of patients selected, the route and dosage of the administration, the period of the trial, and the method to collect and process the data will all influence the results of the trial.

Unfortunately, many of the reported results of clinical studies on herbal medicine so far are not reliable due to more or less unscientific design. Quite often, the results of clinical trial for one herbal medicine obtained by different research groups vary significantly. A well-known example is St. John’s Wort. Some reported this herb to have an effect on mild depression; others reported no such effect. Possible reasons have been mentioned in the above paragraph. A difference in any step of the experimental design will affect the result.

To obtain reliable clinical trial results for herbal medicines, double-blind experiments should be applied with enough patients selected, ideally using the standard of clinical trial for new drug development. Of course, budgetary constraints are often a hindrance to carrying out such trials.

1.3 COMMON MISTAKES SEEN IN RESEARCH ON TRADITIONAL HERBAL MEDICINES

Before starting research on herbal medicines, researchers should carefully search for literature that is related to the study. After reviewing the literature, they should
develop a research plan by writing a detailed procedure design. The following common mistakes should be avoided.

1. **Starting preparations of samples without identification of herbal materials.**
   For many reasons, substituted or adulterated herbal medicines are often seen in the markets. Sometimes they are not easily distinguished from the right material with the naked eye.

2. **Starting biological or pharmacological experiments without chemical identification and standardization of samples.**
   I recall that one day an American friend showed me a bag containing an herbal product. The label on the bag said: No chemicals, all natural. This can lead to a popular misconception among consumers. But as scientists, we should know that chemicals are the fundamental substances of biological activities of herbal medicines, and nature is made up of chemicals. Therefore, chemical identification and standardization must be the primary step in the experiment of modern herbal study. Otherwise, the results are not reliable or accepted.

3. **Using the wrong extraction method or solvent, such that the bioactive compounds are not extracted.**
   Make sure the extraction method will extract the corresponding bioactive compounds. For example, if an extract is for a steroid receptor binding assay, the potential ligands will probably be lipophilic, thus a less polar solvent such as chloroform may be selected. If an extract is for an antivirus experiment, the possible bioactive compounds may be large molecular glycoproteins or polysaccharides; lipophilic solvents or alcohol will not extract them out. The best way is to extract the material with different polar solvents in succession and test them separately in the primary test.

4. **Using a dosage for the bioassay or animal test that is too low.**
   Since the efficacies of bioactive compounds in herbs are relatively weaker than the positive modern drug in most cases, and the concentrations of bioactive compounds are very low in the extract, the negative result of a sample in an assay or animal test may become positive if the concentration of sample is increased. Several dosages at different magnitudes are suggested to prepare for the primary test. Sometimes, the concentration of an herbal extract might be 1000 times higher than that of the positive control. For example, when the estrogenic activity was evaluated for red clover, methanol extract of red clover did not show positive results in the estrogen receptor binding assay until its concentration was increased to 20 µg/mL.

5. **Having a test period in an animal study or clinical trial that is not of sufficient length.**
   Because the effects of bioactive compounds in herbs are relatively moderate in comparison with the positive modern drug, it usually takes a longer time to see the positive result of an herbal extract in animal tests. For example, an estrogenic test for synthetic drug candidates on ovariectomized rats may only need a week, but
positive results of a red clover extract were not observed until the third week of the experiment.

6. Using samples that vary in composition, leading to unrepeatable results.

Ideally, the same batch of herbal sample solution should be used for the same assay or test. If not, chemical analysis should be performed for different batches of samples by HPLC to avoid variable results caused by inconsistent quality or quantity of compounds in samples.

1.4 RESEARCH ON TRADITIONAL HERBS SHOULD REFER TO THEORIES AND CLINICAL APPLICATION OF TRADITIONAL MEDICINE

Many traditional herbs are clinically prescribed by practitioners of traditional medicine under the guidance of theories in traditional medicine, such as TCM in China and Ayurveda in India. This aspect has mostly been ignored by scientists in the field of modern research of herbal medicine for product development, particularly in Western countries. Even in Asia, chemists, biologists, and pharmacologists who have been studying herbal medicine with modern knowledge and technology in labs for many years rarely know enough about theories that guide the applications of herbal treatments in the clinic. One of the reasons is that such study is more challenging.

Traditional herbs might treat a disease in a way different from known modern drugs. Take TCM as an example. A disease can be divided into several “zhengs” based on TCM differentiation. “Zheng” is a Chinese word that is similar in meaning to English symptoms or signs. For example, there is “cold zheng,” “hot zheng,” “internal zheng,” “external zheng,” “excessive zheng,” “deficient zheng,” “yin zheng,” “yang zheng,” “damp zheng,” and “bi zheng” (bi means blocked). Different herbs may be used on different patients with same disease but different zhengs. Sometimes, no animal models can be found to match these zhengs for PD study of herbs that are clinically used for treatment of certain types of zhengs. Thus, a new model with a particular zheng has to be established first. To do this, scientists have to be knowledgeable in both traditional and modern medicines. Otherwise, the study results are not reliable. Up to now, Chinese scientists have found out the biological and pathological foundation for most of the zhengs in TCM and established many animal models for pharmacological study of herbal medicine.9

