COUNTERING THE SIDE EFFECTS OF MODERN MEDICAL THERAPIES WITH CHINESE HERBS

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All medical treatments, whether ancient or modern, are associated with a certain degree of risk for adverse effects, often called side effects. In general, the more drastic the intervention, the more likely and more severe the adverse outcomes. Thus, massage therapy and dietary modifications—examples of external and internal therapies which are usually not considered drastic—have relatively few and minor adverse effects. Nonetheless, there are strong massage techniques and radical dietary modifications that can yield adverse effects, even if the overall outcome is positive. By contrast, surgery and potent drugs—examples of external and internal therapies that are usually deemed invasive or drastic—have more frequent and more serious adverse effects. Still, the overall outcome may be far better than if these techniques were not employed or if gentler alternatives were attempted.

Chinese herbal therapies that have been used in China over the past 2,000 years include toxic herbs, herbs used in large doses, and herbs that are intended to produce strong reactions so as to save the patient from a serious disease. A relatively small group of Chinese herbs have been used to counteract the adverse effects of other herbs for many centuries; this aspect of Chinese medical practice has continued with the introduction of Western medical therapies. There was a great increase in this area of Chinese medicine during the 1970’s (continuing into the present) as the result of intensive adoption of Western medical therapies for cancer (chemotherapy, radiation, and surgery) which almost always produce significant adverse effects.

PERSPECTIVE

In the practice of traditional Chinese medicine, certain adverse effects of treatments have long been known and accepted; some of the adverse consequences are, in fact, the desired actions:

- Acupuncture may cause pain or bleeding. An acupuncture needle reaction (deqi), described as soreness, numbness, or distending feeling, but interpreted by many Westerners as discomfort and pain, is deemed an essential part of effective acupuncture therapy in China; persistence of this reaction is considered an adverse effect of excessive stimulation. Bleeding was a necessary consequence of some early acupuncture practices (using the needles to lance boils) and remains an intended result of certain techniques.

- Moxibustion causes pain and blistering. By the traditional method of application, moxibustion also causes scarring. All these reactions are deemed essential to successful moxa treatment according to the traditional texts.

- Cupping causes pain and bruising; bruising is taken as a sign of good effect.

- Herbs can cause nausea and, if not selected properly, worsening of the disease (or death, according to the traditional commentaries). Further, there can be allergic reactions to herbs. Some herbs used in China are highly toxic, and the dosage of low-toxicity herbs used in some treatments is sufficiently high to produce non-specific toxic reactions, such as dizziness, thirst, and gastrointestinal distress. In some cases, vomiting, diarrhea, or sweating are intended consequences of the herbal therapies, indicating that the therapy is having an effect.
Little has been done about adverse effects of the physical Chinese medical therapies, other than to administer them in a more gentle manner, an adjustment often made in the West (e.g., use finer needles and less stimulation for acupuncture; perform moxibustion only to the point of heating the skin, with no blistering or scarring, etc.). Avoidance of herbs that are problematic is a common approach taken in the West (e.g., eliminate toxic herbs, reduce the dosage of non-toxic herbs, cease administering herbs that appear to cause a reaction). Still, counteracting the adverse effects of herbs has always been a major concern in China and there is a considerable amount of accumulated knowledge and experience in this field that can be transposed to the problem of countering drug side effects. Modern research has helped expand upon the efforts made by traditional doctors in the past.

Some Chinese doctors have argued that the side effects of herbal therapies actually arise from a failure to formulate a prescription appropriate to the full diagnostic picture and with proper compensation for any herbal toxicities. This view would suggest that well-trained, competent, and experienced practitioners can avoid side effects for virtually all their patients. Such an opinion is consistent with the idea that individual herbs may produce side effects, but that those effects can be reduced through proper formulation. This idea is extended to the administration of drugs in carefully designed formulations (with herbs and/or other drugs). However, it is always possible that individuals will have unique and unpredictable reactions to herbal ingredients within a formula (4, 33). Also, such claims of the ability to avoid adverse effects are an ideal that cannot consistently be met, especially by average practitioners who have limited training and experience.

**USING SWEET HERBS TO COUNTER SIDE EFFECTS**

A long-standing principle of Chinese medical practice is that sweet-tasting herbs counter the toxicity and adverse effects of other herbs. One of the fullest elaborations of this principle was reported in *Anticancer Medicinal Herbs* (1) among historical references to the action of *Sophora subprostrata* (*shandougen*):

The drug [*S. subprostrata*] removes toxic materials in many drugs....It is said in the *Elucidation of Materia Medica* that 'It neutralizes toxicity with its sweet taste and eliminates heat with its cold nature. Toxic drugs are usually hot and sweet, and toxicity is removed spontaneously when combined with drugs that are cold, sweet, and bitter.'

The ability of sweet-tasting substances to counteract toxicity has been mentioned in the *Shennong Bencao Jing* (ca. 100 A.D.) and relied upon extensively in the formulations of the *Shanghan Lun* (ca. 220 A.D.), especially in relation to incorporating licorice and jujube. In this case, a concern is mentioned about hot drugs, which was one of the big concerns about the herbs used in ancient times. Hot herbs attained a special status in Chinese medical practice as a result of the concept, developed in Zhang Zhongjing's *Shanghan Lun* (220 A.D.), that cold was the major disease-causing influence. The principle of using cold-natured and bitter-tasting herbs to counter all kinds of hot toxins was elucidated at least as early as the *Neijing Suwen* (ca. 100 B.C.). In the event that a cold toxic herb is to be utilized instead, a sweet and bitter taste with warming nature would be the most likely quality of the herb(s) used to counteract toxicity.

Raw licorice root is sweet, bitter, and neutral, and in the same plant family as sophora (Leguminosae; this is the family of beans, also called legumes). It is well known for its toxicity-relieving properties for both hot and cold natured herbs. In the *Shoushi Baoyuan* (1616 A.D.), it is said that: "licorice is always employed to dissolve all possible poisonous effects of drugs (19)." The detoxifying effect of licorice is described this way in the *Oriental Materia Medica* (2): "Glycyrrhizin [a major active constituent of licorice] and its calcium salt possess detoxifying action on bacterial toxins (diphtherin, tetanin), poisonous foods and drugs, and toxins of metabolic products. Glycyrrhizin, when degraded, yields glucuronic acid, which in the liver will combine with toxic materials to form glucuronide to produce a detoxifying action."

In the *Selected Compilation of Materia Medica*, it is reported that: "When extremely hot and extremely cold drugs are prescribed, licorice must be added to mediate the intensity (1)." An example of this
technique is represented in the traditional formula Liuyi San (Six to One Powder, referring to the ratio of amounts of the two ingredients). The principal ingredient, talc, is used to clear summer heat and promote diuresis; according to the Chinese-English Manual of Commonly Used Prescriptions in Traditional Chinese Medicine (35): "A small amount of licorice is added to inhibit the cold and slippery action of talc."

Another example is Sini Tang, which contains the toxic and hot herb aconite, along with ginger and licorice. According to the Chinese-English Manual of Commonly Used Prescriptions in Traditional Chinese Medicine, licorice serves to "inhibit the toxicity of crude aconite when it is used together with ginger."

Jujube, a sweet herb commonly combined with licorice in formulas, is described (1) this way in the Annotation of Shen Nong's Herbal: "The herb, being sweet in taste, removes poison of any substance, and is used to harmonize drugs in a prescription." The book Chinese-English Manual of Commonly Used Herbs in Traditional Chinese Medicine (36), lists this action of jujube: "moderate the potency of drugs: for counteracting the toxicity or side effects of potent drugs, such as genkwa, euphorbia, lepidium, etc. Recently, also used for anaphylactoid purpura and bronchial asthma." Among the pharmacological actions of jujube listed in this text is "protect the liver from damage."

The use of jujube to counter side effects of genkwa, euphorbia, and lepidium was evident in the Shanghan Lun formulas. In Commonly Used Chinese Herb Formulas with Illustrations (37), the traditional formula Tingli Dazao Xiefei Tang (Lepidium and Jujube Combination) is listed. The two herbs that comprise the formula are described as follows: "Lepidium is bitter, cold, slippery, and sharp in nature. It opens and drains the lungs, purges fire, and expels sputum. To prevent its violent action from harming the lungs, lepidium is subordinated to jujube, which soothes the stomach and harmonizes the action of lepidium so that normal respiration is not harmed." Genkwa and euphorbia appear together in a single prescription of the Shanghan Lun called Shizao Tang, literally, Ten Jujubes Decoction. According to Formulas and Strategies (3), "The name of this formula is a tribute to the importance of the ten jujubes which are taken to moderate the harsh, downward-draining action of the other herbs, and thereby protect the stomach qi."

The hot, spicy herb evodia is a key ingredient of Wuzhuyu Tang (Evodia Combination); according to Formulas and Strategies: "The envoy, sweet jujube, moderates the acrid, drying properties of the chief and deputy ingredients [evodia and ginger]."

Honey, which is sweet and neutral, is described in the Oriental Materia Medica to have these properties: "strengthens the middle warmer, moistens dryness, controls pain, removes toxins." In the text's section on applications, it is mentioned that honey treats aconitine toxification. Aconitine is the main active constituent of aconite, which is the herb that causes more toxicity problems than any other used in China (because of its high frequency of use and high toxicity).

Soybeans are another legume that have a sweet taste and detoxifying quality. According to Chinese Dietary Therapy (48): "For poisoning or untoward reactions caused by taking poisonous food by mistake or hot-natured drugs, take soy bean milk, or soy bean in a decoction made with licorice."

An example of utilizing several of these sweet-tasting herbs together to counter modern drug side effects is the combination of Gancao Fen Mi Tang (Licorice and Honey Decoction) with Gan Dou Tang (Licorice and Soja Decoction), made with licorice, oryza (guya, rice sprout), honey, and soja (dandouchi, processed black soybean; sweet and bitter tasting). In a clinical trial (14), patients undergoing chemotherapy for various types of cancer were administered this combination of herbs or, as a control, just the chemotherapy. Among those receiving the herbs, the white blood cell count either remained above 5.0 (million/liter or thousand/ml) or quickly recovered to that level after chemotherapy in 77% of the patients, and remained above 4.0 or quickly recovered to that level after chemotherapy in 13%. The comparable figures for the controls were 66%
and 5% respectively.