Theories of traditional medicines, such as TCM, cover etiology, pathology, diagnosis, and treatment. Study of these theories can not only help us to explore the mechanisms of herbal treatment, but also help scientists explore possible new etiology and pathology for diseases whose causes are still unknown in modern medicine, thus providing new directions for drug development. For such purposes, a variety of in vitro bioassays on different receptors, enzymes, and other targets and in vivo animal pharmacological tests should be performed on herbs—not only individual ones, but also herbal formulas.
For example, clinical practice has confirmed that Gui Zhi Fu Ling Wan (Cinnamomi and poria composition), a Chinese herbal formula composed of five Chinese herbs, is very effective in decreasing or eliminating uterine fibroids when their diameter is less than 5 cm. This has been confirmed by comparing ultrasound exam results before and after the treatment in the clinic and by pharmacological study on rats. The uterine fibroids are usually removed by surgery in modern medicine if they cause severe abnormal bleeding or if they are too big. Quite often, the uterus will be removed together with the fibroids in order to prevent the regrowth of fibroids in the uterus at a later date. The Chinese formula can not only stop abnormal bleeding and decrease and eliminate the fibroid, but also prevent the regrowth of the fibroid because it regulates the imbalance of the hormones, the cause of fibroid growth. Female hormones, particularly estrogen and progesterone, are known to be related to stimulation of fibroids. TCM considers fibroid formation to be related to accumulation of stagnated blood (called “yu zheng”). Therefore, herbs that invigorate blood circulation are added to the formula. Combining the knowledge about formation of uterine fibroids in modern medicine and TCM, the mechanism of herbal treatment can be explained by chemical, biological, and pharmacological study. To study the treatment mechanism of the formula, not only in vitro assays and in vivo animal tests related to hormone regulation should be performed; those involved in blood circulation should also be carried out.

Research on traditional herbal medicine should be performed on the basis of clinical application and reference to the corresponding theories in each system. The main systems of traditional medicine from different countries will be briefly introduced in Section 1.5. TCM is mentioned below only as an example.

The application of traditional Chinese herbs is not as simple as Western drugs in that not all doctors prescribe the same medicines for the same disease. Quite often in TCM, one herbal formula consisting of several Chinese herbs (most often 5 to 15) is used for different diseases. On the other hand, one disease can be treated with different formulas by different doctors. For example, if an herb is unavailable, experienced Chinese doctors can easily modify a formula by replacing one or two herbs to give similar treatment results. This makes research scientists perplexed and frustrated because explanations by clinical doctors using terminology of TCM are sometimes difficult to understand. Due to the current meticulous division of research areas and a limited amount of energy, most scientists focus on in-depth study in one field, and have no time to spend on other areas that are not closely related to their research. Even to those familiar with both TCM and modern science, if the knowledge on both sides is not extensive, it is still difficult for them to scientifically explain TCM theories with simple modern medicinal terms.

Many patients turn to TCM treatment after they have tried treatment with Western medicines with no effect. Chinese herbal formulas work better than Western drugs for many diseases, not only chronic ones caused by stress, but also on acute infections such as SARS and the H1N1 flu virus. However, research results show that effects of the components isolated from these herbs are mostly less than those of current Western drugs. Thus the question arises: Why or how are the effects of these formulas better?
According to the experimental results, the answer is definitely not the placebo effect. The following might explain the reason.

1. Chinese herbs in a formula can work on different targets, that is, on different receptors and enzymes or other substances in the human body and stimulate the functions of nervous, circulatory, endocrine, immune, digestive, and other systems simultaneously. This is why TCM is a holistic medical system.

2. TCM emphasizes the protection of the digestive function as well as regulation of qi (pronounced “chee”) and blood (details about the definition and explanation of qi and the importance of regulation of qi and blood in TCM will be given in Chapter 10). TCM believes that a good digestive system will guarantee an effective supply of essential nutrients from foods to the human body. It also believes that blocked qi and blood circulation may cause hundreds of types of diseases. For treatment of chronic diseases with Chinese herbs, there are always herbs that improve blood circulation in the formulas; if the patient has a digestion problem together with other symptoms, herbs that regulate the digestive system are usually given first. These actually emphasize the importance of maintaining cell functions with enough nutrients and excluding metabolites in a timely manner through functional blood circulation.

Scientists are currently trying to find out the relationship of mutant genes as causes of diseases, such as Alzheimer’s and Parkinson’s. But what are the main causes of the gene mutations? According to TCM, I would propose that the main cause of such diseases or aging is probably poor capillary blood circulation, which can be caused not only by the fats we eat, but also by the accumulation of metabolites from cells or dead cells. My reasoning is based not only on the above TCM theories and my clinical application of Chinese herbs, but also on the confirmation that the disease of age-related macular degeneration (AMD) is pathologically related to the accumulation of aging retina in the photoreceptor outer segment membrane, part of a research program I performed when I worked as a postdoctoral scientist in the group of Professor Koji Nakanishi from Columbia University. No doubt, further experimentation is required.