Along similar lines, the ancient formula of the *Shanghan Lun*, *Zhizi Gancao Shi Tang*, can be adopted to treat adverse reactions to drugs. The formula is comprised of just three herbs: licorice, soja, and gardenia. Gardenia adds a bitter and cooling component to the therapy described above. This prescription has been utilized as an adjunct to cancer therapy in Japan (especially for esophageal cancer, since the traditional use of the herb formula included swellings in the throat), and for reactions to herbs and drugs such as allergy reaction (urticaria) and nausea. Other processed soybean products, such as miso, have the reputation of protecting against adverse effects of chemicals and radiation.

Dolichos, another legume (hyacinth bean), is described in *Properties of Medicinal Herbs:* "Dolichos is sweet in taste and slightly warm in nature, removes toxic materials of all herbs and plants and is administered through chewing the raw drug or in decoction." A formula used for countering the immune suppression in cancer patients is made with dolichos, astragalus, codonopsis, rehmannia, and tortoise shell (note: all these herbs have a sweet taste). Dolichos is traditionally applied in the treatment of summer heat syndrome, and its action there may be to alleviate bacterial toxins that cause nausea, vomiting, and diarrhea. According to the *Oriental Materia Medica*, dolichos is also useful for "alcohol intoxication."

Phaeseolus (*ludou*; mung bean), another legume, is mentioned in the *Chinese-English Manual of Commonly Used Herbs in Traditional Chinese Medicine* as being able to "relieve metallic and drug poisoning: for preventing and treating the poisoning of lead, arsenic, alcohol, and aconite." *Oriental Materia Medica* simply states that phaseolus "removes all toxins." A traditional prescription, *Mahuang Lianqiao Chixiaodou Tang* (Ma-huang, Forsythia, and Phaseolus Combination) uses one type of phaseolus (*chixiaodou*), along with ginger, jujube, licorice, morus bark, forsythia, and ma-haung to treat pruritis. It was recently shown to treat skin reactions to paint and other toxic and allergenic materials. Both types of phaseolus are characterized as having a sweet taste.

According to *Chinese Dietary Therapy*, phaseolus is applied as follows: "For poisoning or untoward reactions caused by taking hot-natured drugs, such as Sichuan aconite [*chuanwu*] or croton seed, take powdered mung bean steeping in boiling water or together with licorice." In a clinical report on the treatment of aconite poisoning, successful alleviation of severe symptoms was attained by combining the standard Western medical method, including use of the plant drug atropine, with ginger and a decoction of licorice and phaseolus (*ludou*). The licorice plus phaseolus decoction was also applied in the treatment of side effects of the patent remedy *Xiaohuoluo Dan*, which contains aconite. In a report on 93 cases of acute poisoning by various substances, *Ludou Jiedu Tang* was used. It is comprised of phaseolus, licorice, lonicera, imperata, dendrobium, rhubarb, salvia, and bamboo shavings. All patients improved with treatment, with 63 rapidly resolved. All these ingredients, except rhubarb and salvia, are sweet; all the herbs except licorice are cooling.

The flower of pueraria (of the Leguminosae), a sweet-tasting herb, is said to treat "fidgets and thirst after alcoholic intoxication;" this property is also attributed to mung bean flowers.

With these several examples of Leguminosae plants with sweet-taste counteracting toxins and side effects, it is not surprising that when modern Chinese researchers sought new therapies for countering the side effects of cancer drugs, the polysaccharides of astragalus (a member of this plant family, traditionally recognized as having a sweet taste) were evaluated. The polysaccharides were isolated for testing first because they were found to be the sweet fraction of the herb extract. It was soon shown that they counteract the immune-suppressing side effects of cancer therapies. Today, astragalus is one of the most commonly used herbs for this purpose.

An example of a sweet formula developed to treat bone marrow suppression (a common side effect of
both cancer drugs and radiation therapy) is the Astragalus-Jujube Combination (Qi Zao Granule), applied to treating white blood cell suppression from various causes (16). The formula is comprised of astragalus, jujube, hoelen, and millettia (jixueteng). Millettia (from various sources, including the genera Millettia, Macuna, and Spatholobus) is also a member of the Leguminoseae; its taste is sweet and bitter; hoelen, a sweet-tasting tree mushroom, contains polysaccharides similar to those found in astragalus. According to the clinical report, patients with white blood cell counts below 3.5 were treated for 20-30 days with this mixture (given twice per day). 56% of the patients had their white cell counts increased by at least 4.0 above the initial value and 24% had the white cell counts increased at least 1.0 above the initial value; granulocytes similarly increased. The figures for the response of the control group were 25% and 5% respectively.

An expanded version of that formula was clinically tested for cancer patients with impaired immune functions (47). The prescription, Shengxue Tang (Generate Blood Decoction), is made with 30 grams each of astragalus and millettia, and 10-15 grams each of hoelen, lycium fruit, pseudostellaria, ligustrum, and cuscuta (the latter four herbs replacing jujube in the Astragalus-Jujube Combination to yield the new formula; all have a sweetish taste, except ligustrum, which is bitter; lycium contains polysaccharides similar to those found in astragalus). The total formula is notably sweet, with a mild bitter taste, and is slightly warming in nature. According to the clinical report, 242 cancer patients, mostly having stomach or intestinal cancer, and being diagnosed as having spleen qi deficiency, were administered this formula in an attempt to restore impaired immune functions (patients had been treated by surgery, some by chemotherapy). After only a few days of treatment (each course of therapy was only 2-3 day), macrophage phagocytosis, lymphocyte transformation rates, E-rosette formation rates, and killing ability of natural killer cells of peripheral blood were significantly increased.

Yet another version of this formula, labeled Fuzheng Zengxiao Fang, was also tested (21). It is comprised of astragalus, millettia, lycium fruit, ligustrum, pseudostellaria, atractylodes, asparagus, and carthamus (thus, hoelen and cuscuta in Shengxue Tang are replaced by atractylodes, asparagus, and carthamus here). Atractylodes and asparagus are sweet herbs, and both are used to regulate the stomach functions as well as to tonify qi and yin (respectively); carthamus is bitter and vitalizes blood circulation. Patients with tumors affecting the upper body (head, neck, chest; mainly lung, esophagus, and lymphatic cancers) were divided into two groups, one receiving the herbal combination in decoction form daily for four weeks. All received radiation therapy (which is considered to have a burning, therefore hot, impact, and damage the qi and yin while producing blood stasis). It was reported that those taking the herb formulas had significantly less fatigue, gastro-intestinal distress, and loss of body weight; they also had far less inhibition of white blood cells.

It can be seen from the above descriptions that sweet-tasting formulas (particularly those that include herbs of the legume family, such as licorice, astragalus, soja, and millettia) are not only theoretically useful, based on the traditional concept of taste and action, but are also applied in modern clinical work to counter the side effects of toxic drugs with apparent good result. The traditional selection of ingredients also implies that the diet of persons who need to take toxic drug therapies should rely more heavily on legumes, such as soy bean products and mung beans, which can be prepared with rice and other nourishing grains.

**USING STOMACH PROTECTORS**

Licorice, astragalus, and jujube are herbs that enhance the stomach functions. The importance of protecting the stomach from the effects of drugs, and enhancing stomach functions that might be impaired by the drugs, has long been a principle of traditional Chinese medicine. For example, in a discussion of drug poisoning in the Zhangshi Yitong (1695 A.D.), the author, Zhang Lu, argues strongly that the stomach must be protected and that the stomach functions that are damaged must be restored. Zhang's concern was that (19): "The stomach influences [qi] are thrown into disorder by drugs, and, as a result, food and drinks will no longer be transformed into flesh and skin, and the bones will no longer be the firm framework propping up the body." He concluded: "To treat this illness of drug poisoning, one must do away with all the bitter, cold, descending,
draining herbs, and also the acrid, hot, ascending, and stimulating herbs, as well as those that have strong and violent nature and taste. Only small doses of substances that warm and nourish the stomach, such as ginseng and astragalus, are appropriate." Of course, in the case of modern drug therapies, it is not always possible to eliminate the drastic substances; still, the recommendation here is to use sweet herbs, such as ginseng and astragalus, to assure that the stomach can recover. This principle would also apply to treatment of patients who have just completed a course of drug therapy and are suffering from the adverse consequences of both the disease that was being treated and the drugs that were applied.

Herbs that are considered to have particularly cold properties are believed to have the side effect of impairing the stomach functions. An example is gypsum (shigao), which is often described as having an extremely cold property. Despite the extreme nature, it is deemed an important mineral agent to be applied in cases of fire syndromes, such as heatstroke, lung disease, skin eruption, and high fever. One of the best known formulas relying on gypsum is the White Tiger Decoction (Gypsum Combination, Baihu Tang). It includes the two fire-purging herbs gypsum and anemarrhena, with oryza and licorice. Oryza is sweet and warm. According to Formulas and Strategies (3), oryza and licorice "prevent the extremely cold properties of the other ingredients from injuring the middle burner."

Further traditional modifications of this formula listed in the Shanghan Lun include Baihu Jia Renshen Tang that adds ginseng to improve the function of the stomach and spleen, and Zhuye Shigao Tang, in which anemarrhena is replaced by three herbs: pinellia, ophiopogon, and bamboo leaves. This latter formula has been adopted recently to treat the gastro-intestinal side effects of cancer therapies. In a clinical trial (20), this formula was made as a decoction and patients were instructed to drink it in the morning and night, except on the day of chemotherapy (for persons who have a severe reaction to chemotherapy, it would be given a day before the therapy and starting again two days afterward; this avoids any possible interaction between the herbs and the orally-administered chemotherapy drugs). The formula could be modified slightly for specific symptomatic presentation. The patients being treated had bone cancer, and were being treated by polydrug therapies such as VAC (vincristine, cisplatin, and adriamycin), or with methotrexate, cyclophosphamide, etc. In general, only 3-5 doses of the herbs were needed for each cycle of chemotherapy (typical 2-3 week interval between chemotherapy administrations). Of 18 patients so treated, it was reported that 5 had virtually no adverse reactions to the chemotherapy (e.g., nausea, vomiting, dry mouth, sore throat, oral ulceration, etc.) and that 10 had much less reaction than before. Bamboo leaves and ophiopogon have a sweet taste and cold nature. The side effects of the chemotherapy were interpreted as damaging the stomach and yielding stomach-heat reactions, hence the use of gypsum, ophiopogon, and bamboo in this formula for enhancing and normalizing stomach functions.

A traditional formula for clearing lung heat, Morus and Lycium Bark Formula (Xiebai San; literally, Drain the White Powder, where white is the color representing the lungs), is comprised of two heat-clearing herbs, morus bark and lycium bark, and two herbs to protect the stomach, oryza and licorice. According to the Chinese-English Manual of Commonly Used Prescriptions in Traditional Chinese Medicine: "The four drugs used together can purge the lung heat but does not damage the healthy energy."

Protecting the stomach from cold is commonly mentioned in the literature, but protecting the stomach from the heating effects of herbs is also deemed important. Even the commonly-used spicy herb ginger (fresh ginger, shengjiang or dry ginger, ganjiang), is described as having the potential to cause heating and drying of the stomach; this is also true of the warm and spicy herbs pinellia and citrus. The potential problem for the stomach is compensated for by adding licorice and/or jujube. In fact, the stomach-benefiting combination of ginger, jujube, and licorice is used in about 20% of the formulas of the Shanghan Lun and the companion volume Jingui Yao Lue (220 A.D.). A formula combining dry ginger and licorice (honey-fried) is mentioned in the Jingui Yao Lue. Referring to the dry ginger in this formula, Formulas and Strategies mentions that: "its acrid, hot nature can easily deplete the source qi. To prevent this, honey-fried licorice is added to tonify the qi. Together, these herbs warm and strengthen the stomach...."
RECENT RESEARCH EFFORTS

The main effort aimed at finding ways of counteracting side effects of Western medical therapies with Chinese herbs was initiated during the 1970's in an effort to deal with the increasing use of Western medicines to treat cancer. The use of Chinese herbs for treating cancer alone had limited success, as most traditional physicians working at the new hospital facilities set up by the government beginning in the 1950's would attest.

Modern medical cancer therapies are usually difficult to tolerate. Surgery, which can be quite invasive, is the one that causes the least systemic damage, but it is not always a reasonable option. Chemotherapy and radiation therapy cause a number of adverse effects. Of particular concern are: leukopenia (loss of white blood cells due to bone marrow inhibition); reduced appetite and impaired ability to take in nourishing foods; and general weakness (and accompanying depression, lack of exercise, and inability to pursue health-promoting activities). In the attempt to integrate traditional Chinese and modern medicine, the concept arose of relying on the Western therapy as the primary means of killing cancer cells, while using Chinese herbs to protect the bone marrow, improve the appetite and digestion, and increase energy. The Chinese medical aspect of this integrated method was termed Fu Zheng Therapy, where fuzheng means "to support normality." Its actions are to nourish, tonify, and invigorate the body's beneficial qi to help overcome any perverse qi that might be associated with the cancer, the therapies for cancer, and pathogenic influences that attack the body that has been weakened.

In a 1981 report by Tu Gouri (56), the direction and results of this work were summarized:

In recent years, the treatment of malignant tumors with combined methods of traditional Chinese medicine and western medicine has made much progress. Tonics play a part in the therapeutic effect....Patients with advanced malignant tumor usually have the symptoms of deficiency in qi and blood, deficiency of liver and kidney, and dysfunction of spleen and stomach. Tonics may improve the general condition and the immune function of the patients, enhance resistance against diseases, and prolong their surviving period. Furthermore, tonics also have protective effect against immune suppression, lowering of leukocyte count, suppression of bone marrow, and decrease of plasma cortisol level induced by radiotherapy and chemotherapy. All these benefit the treatment of malignant tumor.

The number of clinical journal reports about Fu Zheng Therapy is large, and there have even been books describing this approach, such as the one completed in 1988 and published in English in 1992, Cancer Treatment with Fu Zheng Pei Ben Principle (6). Here, peiben means to shore up the root, meaning to protect the fundamental essence of the body from debilitation; guben is a term sometimes used instead: to firm up the root). If one accepts the findings of any of the Chinese studies, it is evident that cancer patients can experience fewer side effects and, generally speaking, feel better; they can often increase their survival time (compared to persons not using Fu Zheng Therapy).

The herbal basis of Fu Zheng Therapy is, fundamentally, to select ingredients to tonify the qi and yang, nourish the yin and blood, improve digestive function, and, if need be, address specific symptoms that have arisen (either because of the cancer, the cancer therapy, or another influence). The particular ingredients of Fu Zheng Therapies are diverse, though they tend to be sweet and slightly bitter in taste, and the formulas tend to be slightly warming in nature (see section on General Trends in Drug Effects, below, for more on the warming nature of the therapies).

In pursuing the laboratory investigation of herbs for cancer therapy, there is one class of active constituents that stands out. These are the immune-modulating polysaccharides (they are actually polysaccharide-peptide combinations) obtained from numerous herbs, but first investigated among the medicinal mushrooms. Most people in the field of natural healing have heard of some of these materials:
ganoderma (*lingzhi*, Japanese: *reishi*), lentinus (*xianggu*, Japanese: *shiitake*), polyporus (*zhuling*, related Japanese mushroom: *miitake*), and coriolus (*yunzhi*; this is the source of the Japanese drug product called PSK, polysaccharide krestin). Although there have been claims made about the superiority of one source or another, it appears that the mechanism of action of these polysaccharides, also found in astragalus, lithospermum, prunella, lycium fruit, and other non-mushroom herbs, is the same.

The dosage that is needed in clinical application when using oral administration is approximately 3.5 grams of polysaccharides per day. The mushrooms typically contain less than 8% polysaccharides by dry weight, which means that one must ingest the extract of at least 40 grams of the dried mushrooms each day. Because the mushroom extracts that are made into commercially available products are usually quite expensive, and because some commercial preparations have little or no polysaccharides (as is the case with the tinctures), the natural tendency is for these to be used far below the clinically useful dosage, therefore with relatively little effect. This is not, however, because of any basic defect in the treatment strategy. An example of successful treatment was reported (54) for polysaccharides from coriolus in the adjunctive treatment of breast cancer patients. The patients took 9 capsules per day of polysaccharide peptides of coriolus, said to be similar to the drug product PSK. This provided 3.6 grams of the material per day. There was no significant drop in blood counts among 11 patients studied during three cycles of chemotherapy; additionally, half of the patients reported an improvement in appetite.

In the laboratory animals, experimental tumor cell lines usually cause substantial immune impairment, which is rectified by the polysaccharides, causing the tumor to shrink under the attack of the immune system. In humans, cancer-induced immune suppression is less common; instead, the problem of weakened immunity arises from the cancer therapies. Thus, although the polysaccharide extracts of mushrooms were originally developed as treatments for cancer, currently, these (and similar polysaccharides from other plants) are being used as adjunct therapies to protect the patient's stomach, liver, and bone marrow from toxic effects of drugs and damage due to radiation therapy, as in the above-mentioned clinical evaluation.

Westerners first learned about Fu Zheng Therapy when a conference on immune-regulating therapies was held in China (1983) with the support of the M.D. Anderson Medical Center (Houston, Texas) and Newport Pharmaceuticals (Newport, California). At this conference, Dr. Sun Yan presented his data on two of the Chinese herbs that had been shown to be of benefit, astragalus and ligustrum. Subsequently, additional work was done by Dr. Sun during a visit to the M.D. Anderson facilities. Eventually, a polysaccharide fraction of astragalus (fraction 3, F-3) was isolated as the most potent of the herb’s polysaccharides. Unfortunately, because of the inability to patent this type of compound, additional work was not pursued in the U.S. Herb companies have, nonetheless, provided astragalus, ligustrum, the combination of the two (alone or with additional herbs), and even the F-3 component as natural products. Unfortunately, as indicated above, the dosage administered is usually too low to attain the desired effects.

Astragalus plus ligustrum was developed as a cancer adjunct therapy in China, especially to accompany chemotherapy. The Zhenqi Tonic Drink, comprised of these two herbs in liquid extract form (not tincture, however), was evaluated in patients with advanced gastric cancer receiving chemotherapy (mitomycin 5-FU). The herb drink was given to some patients twice daily for eight weeks during chemotherapy. The authors of the study reported that the tonic could reduce the incidence of toxicity, leukopenia, and thrombocytopenia (28). The fact that research on these two herbs held such a prominent position has led to inclusion of astragalus and ligustrum in many *fuzheng* formulations, such as the previously mentioned Shengxue Tang and Fuzheng Zengxiao Fang.

Evaluations of herbs that protect against the immune-suppressing action of radiation therapy begin with studying the ability of herbs to protect animals exposed to whole-body potentially lethal radiation, and develop into clinical trials. In a report on this subject (55), the following herbs were reported to be of benefit to the immune system of cancer patients in clinical trials: eleuthero ginseng, tremella (a medicinal mushroom...
with immune modulating polysaccharides), sophora, and Qi Zao Granule (astragalus, jujube, millettia, and hoelen).

**CLINICAL REPORTS OF TREATING SIDE EFFECTS WITH FU ZHENG THERAPY**

While research efforts continue to aim at analyzing specific herbs and their active constituents, most of the recorded information about treating cancer patients with integrated therapy involves application of complex herbal formulas, not unlike those used for treating other diseases.

The basic principles of treating cancer therapy side effects are outlined in the book *Cancer Treatment with Fu Zheng Pei Ben Principle*. The author, Pan Mingji, based on his long clinical experience, devised a general formula for prevention and treatment of side effects of various chemotherapeutic drugs. This formula, called *Yiqi Buxue Jianpi Tang* (Decoction to Support the Qi, Nourish the Blood, and Benefit the Spleen), is similar to the prescriptions described above for treating immune-suppression, with astragalus, licorice, lycium fruit, ligustrum, millettia, atractylodes, hoelen, and codonopsis as ingredients. However, Pan Mingji shows a preference throughout his book for very large formulas (both a large number of ingredients and a large dosage of each ingredient). His general *fuzheng* prescription also includes rehmannia, ho-shou-wu, polygonatum, glehnia, ophiopogon, euryales, and dioscorea (the formulation to be adjusted, as needed, by adding specific herbs for the toxicity symptoms encountered, sometimes reducing the dosage of other herbs to compensate). According to Pan, the formula is administered along with chemotherapy and during any intervals between therapeutic courses, until symptoms disappear. The overall results of clinical applications are not indicated, though a few case studies are presented in his book.

Clinical trials of cancer therapies, with more specific evaluations of outcomes, have been published in several Chinese medical journals. Due to flaws in research methodology, the outcomes must be interpreted with caution; due to difficulties in evaluating the limited data described in the journals, only a cursory outline of results is given here. Still, the information about what herbs are administered, how they are administered, and what general types of improvements are claimed to result is of interest to practitioners here, especially those who have limited experience treating cancer patients.

There are three main approaches to treating side effects of cancer therapy that are evident in a survey of the Chinese literature:

1. **Attempting to improve overall outcomes.** In the clinical trials, it is common to find that patients with many different types of cancer and undergoing many different Western medical therapies are included in the study and are administered a basic protective herbal therapy, sometimes modified for specific symptoms. The claimed outcomes are fewer side effects, better ability to complete therapy, improvements in tumor shrinkage, and increased survival time.