1.5 BRIEF INTRODUCTION OF DIFFERENT SYSTEMS OF TRADITIONAL MEDICINE

The use of plants for prevention and treatment of diseases is the earliest type of medicine on earth. The practice of traditional medicine developed along with the cultures of ancient China, India, Egypt, and other places. Different species of plants are used as medicines for treatment in different countries because of the different ecological environments. In countries with long histories and cultures, theories of etiology and pathology, methods for diagnosis, and treatment with herbal medicines or other methods under these theories were gradually formed along with the understanding of diseases and accumulated therapeutic experiences, and their own complete medical systems finally established. To fully explore the preventative and
therapeutic mechanisms of traditional herbal medicines, it is necessary to have a deep understanding of the theories in their corresponding medical systems. The following are brief introductions of some ancient but still currently popular traditional medical systems in the world. The systems in which herbal medicine is not a key therapeutic tool are not covered here.

As a summary, “holistic” is one of the most common characteristics of these major popular medical systems and their biggest difference from conventional or allopathic medicine. It is not only reflected in the beliefs of importance of interaction and harmonization between the human body and environment and among organs and tissues, but also implemented in treatment with different herbal components.

1.5.1 Traditional Chinese Medicine (TCM)

TCM originated in China thousands of years ago through meticulous observation of nature, the cosmos, and the human body. Today, it not only remains as a form of primary care in health systems throughout most Asian countries, but also as the most popular complementary or alternative form of medicine in most of the Western countries. It has an extremely complex theory system established mainly on the basis of two philosophical views, the integral and dialectical concepts. The major theories include yin and yang, the five elements, Zang–Fu theory, qi and blood theory, meridians, collaterals, etiology and pathology, and prevention.  

Yin and Yang

Yin and yang reflect all the forms and characteristics existing in the universe. They may represent two separate phenomena with opposite natures, as well as different and opposite aspects within the same phenomenon. While yin is dark, passive, downward, cold, contracting, and weak, yang is bright, active, upward, hot, expanding, and strong.

The basic theory of yin and yang is about their relationship. They are opposing, interdependent, inter-transforming (in a state of constant change), and balanced. The yin and yang theory is applied in TCM for diagnosis and as the principles of treatment. The imbalance and fluctuation of yin and yang are considered the basic causative factors of disease occurrence and development. The goal of clinical treatment is to restore yin–yang balance in the patient. For example, heat syndromes are treated with cold nature herbs, while cold syndromes are treated with hot nature ones.

The Five Elements

In this theory, nature is divided into five elements: wood, fire, earth, metal, and water. Color, taste, emotion, sense, season, organs in human body, and others can all be classified into the five elements. The laws of movement of the five elements are as follows: inter-promoting, interacting, counteracting, and mutual relation. The five elements theory is applied in TCM to explain the physiological and pathological
interrelationship among Zang–Fu organs and guide diagnosis and treatment of diseases.

**Zang–Fu Theory**

In TCM, the heart, lung, spleen, liver, and kidney are known as the five Zang organs, while the gallbladder, stomach, small intestine, large intestine, bladder, and triple energizer are the six Fu organs. The pericardium is a protective membrane of the heart, so it is also considered an organ. The triple energizer is the central body cavity that is connected to Zang organs. There is no biomedical equivalent of the triple energizer in modern medicine. Its function includes transformation, purification, and distribution of air, food, and water. It can be further divided into three parts. The upper part regulates respiration and the circulation of protective qi, the middle part governs the qi of the various digestive system functions, and the lower part controls the qi of the absorption of fluids/nutrients, waste disposal, and sexuality/reproduction. The triple energizer is the central energetic structure and strength of human health and well-being.

The Zang organs are solid and yin in nature. Their physiological functions are to manufacture and store essential substances, including vital essence, qi, blood, and body fluid. They are connected with meridians for the transmission of qi and blood. The Fu organs are hollow and yang in nature. Their physiological functions are to receive and digest food, and transmit and excrete the wastes. Fu organs are also connected with meridians. Interconnected by the meridian system, the Zang and Fu organs have an internally–externally linked relationship.

**Qi, Blood, and Body Fluid**

They are considered fundamental substances that maintain the normal vital activities of the human body and physiological functions of the Zang–Fu, tissue, and meridians.

Qi has such a special meaning in TCM for which no English word exists for translation. It denotes both the essential substances of the human body and the functional activities of the Zang–Fu and tissues. Blood is a red liquid circulating in the vessels, similar to blood in modern terminology. Body fluid is a collective term for all the normal fluids of the body, which include saliva, tears, nasal discharge, sweat, and urine, as well as liquids in stomach, intestines, joint, and other cavities.

**Meridians and Collaterals**

They are pathways in which the qi and blood of the human body are circulated. Meridians constitute the main trunks and run longitudinally and interiorly within the body, while collaterals represent branches of the meridians and run transversely and superficially from the meridians.

The functions of the meridians and collaterals include transporting qi and blood, regulating yin and yang, resisting pathogens, reflecting symptoms and signs, and
transmitting needling sensation to regulate deficiency and excess condition when acupuncture and moxibustion are applied.