2. **Correcting immune suppression.** In clinical trials, the level of white blood cells is monitored; in some cases, more specific immune assays are followed, such as monitoring the numbers of CD4 and CD8 cells (involved in cellular immunity) and levels of immunoglobulins (involved in humoral immunity). Since immune suppression may be reason to prematurely terminate or delay Western medical therapies, and since impaired immunity may result in life-threatening infections, this particular side effect of cancer therapy has been deemed an important area of concern.

3. **Overcoming nausea and other digestive disturbance caused by cancer therapies.** Nausea is a common reaction to chemotherapy and often results in reduced appetite and resulting loss of nutritional status and body weight. Risks associated with malnutrition and wasting are substantial and may be fatal for patients undergoing cancer treatment. Further, nausea and loss of appetite may lead to a situation where a patient is unwilling or unable to consume herbs for their other benefits.
Sometimes the herb treatments are given with the Western medical therapy, but other times they are given afterward, to help recover from the adverse effects of Western medical therapies.

An example of a traditional herb formula that has been recruited to the task of overcoming cancer side effects is Ginseng and Tang-kuei Ten Combination (Shichuan Dabu Tang). The formula:

1. tonifies qi, relying on the base prescription: Four Major Herbs Combination; *Si Junzi Tang*, comprised of ginseng (or codonopsis), licorice (honey baked), hoelen, and atractylodes;
2. nourishes blood, relying on the base prescription: Tang-kuei Four Combination; *Siwu Tang*, comprised of tang-kuei, cnidium, peony, and rehmannia (cooked);
3. invigorates qi and yang, with astragalus and cinnamon bark.

The formulation, with dosage ranges as used to accompany cancer therapies is:

*Shiquan Dabu Tang*

<table>
<thead>
<tr>
<th>Herb</th>
<th>Dosage Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>astragalus</td>
<td>15-30 g</td>
</tr>
<tr>
<td>codonopsis</td>
<td>10-15 g</td>
</tr>
<tr>
<td>hoelen</td>
<td>10-20 g</td>
</tr>
<tr>
<td>atractylodes</td>
<td>10-15 g</td>
</tr>
<tr>
<td>licorice</td>
<td>5-10 g</td>
</tr>
<tr>
<td>tang-kuei</td>
<td>10-15 g</td>
</tr>
<tr>
<td>peony</td>
<td>10-15 g</td>
</tr>
<tr>
<td>cnidium</td>
<td>10-15 g</td>
</tr>
<tr>
<td>rehmannia</td>
<td>10-15 g</td>
</tr>
<tr>
<td>cinnamon bark</td>
<td>5-10 g</td>
</tr>
</tbody>
</table>

This formula has come to the attention of Westerners through some English-language publications, such as the popular book that reviews alternative cancer therapies by Michael Lerner (*Choices in Healing: Integrating the best of conventional and complementary approaches to cancer*), where it is listed by the Japanese name *Jizendaihoto*. Isamu Adachi presented information (17) about using this formula for treating advanced breast cancer patients at a conference on Oriental Medicine held in Japan in 1990, which was relayed by Lerner. Adachi reported on 130 patients entering the study during the period 1985-1987, indicating that patients treated with this formula had a better survival rate than a control group not treated with the formula. The difference was noted after 18 months following the cancer therapy (survival rates were about the same until that time, but better with the herb treated group thereafter) and the improvement was still evident at three years (duration of monitoring at the time of the report).

In a recent report by Wang Yuran (7), 60 patients with a variety of cancers, mainly lung and esophageal cancer, were treated first with chemotherapy or radiation, and subsequently suffered from immune suppression. They were then administered a modified version of *Shiquan Dabu Tang* (added herbs were polygonatum, lycium fruit, ho-shou-wu, cornus, lotus seed, millettia, and dioscorea). This formula is quite similar to the one recommended by Pan Mingji, having 11 of the same herbs, but with lotus seed replacing the related herb euryale (these herbs have virtually the same properties), and with the blood tonics tang-kuei, peony, and cnidium replacing the yin tonics ligustrum, glehnia, ophiopogon, and cornus. After 30 days administration of the herbs, Wang reported that there were statistically significant improvements in total white blood cells, natural killer-cell rate, and ratios of CD2, CD4, and CD8 (to reveal better cellular immune functions; humoral immune functions did not change much, except an improvement in IgG). Of course, one would expect a certain natural improvement in immune functions after the Western medical therapies were completed, so we don't know to what extent these improvements were due to the herbs.
A simplified *Shiquan Dabu Tang* was tested in tablet form by Zhang Yikang and Xiao Ainong (8). Patients with various cancers were treated with radiation and/or chemotherapy and simultaneously given *Bao Yuan Pian* (Tablet for Preserving the Original Qi), comprised of ginseng, astragalus, licorice, and cinnamon bark. Tablets of the extract were given three times daily while a control group received a vitamin tablet. The effects were evaluated according to two related criteria: one was that the patients were able to complete the medical therapies (which requires maintaining sufficient immune status as well as tolerating the adverse symptomatic effects of the therapies), and the other was maintaining a relatively high WBC count. According to the report, the treated group had a better outcome (88% able to complete therapy and maintain good WBC counts) than the control group (61%). *Bao Yuan Pian* focused on the qi and yang invigorating principles of *Shiquan Dabu Tang*.

A modified *Shiquan Dabu Tang* recipe, with peony, cnidium, and cinnamon bark deleted and adenophora and salvia added, was used to treat gastric cancer patients with advanced stage of disease (68). The patients had undergone surgery and were then treated with chemotherapy along with the herbs. A control group received chemotherapy plus herbs that were aimed specifically at alleviating gastric distress, with citrus, magnolia bark, cardamon, oryza, and malt. Those treated with the modified *Shiquan Dabu Tang* had significantly increased CD8 levels and reduction in the high platelet-aggregation rate that is characteristic of advanced cancer patients; the survival time of this group was greater than that of the control group.

Another treatment that may be considered a modification of *Shiquan Dabu Tang* is the one described by Cheng Huiha, et al., (9), using astragalus plus *Liu Junzi Tang*. Like *Shiquan Dabu Tang*, it incorporates *Si Junzi Tang* plus astragalus, but it does not include the blood nourishing herbs or cinnamon bark, and instead contains pinellia and citrus, two herbs that promote digestive functions and help alleviate nausea and vomiting. Patients with primary hepatic cancer were treated by chemotherapy infused directly into liver arteries by catheter, and were given the herbal formula orally (each batch taken in two divided doses per day, 6 batches per week, 30-40 batches per treatment. The herbs were taken during the overall course of chemotherapy but not for three days before or during each catheter administration of the drugs (typically four times per patient). According to the authors, the use of herbs led to lessening of: nausea, vomiting, pain in the liver region, and WBC decline. There was a slight improvement in the shrinkage of the tumor as well.

Countering immune suppression due to thiamazole (methimazole) or propylthiouracil (thyroid-inhibiting drugs used for treatment of hyperthyroidism, such as Grave's disease), was also accomplished by using a modification of *Shiquan Dabu Tang*, in which hoelen, cnidium, and cinnamon were deleted (these are the three herbs of the traditional formula that are most often sacrificed in Fu Zheng Therapy to make room for various additions) and millettia and buffalo horn added. In the study of its effects, a control group used Western medicine, such as leucogen (nupigen) and vitamins. Patients continued using the thyroid drugs, except two who had such severe leukocyte-inhibition that they stopped. Patients treated with the herbs had significant increases in hemoglobin, white blood cells, and platelets, indicating restoration of bone marrow functions. The control group treated with Western medicine showed some improvements in these parameters, but to a much lesser degree.

*Shiquan Dabu Tang* has become so well known as a treatment for minimizing cancer therapy side effects and post-cancer therapy recovery of immune functions that it was used in a clinical trial (10) as the control treatment to test a new herbal therapy. The formula, *Yangyin Shengbai Yin* (Support the Yin, Generate White Blood Cells), is made with an unusual mixture of herbs (compared to most Fu Zheng Therapies) aimed at treating qi, blood, and yin deficiency, and digestive disturbance. Of 14 ingredients used, only three were commonly found in other formulations, namely hu-chang, tang-kuei, and peony. According to the report, *Yangyin Shengbai Yin* and *Shiquan Dabu Tang* were both associated with substantial improvements in WBC counts, but the former group had a better total effective rate (87%) than the latter (69%) after three weeks of treatment. This difference may not reveal any flaw in *Shiquan Dabu Tang* or benefit in the alternative formula because the control group was too small and the trial was not blinded.
A more representative Fu Zheng formulation that is not a strict derivative of *Shiquan Dabu Tang* is that presented by Zhang Haifan in a study (11) on the side effects of cancer therapy in patients with many types of cancer. His formula is:

**Huten Tang**

- astragalus 40 g
- hu-chang 30 g
- millettia 30 g
- lycium fruit 15 g
- atractylodes 12 g
- hoelen 30 g
- tang-kuei 15 g
- psoralea 15 g
- cuscuta 20 g
- licorice 10 g

This formula, which is similar to *Shengxue Tang* mentioned earlier, is relatively devoid of the yin-nourishing herbs (lycium is a blood tonic that nourishes yin), but does contain yang-tonic herbs (psoralea and cuscuta) as well as qi tonics (the combination of astragalus, atractylodes, hoelen, and licorice). Hu-chang and millettia (which are both used in modern China to boost white blood cells) were deemed main herbs in the formula. This prescription is an elaboration of one described for leukopenia due to radiotherapy (1) which is comprised of 30 grams each of hu-chang, millettia, and tang-kuei (all used for building blood), along with 9 grams of licorice. In this instance, Zhang initiated the herb therapy 3-5 days prior to starting chemotherapy and continued it until one week after finishing chemotherapy. The effectiveness of the therapy was evaluated by considering a broad set of indicators, such as red and white blood cell levels, extent of gastro-intestinal reactions, avoiding loss of hair, and improving tumor shrinkage. According to the author, 39% of the patients had an excellent outcome, and 43% had a notably effective response, while only 7% failed to respond at all, yielding a benefit that seems comparable with other claims that have been made for Fu Zheng Therapy.