**Causes of Diseases**

TCM believes that the causes of disease include the six exogenous factors (wind, cold, summer heat, damp, dryness, and fire), the seven emotional factors (joy, anger, melancholy, worry, grief, fear, and fright), improper diet, overstrain, lack of physical exercise, traumatic injuries, bites by insects or wild animals, as well as stagnant blood and phlegm fluid.

**Diagnostic Methods**

TCM diagnosis includes inspection, auscultation and olfaction, inquiry, and palpation.

**Treatment Methods**

The TCM treatment methods include herbal medicine, acupuncture, dietary therapy, Tui na, and massage. Qi gong and Tai ji are also strongly affiliated with TCM.

Information about properties, current researches, and modern pharmacology of Chinese herbal medicines, and the understanding of TCM theories with modern medical terminology will be given in Chapter 10.

### 1.5.2 Kampo Medicine

Kampo is the Japanese study and adaptation of Chinese medicine. The first Chinese medical works were introduced to Japan around the fourth or fifth century AD. Since then, the Japanese have established their own herbal medical system and diagnosis based on TCM. Kampo utilizes most of the TCM treatment methods, including herbs, acupuncture, and moxibustion.

Kampo is currently integrated into the national health-care system in Japan. Different from modifying formulas applied in TCM clinics, the Japanese Kampo uses standardized, fixed, and precise combinations of herbs. Today, about 75% of Japanese physicians prescribe Kampo formulas. Since 1967, the Japanese Ministry of Health, Labor, and Welfare has approved 148 Kampo formulas for coverage and reimbursement in the national health insurance plan. The formulas are prepared under strict manufacturing conditions with the Ministry’s standardization methodology.

### 1.5.3 Indian Medicines

Indian medicines include three different systems: Ayurveda, Siddha, and Unani. They are different in origin and practice areas, as well as the theory and application.
Chapter 1 Introduction to Traditional Herbal Medicines and Their Study

Ayurveda

The term means “the science of life.” It is another one of the oldest systems of medicine in the world. According to the web site of the U.S. National Center for Complementary and Alternative Medicine (NCCAM) in NIH (http://nccam.nih.gov/health/ayurveda/introduction.htm), Ayurveda medicine originated in India several thousand years ago and continues to be practiced in India, where nearly 80% of the population uses it exclusively or in combination with Western medicine. It is also practiced in Bangladesh, Sri Lanka, Nepal, and Pakistan. Two ancient books, Caraka Samhita and Sushruta Samhita, written in Sanskrit more than 2000 years ago, are considered the main texts on Ayurvedic medicine.

Ayurvedic medicine aims to integrate and balance the body, mind, and spirit; thus, it is also viewed as “holistic.” This balance is believed to lead to happiness and health, and to help prevent illness. A chief aim of Ayurvedic practices is to cleanse the body of substances that can cause disease, thus helping to reestablish harmony and balance. Ayurvedic medicine has several key foundations that pertain to health and disease. These concepts have to do with universal interconnectedness, the body’s constitution (prakriti), and life forces (doshas).

Interconnectedness  This is about the relationships among people, their health, and the universe as the basis for how Ayurvedic practitioners think about problems that affect health. It believes that disease arises when a person is out of harmony with the universe. Disruptions can be physical, emotional, spiritual, or a combination of these.

Constitution (Prakriti)  This refers to a person’s general health, the likelihood of becoming out of balance, and the ability to resist and recover from disease or other health problems. It is called the prakriti, which means a person’s unique combination of physical and psychological characteristics and the way the body functions to maintain health. It is believed to be unchanged over a person’s lifetime and influenced by such factors as digestion and how the body deals with waste products.

Life Forces or Energies (Doshas)  Different from TCM, the five fundamental elements in Ayurveda that make up the universe and also human physiology are space, air, fire, water, and earth. Ayurveda believes that health is maintained by the balancing of three subtle energies known as doshas. There are three doshas, called Vata, Pitta and Kapha, and each is mainly a combination of two elements. Vata dosha is made up of space and air. Pitta dosha is a combination of fire and water. Kapha dosha is made up of water and earth. Together, the doshas orchestrate all the activities that occur within us. A person’s chances of developing certain types of diseases are thought to be related to the way doshas are balanced, the state of the physical body, and mental or lifestyle factors.

Ayurvedic practitioners first determine the patient’s primary dosha and the balance among the three doshas by Asking, Observing, and Checking a pulse (each
dosha is thought to make a particular kind of pulse). The goals of treatment include eliminating impurities, reducing symptoms, increasing resistance to disease, and reducing worry and increasing harmony in the patient’s life.

Ayurvedic treatments rely heavily on plants, including herbs, oils, and common spices. Currently, more than 600 herbal formulas and 250 single-plant drugs are included in the “pharmacy” of Ayurvedic treatments. According to their effects, for example, healing, promoting vitality, or relieving pain, Ayurvedic medicines have been divided into categories.

**Siddha**

Siddha is mainly practiced in south India. This system of medicine is believed to be developed by the Siddhars, the ancient supernatural spiritual saints of India, who developed methods and medications that are believed to strengthen their physical body and thereby their soul, including intense yogic practices and years of fasting and meditation.

**Unani**

Unani means Greek. Unani medicine originated around 980 AD in Persia. The basic knowledge as a healing system was collected by Hakim Ibn Sina. This system is based on the theory of the presence of the elements, which are fire, water, earth, and air. These elements are present in different fluids (phlegm, blood, yellow bile, and black bile). The balance of these element leads to health, and imbalance leads to illness. Most medicines and remedies used in Unani are also used in Ayurveda. The base used in Unani medicine is often honey. Real pearls and metal are also used in making Unani medicine, based on the kind of ailment it is aimed to heal. In India, Unani practitioners can practice as qualified doctors.

**1.5.4 Tibetan Medicine**

Tibetan medicine combines elements of Indian, Chinese, and Greek medical traditions. Dietary modification, medicines composed of herbs and minerals, acupuncture, and moxabustion are applied for the treatment of illness. Tibetan medicine is currently practiced in Tibet, India, Nepal, Bhutan, China, and Mongolia, and is spreading to North America and Europe.

**1.5.5 Muti**

Muti is a term for traditional medicine in Southern Africa. The word means tree. African traditional medicine makes use of various natural products, many of which are derived from trees. For this reason, medicine generally is known as Muti. In Southern Africa, the word muti is in widespread use in most indigenous African
languages, as well as in South African English and Afrikaans, where it is sometimes used as a slang word for medicine in general.

1.5.6 Islamic Medicine (Arabic Medicine)

Islamic medicine (Arabic medicine) refers to medicine developed in the medieval Islamic civilization and written in Arabic. Its development was closely related to the history of Arab tribes.

In the seventh century, the prophet Mohammed united the Arab tribes and declared a new religion, Islam. By the tenth century, the Muslims not only controlled Italy and Spain, but also extended their raids through the Alpine passages into mid-Europe. The Islamic Empire extended from the Atlantic Ocean on the west to the borders of China on the east, and became the most advanced and civilized nation in the world between the ancient civilizations and the Renaissance era in Europe (the seventh to thirteenth centuries).

According to the online book *Islamic Medicine*, a compilation of articles published in the *Journal of Islamic Medical Association* over the last several years edited by Shahid Athar, the Muslims were avid for the wisdom of the world of Galen, Hippocrates, Rufus of Ephesus, Oribasius, Discorides, and Paul of Aegina. By the tenth century, their zeal and enthusiasm for learning resulted in all essential Greek medical writings being translated into Arabic.

Ibrahim B. Syed, the author of the chapter “Islamic Medicine: 1000 Years Ahead of Its Times,” believes that Islamic medicine was advanced in the fields of medical education, hospitals, bacteriology, medicine, anesthesia, surgery, pharmacy, ophthalmology, psychotherapy, and psychosomatic diseases; he even thinks that the European medical system is Arabian not only in origin but also in its structure. The Arabs are the intellectual forebears of the Europeans. Meanwhile, Dr. Abouleish, the author for the chapter “Contributions of Islam to Medicine,” admits objectively that the Arabs were assimilated by the countries they reached. It is difficult to identify this new breed as Arabs, because although the language was Arabic, not all the scientists were from the Arabian Peninsula. It is also equally difficult to describe it as Islamic, because although the majority of the scientists were Muslims, sponsored by Muslim rulers, and governed by the Islamic law, some scientists were Christians or Jews. The book also mentions that Islamic medicine was integrated with the elements of TCM and Ayurveda by trade with China and India.

In Islamic medicine, the patients were treated through a scheme starting with physiotherapy and diet; if this failed, drugs were used, and last, surgery would be resorted to. The physiotherapy included exercises and water baths. The Arabs had an elaborate system of dieting and were aware of food deficiencies. Proper nutrition was an important item of treatment. Drugs were divided into two groups: simple and compound drugs. They were aware of the interaction between drugs; thus, they used simple drugs first. If these failed, drugs that are made from two or more compounds were used. If these conservative measures failed, surgery was undertaken.
1.5.7 Mexican Folk Medicine

According to Sandoval’s 1998 book, *Homegrown Healing: Traditional Home Remedies from Mexico*, Mexican folk medicine is a healing philosophy that significantly influenced the American Indian and the Spanish conquistadors.

Before the arrival of the Spaniards, Meso-America (the area of central Mexico, Belize, Guatemala, and parts of Honduras) had been agricultural for over 3000 years. The Aztecs believe that there is a delicate balance or “harmony” between themselves and nature, and disease was caused by the gods to punish sinners. Tilting one’s balance would cause serious illness or death. Similarly, the Spaniards believed that health was “God’s will,” and could be taken away as rectification.