In a clinical trial (61) involving cancer patients with severely lowered white blood cell production due to chemotherapy agents, a formula focusing on qi and blood nourishing herbs was given:

**Fuzheng Shengbai Tang**

- astragalus 30 g
- codonopsis 30 g
- atractylodes 12 g
- hoelen 12 g
- tang-kuei 9 g
- psoralea 12 g
- ligustrum 12 g
- polygonatum 30 g
- ho-shou-wu 15 g

The formula was modified with additional herbs to treat specific manifestations. These herbs were given when chemotherapy was stopped, in order to help restore the reduced leukocyte levels. The control group received leucogen. The Chinese herb group was reported to have greater recovery of white blood cell counts and also showed significant improvement in other chemotherapy symptoms, such as nausea, poor appetite, weariness, and thin stools.
The same basic principle was utilized in another trial (62) that focused mainly on upper body tumors (lung, breast, and stomach), with the following formulation:

**Fuzheng Guben Fang**

- astragalus 40 g
- atracylodes 15 g
- licorice 20 g
- pseudostellaria 30 g
- tang-kuei 15 g
- peony 15 g
- rehmannia 20 g
- ho-shou-wu 40 g
- gelatin 20 g
- oldenlandia 30 g
- millettia 30 g
- ligustrum 20 g

Here, ho-shou-wu and gelatin are additional blood tonics and oldenlandia serves as an anticancer herb that increases leukocyte counts. The formulation was modified to address specific symptoms. The herbs were given along with chemotherapy, while a control group received Western drugs, vitamins, and berbamine (an herbal leukocyte raising alkaloid derived from *sankezhen, Berberis soulieana*) along with the chemotherapy. According to the report, the Fuzheng formula prevented the decline in leukocytes better than the control treatment, and the patients also had fewer other side effects, such as nausea and weariness.

Zhang Xinqi and his colleagues (25) described another fuzheng formula that relied more heavily on nourishing the kidney and liver. It contains:

- astragalus 30 g
- codonopsis 15 g
- lycium 15 g
- psoralea 15 g
- cuscuta 10 g
- ligustrum 10 g
- drynaria 10 g
- rehmannia 10 g
- cornus 10 g

The herbs were administered once per day for 7 days, given after the occurrence of leukopenia from chemotherapy or radiation therapy. A patient group was randomly assigned to receive or not receive the herbs; chemotherapeutic agents included cyclophosphamide, cisplatin, 5-FU, and Adriamycin. According to the report, improvements were noted in nausea, lassitude, dizziness, and insomnia, and the leukocyte counts improved markedly (from an average of 2.8 to an average of 5.9).

A similar approach was presented by Liu Jiaxiang in a lecture on combining Chinese and Western therapies (18). He described the case of post-operative treatment of stomach cancer (stage III). The herb formula given was Jianpi Yisheng Tang comprised of codonopsis, atracylodes, cuscuta, ligustrum, lycium, and psoralea (all these herbs are in the above formula). This formula invigorates the spleen and the kidney and was utilized to "lessen the toxic and side-reactions of the drugs" that were given to the patients (a triple drug combination). The effectiveness was rated by survival time, with 99% of patients surviving one year,
79% surviving three years, and 55% surviving 5 years; these survival rates are considerably higher than those attained by surgery plus chemotherapy alone.

In a case (42) of cardiac distress (palpitation, small and slow pulse with irregular intervals, premature systole occurring occasionally, lower-wall myocardial ischemia) caused by the cancer therapy adriamycin (doxorubicin), the attending physician applied a modified Baked Licorice Combination (Zhigancao Tang), which is traditionally employed to treat cardiac irregularities. The formula applied was 20 grams licorice, 30 pieces jujube, 10 grams ginseng, 15 grams fresh ginger, 10 grams cinnamon twig, 30 grams rehmannia, and 15 grams cannabis seed. After six days of using this decoction the patients symptoms were eliminated; then, when adriamycin therapy was begun again, she was given the decoction along with it and the cardiac irregularities did not occur. This formula has a notable sweet taste, and, like Bao Yuan Pian, contains ginseng, cinnamon, and licorice.

The above examples reveal the following:

1. Herbal therapies may be applied along with cancer therapies or after the completion of cancer therapy.
2. Treatment times with the specific formulas mentioned are a few weeks.
3. High dosage decoctions are usually utilized, with daily doses of 100-200 grams.
4. Tonic herbs and herbs that are uniquely reputed to raise blood counts are relied upon most heavily.
5. Sweet-tasting formulas with warming nature are the rule.
6. Specific ingredients vary somewhat; astragalus is the most frequently included. The other common herbs are: the qi tonics codonopsis, atractyloides, and licorice; the blood tonics tang-kuei, peony, rehmannia, and lycium fruit; the yang tonics psoralea and cuscuta; and the blood cell raising hu-chang, ligustrum, and millettia that belong to miscellaneous categories of herbal therapy.
7. The claimed benefits are fewer side effects from cancer therapy, faster and better recovery of immunity after completion of the therapy, and improved outcomes measured in terms of survival time.

TREATING SPECIFIC SYMPTOMS OF CHEMOTHERAPY
Several clinical trials published in the medical literature focused on the specific herbal treatment of nausea and vomiting. These included modified versions of Inula and Hematite Combination (Xuan Fu Dai Zhe Tang; (59)), Six Major Herbs Combination (Liu Junzi Tang, (60)), Ginseng Stomach Combination (Renshen Yangwei Tang; (65)), and Bamboo and Gypsum Combination (Zhuye Shigao Tang; (67)). Beneficial results were described in each of the clinical reports. Acupuncture therapy is sometimes used instead of herbs, relying on standard point selections, such as using ST-26 or PC-6. In fact, in one clinical trial (64) these two points were needled along with LI-4 and LI-11 to counteract numerous side effects of chemotherapy and radiation therapy (with daily acupuncture six days each week). This treatment, carried on for three weeks, was reportedly able to help alleviate the symptoms of loss of appetite, nausea and vomiting, abdominal distention and diarrhea, as well as helping with dizziness, insomnia, and lassitude. In another study (66), these same four acupoints, along with other points, were used to treat gastrointestinal reactions to cancer therapies, administering acupuncture daily for ten days. The treatment was claimed to alleviate vomiting, diarrhea, nausea, and fullness and distention. Unfortunately, daily acupuncture is rarely possible in the current Western setting.

Oral ulceration, a common effect of some chemotherapies, was treated with success (26) by the following herbal combination:
Astragalus 30 g  
Ligusticum 6 g  
Phellodendron 8 g  
Trichosanthes root 15 g  
Forsythia 20 g  
Tien-ki ginseng 4 g [as powder]  
Bletilla 15 g [as powder]

The first five herbs are decocted (200 mls decocted to yield 50 mls finished, strained liquid) and the powders are then added and the mixture homogenized; this mixture is given several times daily. The taste is quite bitter so honey is added to ameliorate that problem. The herbs were administered for 3-9 days as needed to resolve the condition. It was reported that 76% of the patients had their oral ulcerations resolved (compared to a control group receiving vitamins and Western drugs, with 23% resolved).

Although clinical results were not mentioned, the following formula is of interest for reference purposes in the treatment of oral ulceration and pharyngeal ulceration following chemotherapy (52):

Astragalus 15-30 g  
Sophora subprostrata 15 g  
Rehmannia 15-30 g  
Isatis root 12-15 g  
Scrophularia 9 g  
Coptis 6 g  
Lonicera 15 g

This prescription is prepared as a decoction and taken in two divided doses, morning and evening. As with the above formula, this one is derived from treatment of sore throat and oral ulceration that might arise from other causes, such as infection. The high dose of astragalus is one of the key differences in addressing the side effects rather than infection-caused inflammation. In a section below, formulas for treating similar symptoms due to radiation therapy are mentioned.

OTHER CASES OF COUNTERING SIDE EFFECTS OF WESTERN DRUGS

While Fu Zheng Therapy has been the primary focus of countering side effects, the use of Chinese herbs to overcome the toxicity of other types of drugs has also been investigated, to a limited extent.

In traditional literature, the ferns have been reported to counteract toxicity. According to one report (39), Stenoloma chusanum (wujue, of the Polypodiaceae; known as a "universal antidote") was shown in laboratory animal studies to reduce the toxicity of arsenic. Another member of the Polypodiaceae, drynaria, has been shown to counteract the ototoxicity of kanamycin (40). The tests were done in guinea pigs, with extensive testing of the ears (including light microscope and scanning electron microscope) after the experimental period. Animals were treated with 300 mg/kg of kanamycin and the extract from 15 grams/kg of drynaria. At this time, the active constituents of drynaria that might contribute to this effect have not been established; however, drynaria is known to contain naringenin, which is a flavonoid. A rarely used relative of drynaria, onychium (leaves of O. japonicum), is reported in Modern Study and Application of Materia Medica (46) to be an antidote to several kinds of poisoning, including arsenic, mercury, DDT, and plant-drug poisoning. This herb is closely allied with another fern, pteris (fengweicao), for which the leaves are also used; according to the Oriental Materia Medica, pteris is sweet, with a mild bitter flavor, a cold property, and diuretic action (thus, having an effect on the kidneys and, possibly, on the elimination of toxins). Pyrrosa (shiwei; bitter, sweet, and slightly cold), another member of the Polypodiaceae that is employed as a diuretic, is mentioned in Chinese-English Manual of Commonly Used Herbs in Traditional Chinese Medicine to
be "effective for cyclophosphamide-induced leukopenia in mice." In *Treatment of Cancer by Integrated Chinese-Western Medicine*, a simple formula for leukopenia is 30 grams each of pyrrosia, jujube, and dendrobium.

Cnidium (*chuanxiong*) contains an active constituent, ligustrazine, that has been employed for numerous medical purposes (especially for cardiovascular disorders), and has been shown to inhibit toxicity of certain drugs. In another study of ototoxicity of kanamycin (27), evaluated in guinea pigs, the authors of the investigation concluded that part of the toxicity process was due to lipid peroxidation, which could be treated by antioxidants. They used ligustrazine in order to successfully reduce kanamycin ototoxicity; this compound has antioxidant activity. Gentamicin, a drug often used as a last resort for infections, is given by intravenous administration and may cause nephritis. In an attempt to counteract this, Chinese physicians have tried the combination of astragalus (30 grams per day taken orally in decoction form) and ligustrazine (80 mg/day by IV). This treatment was reported to improve the kidney functions (29). The anticancer plant drug camptothecin (obtained from Camptotheca acuminata) is highly toxic, but the toxicity may be reduced, according to the *Chinese-English Manual of Commonly Used Herbs in Traditional Chinese Medicine*, by glycyrrhizin from licorice and by cnidium.

A new type of immune-based therapy with injection of IL-2 (interleuken-2, a cytokine) tends to cause kidney toxicity. A decoction of astragalus, millettia, dioscorea, leonurus fruit, and imperata (dioscorea, leonurus fruit, and imperata all have a sweet taste), 30 grams each, was given to patients in an effort to counter that toxicity (41). It was reported that this treatment was effective (all 150 patients showed normal values of kidney function; in the control group, 15% of patients showed abnormalities that could be normalized by giving them the decoction for one week). In laboratory animal experiments (53), it was shown that cordyceps could inhibit the renal toxicity of cyclosporine A.

*Centella asiatica* (*jixiecao*) is reported in the *Chinese-English Manual of Commonly Used Herbs in Traditional Chinese Medicine* to relieve drug poisoning. Specifically, mushroom poisoning, *Gelsemium elegans* (a very poisonous herb; the alkaloid is a spinal poison), cassava (used as a source of starch, it contains hydrocyanic acid), *Derris trifoliata* (a poisonous herb used as an insecticide, containing rotenone), organic phosphorus, and arsenic. For treatment of poisoning, the juice of fresh *jixiecao* leaves is recommended, using 500-1,500 grams of herb for a one day dose.

Numerous Chinese herbs have been shown to have liver-protective actions in laboratory tests where liver toxins (notably carbon tetrachloride) are administered. In *Pharmacology and Applications of Chinese Materia Medica*, the following commonly used herbs were said to have a hepatoprotective property: atractylodes, mentha, bupleurum, tang-kuei, rehmannia, hoelen, licorice, lycium fruit, magnolia bark, astragalus, forsythia, ganoderma, gentiana, dandelion, schizandra, capillaris, alisma, and gardenia. The *Modern Study and Application of Materia Medica* also lists liver-protecting herbs, most of which are the same, but also included are: salvia, rehmannia, and hu-chang. In a search for herbs that would be useful in treating viral hepatitis, Hiroshi Hikino (31) first determined their anti-hepatotoxic activity (liver protection against a calcium transport drug; calcium flooding is thought to be one of the mechanisms of hepatic inflammation in viral and toxic hepatitis). Aside from glycyrrhizin in licorice, the following herbs were found to inhibit liver damage: curcuma, atractylodes, capillaris, swertia (a relative of gentiana), dianthus, tetrapanax, ginseng, and schizandra. Similarly, Zhou Qingjun (32) examined herbs that protect against carbon tetrachloride damage and found these to be effective: schizandra, sedum, ganoderma, astragalus, tang-kuei, salvia, scute, capillaris, licorice, and *Sophora subprostrata*. Several of the liver-protective herbs have been used in the formulas for protecting against immune-suppression side effects, notably atractylodes, tang-kuei, licorice, lycium fruit, astragalus, rehmannia, and hu-chang.

Numerous pharmaceutical drugs are known to adversely affect the liver. In one Chinese clinical trial (12), patients suffering from hepatotoxicity from isoniazide, erythromycin, griseofulvin, ibuprofen, and
Furadantin were treated with a combined Western and Chinese medical approach. The Western part was an IV drip with coenzyme A (200 units), ATP (60 mg), and inosine (400 mg), as well as a tablet containing vitamin B6 (20 mg), ATP (20 mg), and polyenzyme mixture (600 mg) (one tablet taken three times per day). The Chinese portion was a decoction of 10 grams scute, 20 grams sedum, 12 grams hu-chang, 15 grams lycium, 10 grams dandelion, and 20 grams capillaris, in two divided doses per day. A control group received the Western portion but not the Chinese herbs. Both the groups had improvements in the hepatic inflammation and bile accumulation, but the Chinese herb group had more patients with complete normalization of liver enzyme levels.

Inositol and its derivative inosine, used in the above-mentioned experiment, are deemed protective of the liver (often given in Chinese treatments for viral hepatitis, usually as part of a Western medical approach). Additionally, in one laboratory study (38) inositol was reported to antagonize multiple toxic actions of cyclophosphamide in mice. Inositol is extracted from the leaf of *Apocynum venetum* (*luobuma*), which is a folk remedy for hepatitis and nephritis.

Allergy reactions are a problem with some drugs (actually, the problem is more with the sensitivity of the patient rather than the inherent nature of the drug); in most cases, this is simply resolved by changing to a different drug. However, in recent years there has been a situation where changing drugs was not a workable solution. In patients infected by HIV who had developed AIDS, a prophylactic treatment for potentially fatal pneumocystis infection was administered. The most effective drugs, sulfa drugs, caused allergic skin rashes, often severe, in some persons. Ultimately, this was resolved by administering corticosteroids (e.g., prednisone) along with the drug; this solution is not entirely satisfactory because the steroids have side effects including immune-suppression. Several non-toxic Chinese herbs have been shown to inhibit allergy reactions (see: *Treatment of allergy with Chinese herbs*). In *Modern Study and Application of Materia Medica*, the following commonly used herbs were reported to inhibit allergy reactions: mume, earthworm, moutan, placenta, astragalus, stephania, licorice, ma-huang, chin-chiu, bupleurum, cicada, atracylodes, tribulus, and ginseng.

Certain herbs mentioned in *Modern Study and Application of Materia Medica* for anti-allergy effects were also mentioned above as being used for protecting against immune-deficiency side effects and liver damage from chemical exposure, notably astragalus, licorice, and atracylodes. In fact, the formula *Shichuan Dabu Tang* contains these three herbs and others that have been described in this section: ginseng, tang-kuei, cnidium, and rehmannia. In fact, *Shiquan Dabu Tang* has been shown helpful in treatment of refractory urticaria (58), a skin condition that is often the result of repeated exposure to allergens. This formula is clearly worthy of consideration when faced with treating all kinds of adverse reactions to drugs.

**GENERAL TRENDS IN DRUG EFFECTS AND SIDE EFFECTS**

Side effects vary from drug to drug, so the approach to compensating for the effects needs to be tailored appropriately. Still, among commonly-used drugs that are of concern with regard to side effects, there is a trend towards them having a cooling action. Western drug therapies are frequently employed for their inhibitory effects. For example, one can immediately think of drugs that inhibit bacteria, cancer cell growth, stomach acid, and nerve impulses (e.g., beta blockers). In general, and keeping in mind the diversity of drugs that will generate some exceptions, these inhibitory effects correspond to having cooling actions, even if some of the drug side effects are of a hot nature (e.g., causing mouth ulceration). Hence, antibiotics, understood in Western terms as treatments for bacterial infection, often alleviate fever (a hot condition) and colored discharge (a traditional sign of heat). Cancer drugs clearly reveal their side effects before their positive effects (tumor shrinkage), and induce lowered blood-cell production, lowered appetite, lowered energy, and other inhibitory actions that would be interpreted as involving a lowering of qi and yang. Steroidal drugs that inhibit inflammatory processes are used in Chinese pharmacology experiments to induce laboratory animal models of yang deficiency, because of their ability to impair the adrenal cortical output of
hormones, which corresponds to a weakening of yang.

Much of the effort to overcome the effects of prolonged drug therapy involves the application of qi- and yang-tonifying herbs (warming the spleen and kidney). In the article by Zhang Xinqi (25) about cancer therapies, the situation was summed up this way: "The leukopenia caused by chemo-or radiotherapy is classified to the deficiency type of illness which is referred to as the morbid condition showing deficiency of genuine qi, lowered body resistance, and declining of function. Then, supplementing qi and nourishing the blood, warming and invigorating the spleen and kidney are the essential therapeutic principles for remitting the toxic and side effect of chemo- and radiotherapy." By contrast, short-term drug effects (e.g., acute toxicity after a single exposure or very few exposures) may be treated with traditional "antitoxin" herbs, which are usually cooling in nature.

From time to time, a yin- or blood-nourishing herb is found to have properties similar to the qi- and yang-tonifying herbs. For example, lycium fruit, noted for nourishing yin and blood, contains polysaccharides that have the same effects as those found in qi- and yang-tonifying herbs, such as astragalus and epimedium. Thus, while there are no strict rules, and while the complex formulas for treating side effects usually contain a mix of herbs having different therapeutic actions, the above analysis helps explain why a large portion of the herbs and formulas for treating adverse effects (in modern clinical trials) are qi and yang tonics and are warming in nature. Even when the drug therapy produces symptoms of thirst and dryness, qi-tonifying herbs may be used since the spleen qi generates fluids (pseudostellaria is one of the favored herbs for tonifying qi when there is thirst and dryness; American ginseng is sometimes substituted). An exception is protection against liver toxicity, which tends to rely more on cooling herbs. Liver toxicity reactions often appear as damp-heat, thus indicating the use of cool and bitter herbs.

Yin-nourishing therapies may be an essential ingredient in the treatment of patients who are elderly or who have been ill for a long time. It is generally accepted that such patients will suffer from yin-deficiency syndrome, regardless of the particular drugs being utilized. Because the drugs have an impairing action on the stomach and spleen (as well as other organs), the yin deficiency will be worsened.

POST-SURGICAL TREATMENTS
Despite the great advances in surgical techniques, persons undergoing any major surgery often experience the problem of blood stasis, the direct result of cutting through numerous vessels. Surgical interventions are somewhat like injuries, like a stab-wound, though far less traumatic due to the finely-honed knives, the skill of the surgeons, and the specific aim of not causing harm. Therefore, unlike treatments strictly aimed at wound-healing, the emphasis in post-surgical therapy is only partly focused on vitalizing blood, with much greater focus on strengthening the individual. Surgical interventions themselves usually cause some weakening of the qi, partly the result of any prolonged anesthesia and partly the result of damage to the normal interaction of the organs via the natural blood circulation. However, the qi of patients requiring surgery may already be weak. Surgical interventions often cause temporary weakening of the blood due to the blood loss that occurs during the procedure; patients may also suffer from blood deficiency due to malnourishment. When the lymphatic system is damaged by surgery, as is often the case with breast cancer surgery (in which the lymph nodes are removed), fluid accumulation arises. Finally, in cases of cancer therapy, there is a concern about cancer cells that are left behind (either at the original tumor site or that have already metastasized).