In the fifteenth century, several thousand medicinal plants were collected in the Huaxtepec garden. Academic priests conducted research with plant derivatives for their pharmacological benefits. Meanwhile, Spain was leading medical advancement in Europe. Its superiority in medicine had been due, in part, to the knowledge acquired while under Arabic rule. When Catholic priests came with the Spanish conquistadors to the New World, they considered ancient codices of the Aztec priests blasphemous, prompting Hernan Cortes to order all works on botany and science to be destroyed. The values, convictions, and traditions of the Aztec people were almost completely eradicated by Spain in a relatively short period of time.

Fortunately, the early missionaries played a paradoxical role in salvaging the remnants of Aztec knowledge. They traveled throughout Nuevo Espana collecting and documenting materia medica, while integrating European healing philosophies. Some of the native remedies have survived the conquest due to quick thinking Indians who renamed the plants used in ancient ceremonial practices, using the names of benevolent saints. Therefore, many remedies survived the conquest and are still used in Mexico.

The Spaniards introduced humoral pathology, Hippocrates’ theory of health being dependent on the proper distribution of the body’s four humors: blood, phlegm, yellow bile, and black bile. From humoral pathology, the hot and cold theory of disease has survived in Mexico and in the Southwestern United States. In order to restore the body’s symmetry, plants with opposing qualities are still taken.

The Mexican Institute for the Study of Medical Plants was established in 1975. Researchers at the institute have been examining the sixteenth century records to determine the validity of indigenous medicines, with great success. The science, which had dismissed traditional remedies, has begun to reevaluate therapeutic values of botanical lore.

1.5.8 Other Indigenous or Folk Medicines

In China, the definitions of Chinese materia medica and folk or indigenous medicines are different. The former refers to those herbs that are recorded in TCM books and prescribed by the Chinese doctors under the guidance of TCM theory after diagnosis;
Folk or indigenous medicine refers to herbs that are used by folks in only certain regions or minority areas without TCM theory.

Similarly, except some major traditional medicine systems from these older countries with longer cultural history such as India and Arabic countries, not every traditional herbal medicine has its own complete theories for supporting the application. Examples include herbs used by Indian American and many other tribes over the world.

1.6 REGULATION OF HERBAL MEDICINES AND THEIR PRODUCTS

With more and more application of herbs all over the world, regulation of herbal medicines and their products is called for due to quality and safety concerns. The most commonly seen quality issue of raw herbal materials is adulteration with counterfeit species or contamination with microorganisms, pesticide residues, and heavy metals. In order to gain higher profit, some merchants may sell moldy materials, or even adopt unethical and unscrupulous means on herbal materials, for example, dyeing Goji berry with sulfur. The manufacturers of herbal products could secretly mix them with Western drugs without giving note on the label and deliberately give false ingredients on the label. Thus, considering the safety of consumers, strict regulation on herbal products is imperative.

Different countries, such as China, the United States, Japan, and Germany, have taken different actions and formulated various regulations on quality control of raw materials of herbs and their products as well as registration of herbal products. World organizations such as WHO and International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) are also involved in performance of research and clinical practice of herbal medicine.

In 2005, WHO published a report of a global survey about National Policy on Traditional Medicine and Regulation of Herbal Medicines. This report indicated that about 50 countries already have their national policy and laws or regulations on traditional medicines or CAM.

ICH is a unique project that brings together the regulatory authorities of Europe, Japan, and the United States, and experts from the pharmaceutical industry in the three regions to discuss scientific and technical aspects of product registration. According to the ICH web site, its purpose is to make recommendations on ways to achieve greater harmonization in the interpretation and application of technical guidelines and requirements for product registration in order to reduce or obviate the need to duplicate the testing carried out during the research and development of new medicines. The objective of such harmonization is a more economical use of human, animal, and material resources, and the elimination of unnecessary delay in the global development and availability of new medicines while maintaining safeguards on quality, safety, and efficacy, and regulatory obligations to protect public health.
In China, good manufacturing practice (GMP) has been applied to herbal medicine. Management of herbal medicine covers raw herbal materials and their processing, herbal products, export and import, registration, and others. Among thousands of herbs, 87 are allowed to be used as healthy foods, defined as foods that are suitable for a specific population and capable of regulating bodily functions but not taken for therapeutic purposes; nearly 600 individual herbs and 600 herbal products are listed in the *Chinese Pharmacopoeia* (2005 edition) with established quality standards. New herbal products must be registered with required chemical, pharmacological, clinical, and safety data depending on its category in the new drug list (there are five categories for Chinese drugs).

Herbal medicine systems used in Japan include the Japanese traditional medicines, Kampo formulas, and combinations of the traditional medicines with vitamins and pharmaceuticals. Except Kampo formulas, regulation of herbal medicines is the same as the approval for both prescription and over the counter (OTC) drugs. Regulation of quality standards of those herbal products was established in Japanese Pharmacopoeia for more than 90% of them.\(^{20}\)

Regulatory standards of herbal medicine in Europe were introduced by De Smet in his article written in 2005.\(^{21}\) Germany and France are indisputably in the lead in OTC sales of herbal medicine among European countries, and they have also had noteworthy markets for prescription herbal preparations.

There was no proprietary regulation on herbs in the United States until the 1990s. According to the U.S. Food and Drug Administration (FDA) website, FDA regulates dietary supplements including herbs under a different set of regulations from those covering “conventional” foods and drug products (prescription and OTC). The U.S. Congress defined the term “dietary supplement” in the Dietary Supplement Health and Education Act (DSHEA) of 1994 as a product taken orally that contains a “dietary ingredient” intended to supplement the diet. The “dietary ingredients” in these products may include vitamins, minerals, herbs or other botanicals, amino acids, and substances such as enzymes, organ tissues, glandulars, and metabolites. It says that the manufacturer is responsible for ensuring that the product is safe and the product label is truthful and not misleading. Manufacturers do not need to register their products with FDA nor get FDA approval, unlike OTC and prescription drugs. The FDA monitors voluntary adverse event reporting, labeling, and claims, and can take action against any unsafe dietary supplement after it reaches the market.

In August 2007, the FDA issued the Dietary Supplement Current Good Manufacturing Practice (CGMP) Final Rule 21 CFR Part 111. In essence, this final rule requires that the proper controls be in place for dietary supplements during manufacturing, packaging, labeling, and holding operations. The move was in response to concerns about substandard dietary supplement manufacturing practices, as well as mislabeling practices. The 21 CFR 111 ruling addresses the quality of the manufacturing processes for dietary supplements and the accurate listing of supplement ingredients. It does not limit consumers’ access to dietary supplements, nor does it address the safety of the ingredients in dietary supplements, or their effects on health, when proper manufacturing techniques are used. The rule applies to all
domestic and foreign companies that manufacture, package, label, or hold dietary supplements, including those involved with testing, quality control, and dietary supplement distribution in the United States. This regulation has been fully implemented to all involved companies as mentioned since June 2010.

1.7 ACHIEVEMENTS AND CHALLENGES OF RESEARCH ON CHINESE HERBAL MEDICINES

Since TCM is one of the oldest medical systems with complete theories, Chinese herbs have been applied worldwide with the largest population and studied by scientists all over the world. The achievement of research on Chinese herbal medicine is summarized here as a reference to learn the developmental process and current status of herbal study.

Chinese material medica is the official name for Chinese medicines, which include materials from all parts of plants, substances related to animals, and minerals. There are also many folk medicines in China. The difference between Chinese material medica and folk medicines is that the former are usually prescribed by Chinese doctors on the basis of diagnosis along with the guidance of TCM theory, while the latter are used by laypeople based on personal experience or are given by minority practitioners. In this book, Chinese herbal medicine is used to simply refer to Chinese material medica originated from plants.

In 1999, Zhong Hua Ben Cao, the most authoritative Chinese book with a complete record of Chinese materia medica, was published. Its editorial board was composed of experts all over the country and organized by the State Administration of Traditional Chinese Medicine (SATCM). This book records a total of 8980 Chinese medicines that are divided into 34 volumes and summarized the contemporary research of Chinese medicine with modern science and technology. The 2005 edition of Pharmacopoeia People’s Republic of China listed around 600 individual Chinese materia medica used in clinics, most of them with identification methods. Clinically, about 300 of them are most commonly used by Chinese doctors; many others are generally used locally as folk medicines.

Modern study of Chinese herbal medicine started in the 1920s when Chinese scholars found the biological activity of ephedrine from ephedra. The progress of the study was slow before 1949 due to continuous wars in China. Since the 1950s, the Chinese government has given great support for the development of Chinese medicine. Many provinces established TCM colleges with affiliated hospitals. Now, almost all of the provinces in China have their own TCM colleges or universities that include a department of Chinese Pharmacology; many Western medical universities in China also have either a department or a research institute of Chinese Pharmacology. Due to the emphasis on scientific research since the nationwide economic reforms starting three decades ago, the Chinese government has been investing more money on TCM research. Research of Chinese herbs has been performed nationwide, from chemical isolation and identification, analysis for quality control and standardization, to bioassay and pharmacological study, and clinical
trial. Meanwhile, scientists in Japan, Korea, Germany, and other countries have also made great contributions to the Chinese herbal study.

1.7.1 Chemical Isolation, Identification, and Standardization of Chinese Herbs

Isolation of chemical compounds from Chinese herbal medicines in China just started in the 1920s, about 100 years after the isolation of salicin from white willow by Western scientists. However, since the 1950s, more and more Chinese chemists have been using all kinds of column chromatography, MPLC or HPLC, SFE, DCC, HSCC, and other methods for isolating compounds from extracts, and different spectral equipments such as IR, UV, NMR, and MS for identification of the isolated compounds. Theses of most graduate students in phytochemistry majors are about chemical studies of Chinese herbs. Because of the contribution from scholars nationwide in the past half century, most commonly used Chinese herbs have been widely studied up to now. Major compounds in many of them have been isolated and identified. Based on these identified major compounds in herbs, HPLC quantitative and qualitative analysis of many herbal materials and their products are available for quality control and standardization.