As examples of helping the patient recover from surgery, the following are offered. The first example is the post-surgical treatment of breast cancer. The herb formula outlined below was presented by Pan Mingji. It has the purpose of promoting early recovery from surgical trauma, enhancing immune functions, and inhibiting residual cancer cells:

| Astragalus | 15 g |
pseudostellaria 15 g  
white ginseng 4.5 g  
peony 10 g  
tang-kuei 9 g  
tien-chi ginseng [taken separately as powder] 1.5 g  
placenta 12 g  
polyporus 15 g  
hoelen 15 g  
asparagus 15 g

In addition to the above herbs, which tonify qi, nourish blood, vitalize blood, and drain dampness, herbs for inhibiting tumor cells were also included: prunella (15 g), trichosanthes fruit (20 g), oldenlandia (15 g), cremastra (12 g), lonicera (12 g), and toad skin (10 g). The total dosage of herbs is about 200 grams, though just over half of it is aimed at the recovery from surgery. The herbs are to be made as a decoction and consumed in two or three divided doses. One or two additional herbs may be added to address specific symptoms. According to Pan, for cases of the incision not healing well, use 30 grams each of astragalus and salvia; 20 grams each of tang-kuei and wild chrysanthemum; and 10 grams each of catechu, licorice, and atracytloides for several days in place of the above formula.

A second example is the surgical treatment of gynecological disorders, such as ovarian cysts and uterine fibroids. Since malignant tumor cells are not a concern, the anti-cancer herbs (such as oldenlandia and cremastra) are not required. Because the treatment involves the lower body rather than the upper body, herbs for nourishing the kidney and liver are relied upon more than herbs for benefiting the spleen and lungs (qi-tonic herbs). A formula, Yomeishu, given as a medicinal wine, was described by Toshifumi Takabayashi and his colleagues (13). The formula (proportions not given) is:

rehmannia  
clove  
cinnamon bark  
lemonurus  
epimedium  
turmeric  
eucommia  
lindera  
cistanche  
agkistrodon  
ginseng  
siler

This formula nourishes the kidney and liver, tonifies qi and vitalizes blood. It was tested among a group of 100 post-operative patients, of which 24 had radical hysterectomies, 66 had simple hysterectomies, and 10 had oopherectomies; half of all patients received the formula. Those receiving the formula, which was administered during the three months after surgery, showed faster recovery and improvements in virtually all symptoms monitored. One can guess that the proportions of most of the herbs are roughly equal (e.g., 9-15 grams in decoction form), with lesser amounts of cinnamon bark, ginseng, clove, siler, and agkistrodon (e.g., 3-6 grams in decoction form).

Both formulas rely primarily on tonification therapy and have only a small component aimed at overcoming blood stasis. Surgical treatment of stomach cancer, one of the common types of abdominal surgery for cancer, is frequently mentioned in the medical literature and mainly treated by herbs that tonify qi and aid digestion.

**THE PROBLEM OF RADIATION BURNS**

Radiation therapy causes damage to the tissues adjacent to those being targeted, which is similar to the
experience of a burn. In terms of herbal therapies, tonics like those used for countering immune suppression and drug toxicity turn out to be of benefit. The general theory is that the spleen function needs to be improved to assure adequate nutrition to help heal the burn (43). For example, Zhang Yin (44) reported on successful treatment of patients with severe burns (not from radiotherapy but from fire), using the following formulas:

Shen Fu Tang

ginseng 16 g  
jujube 5 pieces  
aconite 9 g  
fresh ginger 3 slices.

Modified Yupingfeng San

astragalus 30 g  
aticylodes 9 g  
jujube 5 pieces  
siler 9 g  
wheat 16 g  
longan 16 g

In another report (44), reviewing 1,000 cases of burns treated topically and orally, the decoction applied orally was derived from Ginseng and Astragalus Combination (Buzhong Yiqi Tang), Four Major Herbs Combination (Siwu Tang), and Tang-kuei and Astragalus Combination (Danggui Buxue Tang). In laboratory animal studies (51), it was reported that Ginseng and Astragalus Combination, Minor Bupleurum Combination (Xiao Chaihu Tang), and Shiquan Dabu Tang all offered significant protection from radiation. The herbs were administered for three weeks prior to beginning radiation exposure and continuing throughout radiation exposure. Ginseng, astragalus, licorice, and jujube are common components of these various formulas.

Although clinical reports about treating the oral and esophageal damage due to radiation burns have not appeared in the medical literature, Chinese doctors have mentioned remedies that they believe to be effective. For example, in Prevention and Treatment of Carcinoma in Traditional Chinese Medicine (49), the author, Jia Kun, describes treating a woman with breast cancer who had just undergone radiation therapy. This treatment had left her with symptoms of sore throat, cough, dry mouth, and pain when swallowing food. To his basic formula for treating her overall condition, he added trichosanthes root (or a related herb, bulbopestema, tubeimu) and sophora root (30 grams each). A patent remedy, Bi Yan Ling Pian (nose throat effective tablets) contains Sophora subprostrata, codonopsis, scrophularia, ophiopogon, oldenlandia, and selaginella (shishangbo, an antitumor herb used for lung, nasopharyngeal, and esophageal cancers), and was developed to be used for "acute and chronic pharyngitis and a subsidiary after radiotherapy." According to the package insert (50): "The rate of effectiveness for side effects after radiation therapy, such as nausea, bad appetite, dry and sore throat, nose bleeding, and oral erosion is 89%.

In an attempt to ward off side effects of radiation therapy, the following formula was mentioned in Treatment of Cancer by Integrated Chinese-Western Medicine for use starting 3-4 days prior to initiating the radiation treatments:

astragalus 15-30 g  
aticylodes 9 g  
Sophora subprostrata 15-30 g  
rehmanna 15-30 g  
forsythia 15-30 g
isatis root 15-30 g
scrophularia 9 g
trichosanthes fruit 15-30 g
belamcanda 9-15 g
shen-chu 15-30 g

Most of the herbs in this formula are aimed at treating inflammation of the lungs, esophagus, and oral cavity. Shen-chu helps protect against loss of appetite.

**DO HERBS THAT COUNTER SIDE EFFECTS ALSO COUNTER DESIRED EFFECTS?**

A concern raised by medical doctors regarding the use of herbs to counter side effects is whether or not the desired effects of the therapies will also be countered. For example, will the herb formula that prevents leukopenia (bone marrow inhibition) induced by the drug also prevent the drug from inhibiting the tumors?

In general, this is not a problem, as revealed by the clinical outcomes reported by the Chinese: not only are the side effects lessened, but the survival rates improve. To understand how this works, the situation can be illustrated by the use of immune-enhancing polysaccharides to counter the leukopenia induced by cancer therapies. The action of the polysaccharides is to maximize the effectiveness of the bone-marrow production of white blood cells, in much the way a medical doctor might apply a stem cell growth stimulating factor (e.g., Nupigen). The mechanism of action is via stimulation of various immune system components, through a cascade of events that take place within the immune system. The polysaccharides do not stimulate other cell lines, nor do they protect bone marrow cells by directly blocking the entrance of cancer drugs into cells. Therefore, while the polysaccharides will be able to partially counteract the bone marrow suppression induced by chemotherapy (or radiation), they will not counteract the suppression of or damage to cancer cells.

On the other hand, there are some Western medical interventions (not for cancer) relying on immune-suppressive drugs, such as cyclophosphamide, that are specifically intended to stop bone marrow production of immune cells. In that case, the use of the immune-enhancing polysaccharides is inappropriate, as it can counteract the intended action of the drugs (e.g., halting immune attack against grafted cells).

Chinese herbs applied to counteract side effects are usually aimed at improving the functional status of the organs, tissues, or cells that are subject to the side effects and are not aimed at reducing the absorption, distribution, or utilization of the drug. Thus, as another example, herbal therapies used to overcome the nauseant action of cancer drugs are aimed at rectifying the functions and condition of the stomach, but are not aimed at impairing the overall function of the drug towards inhibiting rapidly growing cells.

An example of an area of concern that can be addressed relatively easily is the use of antioxidant herbs, herbal components, and vitamins in patients undertaking radiation therapy. Some recent popular publications have cautioned patients to avoid this approach, as it might impair the ability of radiation to destroy the tumor cells. Radiation has two major effects at the target site:

1. In the zone of highest density of radiation, the cells are either literally torn up by the energy of the radiation, which smashes into critical components, notably the large DNA strands, or they are sufficiently damaged that the cell recognizes itself as being unrepairable and apoptosis (programmed cell death) is initiated.

2. As the distance from the focus of radiation increases, the total destruction of cells diminishes and the main effect of radiation is generation of damaged molecules, many of them in the state of free radicals (oxidized state). These free radicals can lead to the ultimate destruction of the cells over time (within hours, or even days), though they are present in large numbers only for a few
minutes, since they are highly reactive molecules.

When conducted properly, radiation is focused on the tumor mass and its cells are either immediately damaged beyond repair (#1 above), or eventually damaged beyond repair (#2 above). Radiation is usually administered several times to assure that none of the tumor cells escape destruction.

Antioxidants, when administered in high dosages, enhance the natural antioxidant system that the body maintains. This enhancement is not enough to counteract the massive number of free radicals generated at the tumor site, but it is enough to help counteract the small numbers of extra free radicals at a distance from the tumor site, namely, in the healthy cells that receive unintended but unavoidable collateral damage (by either being in the path of radiation in front of or behind the tumor, or by being to the side of the radiation path, where the peripheral rays and deflected rays pass). Thus, antioxidants can reduce some of the side effects of the radiation, but they would be woefully inadequate to stop the radiation effects at the focus of the treatment, the tumor, even if that were the aim of their use.

One may get the impression that antioxidants can protect all cells from radiation if one examines certain animal studies, but these studies are not indicative of what happens under directed radiation to the tumors. If animals are irradiated (full body irradiation is given), those that receive antioxidants (and other herbs with beneficial properties) will survive better than those who do not receive these substances. However, these experiments are not performed with the tumor-cell-smashing focused radiation, but with a lower level radiation more similar to that experienced by the healthy tissues outside the primary focus of radiation. This whole body radiation can be lethal, but antioxidants protect against the outcome up to certain high levels of radiation.

In a literature review and summary of natural health care interventions to aid cancer patients, Paul Reilly (63) mentions several instances where substances reduce the adverse actions of cancer therapies while preserving the desired actions. These favorable combinations with drugs included the antioxidant vitamins A, C, and E with adriamycin and the antioxidant glutathione with cisplatin. Favorable combinations with radiation therapy included vitamin A, beta carotene, and vitamin E.

Thus, one must consider carefully the target of the drugs (or other therapy) and the nature of the herbal effects in order to understand the potential of herbs to counter any intended effect of the drugs. According to the Chinese clinical reports, patients receiving herbs with chemotherapy or radiation not only experience fewer side effects, but also have better short-term and long-term outcomes in relation to their disease.