1.7.2 Biological and Pharmacological Studies of Chinese Herbs

Extracts or major compounds of most commonly used Chinese herbs have been screened for many types of in vitro bioassay tests and in vivo animal studies. Most of the results, from the levels of enzyme, receptor, gene or cell to tissue and animal, strongly support their preventative and therapeutic functions. So far, pharmacological studies have been performed on most of the commonly used Chinese herbs listed in the herbology textbooks. The modern pharmacological characteristics of all the Chinese herb groups, categorized according to their functions with terminology of TCM, have been documented. Unfortunately, most of the study results were published solely in Chinese journals due to obvious language translation barriers. Nevertheless, some research results are available in English international journals.

1.7.3 Challenge of Studies on Chinese Herbal Formulas

One of the special characteristics of Chinese herbal treatment is that Chinese doctors like to treat diseases with herbal formulas that are usually composed of several herbs. Each herb in one formula plays its own role; herbs within the formula may also interact with each other (see Chapter 10). The aim of the formula is not only to simultaneously stimulate functions of different organs and systems of the body for respective symptoms, but also to seize synergetic effects of the herbs or suppress side effects of each other. For example, licorice is often used in formulas because
it contains glycyrrhizin type saponins, which have sweetening and surfactant properties. Thus, it is used to harmonize the taste of other bitter herbs, and to help dissolve components of other herbs when cooked together.

If studies on a single herb are difficult enough, it is even more challenging to do research on an herbal formula. Not only do the components become more difficult for analysis, but the interactions between herbs further complicate the pharmacological study. The study of formulas is currently the biggest challenge to TCM researchers.

Take the Six-Ingredient Pill with Rehmannia as an example. This is a famous Chinese herbal formula that is composed of six herbs. It is often used for diabetes, chronic nephritis, chronic prostatitis, and menopause symptoms in clinics. Pharmacological study showed that this formula could lower the ALT level of mice with liver damage induced by CCl4, thioacetamide, or hydrocortisone. However, when the six herbs were split into three pairs, the results showed that none of the pairs had any deductive effect on ALT levels in the mice with CCl4-induced liver damage. This example demonstrates the synergetic property of herbal formulas—only when the herbs worked together were they able to be effective.

1.7.4 Formulations of Chinese Herbal Preparation

In ancient China, herbal formulas were mostly cooked with water, which is called a decoction in English. For convenience, pills were made by mixing water extract of some herbs with other powdered ones; honey was added as necessary. Few herbs or formulas were soaked in wine or were simply ground for administration. The preparation of such formulas was either time-consuming or easily contaminated.

Now, with recognition of bioactive components from herbs and their pharmacological activity, many Chinese herbal extracts have been developed into many forms of preparation, including capsule; tablet; granule; soft gel; true solution; colloidal-, suspension-, or emulsion-type liquid formulations; suppositories, and ointments for external use. A few have even been made into liquid or powder injections.

1.7.5 Standardization and Quality Control of Chinese Herbal Materials and Products

Standardization of an herb usually refers to the chemical analysis of the characteristic bioactive and main components for identification or comparison of species. At present fingerprints of HPLC chromatograms are the most popular method. Thin layer chromatography (TLC) is another common one with lower cost.

Quality control for an herbal material usually includes not only the quantitative analysis of the main compounds from herbs, but also other analyses related to hygiene or safety examination such as heavy metal, pesticides, and microorganisms. For each individual formulation of the preparation, quality control has different requirements, such as precipitation test of an oral liquid and time for disintegration of a tablet.
Currently, the contamination of heavy metal, pesticides, and microorganisms is still a problem for many raw materials and their products. To a large extent, the efficacy and toxicity of a product depend on quality control. Toxicity or death reports by consumers by herbal products are mostly related to poor quality control during preparation, storage, or transportation. Recently, several deaths caused by Chinese herbal injections have been reported in China. Therefore, more and more strict quality controls are required from the Chinese government.

1.7.6 Clinical Studies of Chinese Herbs and Herbal Formulas

Although many Chinese herbs and herbal formulas have been in practice for hundreds or thousands of years and evidence of their therapeutic effects is ample in many books, there are not enough data to convince modern people, especially scientists in Western countries, to accept them.

In Chinese TCM journals, many more reports about clinical case studies of herbal formulas or products with dozens of patients were found than were those about the standard double-blind clinical trial with several hundred patients, which are usually performed for new drug development. The reason is that there is no requirement of clinic studies for herbal products that are already on the market. Moreover, clinical studies require a greater investment of time, money, and manpower.

1.7.7 Mechanisms of Chinese Herbal Processing Revealed by Chemical Investigation and Pharmacological Studies

Many Chinese herbs need to be processed when used for treatment of certain types of diseases. Methods of processing include boiling, steaming, frying, or heating with some accessories such as wine, vinegar, salt, honey, sand, and mud. The purposes of such processing are to decrease the toxicity and side effects of herbs, increase their therapeutic effects, change their properties or functions, make them easier for preparation and storage, and others. Chemical and pharmacological studies have revealed that the processing can either decompose the structures in herbs by breaking down the bonds of esters or glycosides, or change the solubility or properties of compounds such as alkaloids, acids, and proteins, or decrease the concentrations of components such as essential oil. Processing mechanisms of commonly used herbs are well known now. 22

REFERENCES