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APPENDIX 1: Survey of Herb Side Effects

Since the treatment of drug side effects with Chinese herbs began with the treatment of herb side effects, a brief review of the related concerns is warranted. There are three basic types of problems:

1. There are adverse reactions to the herbs that are essentially non-toxic. Such adverse reactions may not affect everyone, but herbal formulations may take into account the tendency for reactions to occur.

2. There are the toxic herbs that are of concern to any potential users. These herbs are not used in the Western practice of Chinese medicine, but have long been used in China.

3. There are cases where herbs that are otherwise non-toxic produce severe reactions in a small number of users. These are unexpected reactions, but they can occur. Such reactions may also be more prevalent when new methods of administration are developed, such as intravenous injection of herbal extracts or ingestion of highly concentrated active constituents of herbs.

An outline of the principal side effects of commonly-used herbs that can have adverse reactions without being specifically toxic was presented by Toyohiko Kikutani in the International Journal of Oriental Medicine (4). With some modifications of his commentaries and some additions, the problems are:

1. Surface-relieving herbs and formulas may produce itching skin or rashes as the response to dilation of the surface blood vessels and the presence of essential oils with irritant actions. According to Kikutani, herbs that are potentially problematic include cinnamon twig, ma-huang, chiang-huo, tu-huo, siler, schizonepeta, and perilla leaf. Surface-relieving herbs, such as siler and schizonepeta, are frequently used in formulas to treat skin rashes. The dilating action of these
herbs is often compensated for by including peony in the formulas, as often mentioned in relation to the elegant formulation principle behind Cinnamon Combination (Guizhi Tang). Fire-purging herbs included in several prescriptions may inhibit the skin rashes, and sweet herbs, especially the combination of jujube and licorice (components of Cinnamon Combination), also limit the adverse effects of surface relievers.

2. Diuretic herbs may induce frequent urination, and may lead to constipation by removing water from the intestines. The main diuretic herbs are hoelen, polyporus, stephania, atractylodes, and alisma. Such effects are counter-balanced by including herbs to recirculate the fluids (e.g., cinnamon twig in Hoelen Five Formula, Wuling San), or by including an astringent herb (e.g., schizandra) to limit excretion and to help generate fluids. Constipation is avoided by including moistening herbs (e.g., apricot seed) or mild laxatives (e.g., gardenia).

3. Blood-vitalizing herbs may cause increased uterine bleeding, including bleeding between menstrual periods; this is especially true when there are fibroids present, which are to be treated by blood-vitalizing herbs. The herbs moutan, persica, red peony, carthamus, rhubarb, typhus, and tang-kuei are often found in the blood-vitalizing prescriptions and may contribute to such side effects. Blood-vitalizing herbs are often used to treat bleeding, following the theory that blood stasis leads to bleeding, but hemostatic herbs (e.g., agrimony, thistle) are included in many of the prescriptions to avoid the undesired increase in bleeding.

4. Blood-nourishing formulas may cause loss of appetite, nausea, loose stool, or vomiting. Tang-kuei, cnidium, zizyphus, and cooked rehmannia are the herbs that are most often the cause of such problems due to the presence of oily compounds. This effect can be countered, in some cases, by inclusion of aromatic herbs such as aquilaria, cardamon, citrus, or ginger. At the Ming Dynasty pharmacy, Tong Ren Tang, that still operates in Beijing, cardamon is automatically added to most formulas containing cooked rehmannia, even if not specified in the doctor's prescription.

5. Purgative formulas may cause abdominal cramping and loose stool or diarrhea. Rhubarb is the main purgative of Chinese medicine; senna leaf, aloe, and prunus are alternative purgatives. However, gardenia, persica, apricot seed, and mirabilitum, as well as some others herbs (e.g., bupleurum used in doses of 20 grams or more; ho-shou-wu; hu-chang; and cistanche) might be used for various purposes without intending to be purgative, yet produce an unintended purgative action and accompanying side effect of intestinal discomfort. Purgative effects are ameliorated by adding warming herbs that disperse moisture (e.g., including dry ginger or aconite with rhubarb).

6. Fire-purging formulas may cause loss of appetite and loose stool. Coptis, gardenia, forsythia, gentiana, and raw rehmannia are examples of ingredients that may produce this effect. Gentiana is of particular concern to Chinese physicians because this herb frequently causes reactions in patients with various deficiency syndromes. As an example of an herbal therapy disrupting the stomach function, dichroa, an herb traditionally used to treat malaria (and recently to treat giardia), tends to cause nausea and even vomiting in nearly all users. Therefore, antinauseant herbs are combined with it. According to Pharmacology and Applications of Chinese Materia Medica (5), the emetic effect may be reduced by "using it with pinellia, pogostemon, or citrus." These are herbs traditionally used to open and settle the stomach. It is reported that by combining dichroa with pogostemon, the incidence of nausea and vomiting on the first day of medication was reduced to 40% and that this incidence gradually decreased over several days so that only 20% of patients reported these reactions. It should be noted that most of the heat-clearing herbs classified in the subdivision of removing toxins (herbs used in cancer therapies, for snake bites, and viral infections) usually do not produce this adverse reaction. As mentioned above, stomach-protecting herbs, such as oryza and licorice may be used to protect the stomach from cold natured herbs; a small amount of warming herbs may compensate the extreme cold nature of the other ingredients.
7. Chill-dispelling and yang-tonifying formulas may cause feverish feeling, headache, nose bleeds, palpitations, sensation of pressure in the chest, or hyperactivity. Cinnamon bark, aconite, and evodia are examples of chill-dispelling herbs that may be problematic. Coptis is added to some prescriptions to counter these effects. While problems may be avoided by proper diagnosis, imbalance in the kidney system can lead to unpredictable responses to yang tonic herbs (e.g., deer antler, morinda, or curculigo). This is usually compensated by inclusion of a large dose of cooked rehmannia (or mixed cooked and raw rehmannia), which will prevent the kidney yang from becoming overly agitated.

8. Minerals may cause gastric discomfort, loss of appetite, and (with long-term use) aching of muscles. Materials high in minerals, such as seaweeds, sea shells, and dragon bone, as well as mineral agents (e.g., gypsum, fluorite, magnetite) may also inhibit stomach function (by reducing stomach acid) and cause some disturbance when used in high dosage. This problem may be countered, to some extent, by inclusion of sprouted wheat or barley (malt), licorice (not suggested for seaweeds, however), or warm spicy herbs, such as raphanus or sinapis. Gallus is reported to help restore natural levels of stomach acid production.

9. Ma-huang formulas may produce tachycardia, insomnia, increased blood pressure, or excessive sweating. Persons who are hypersensitive to the herb may experience such responses with relatively low doses. In addition, herbs with cardiotonic glycosides, such as periploca and cynanchum, can cause heart palpitations or arrhythmias (an effect that is a toxic reaction if large enough amounts are used). In general, avoidance of the herb is the rule, though counterbalancing effects of other herbs, such as coptis, are a potential solution.

10. Saponin-rich formulas may cause headaches, nervousness, spontaneous bleeding, and changes in appetite. Bupleurum, platycodon, and ginseng are examples of saponin-rich herbs. Also, several of the folk remedies for arthritis used in China contain herbs high in saponins. These problems are traditionally interpreted as the result of blood deficiency and rising yang, which is compensated by incorporating blood nourishing herbs (e.g., tang-kuei and peony), and by including herbs that settle the yang (e.g., dragon bone).

11. Polysaccharide-rich formulas may cause abdominal bloating, flatulence, and mushy or loose stool. Astragalus and ganoderma may present this problem. The concern that qi-tonic herbs may cause a stagnancy syndrome in individuals with poor spreading of central qi is largely attributable to experience with the use of astragalus. Further, the polysaccharides in some members of the Leguminosae, such as licorice, albizzia, erythrina, soja, and dolichos, might cause similar problems. Citrus, ginger, cardamon, or other spicy herbs may help counteract such reactions.

12. Formulas with large amounts of licorice can cause sodium/potassium imbalance, resulting in edema and heart palpitations or arrhythmias. Glycyrrhizin in licorice promotes adrenal production of aldosterone, which produces this effect. Nonetheless, processed licorice, used in large doses in the Chinese clinical application of Baked Licorice Combination (Zhigancao Tang) is prescribed in the treatment of heart irregularities. Sodium/potassium imbalance might also occur with therapies that produce a diuretic or laxative effect. For example, senna-leaf based weight-loss formulas can have this adverse reaction. High dosage of licorice and strong laxative therapies should be used for a limited duration. Nonetheless, kidney warming formulas have been used by Chinese physicians to compensate for high dose licorice when its use is deemed important.

13. Hormone-influencing formulas can cause changes in the menstrual cycle; ginseng, tang-kuei, deer antler, epimedium, and bupleurum may have such influences. Changes in length of the cycle, amount of bleeding, the possibility of mid-cycle bleeding, or changes in fertility might be associated with their use. While these herbs can be used in formulas intended to alter the menstrual cycle, they can also be used in treatments for which no menstrual changes are expected or desired. Some women who recently entered menopause may resume menstrual bleeding as a
result of using tonic herb formulas. These effects are not necessarily problematic, but rather need to be understood so that the changes that occur are not surprising or disturbing. According to traditional thinking, if the formulation strategy is correct, including proper consideration of yin/yang balancing, then the menstrual cycle will remain regular.

14. Some herbs may cause changes in blood-sugar levels during the first hour or two after ingestion, producing a feeling of dizziness, hunger, or other sensations. Xanthium, platycodon, bupleurum, and morus leaf are examples of herbs not usually used to treat diabetes (where blood-sugar lowering is a desired action) that may produce a reduction in blood sugar. This problem is usually corrected by adjusting the time of taking herbs in relation to meals, and, if necessary, adjusting the diet to compensate.

15. Materials containing tough gelatinous substances, as found in turtle and tortoise shell, deer antler, donkey skin (gelatin), and fish swim bladder, may cause lower-intestinal cramping when imbalances of intestinal flora and weak digestion permit adverse bacterial digestion of the materials to occur in the intestines. This is compensated by treating spleen/stomach deficiency, gallbladder stagnation, and qi disturbances simultaneously with administering the herbs of concern.

Wang Yunmo and Hu Juanyue (33) surveyed the recent Chinese medical literature and reported on toxicity and side effects of Chinese herbs. They pointed out that:

Generally, toxic actions are related to overdosage, or overly long period of drug administration, due to accumulation. Anaphylaxis is associated with allergic constitution. Poisoning and hypersensitivity is a quantitative action, while allergy is a qualitative sensitive effect. People with idiosyncrasy may show urticaria, pyrexia, and rashes in spite of small dosage, even a little amount.

Combining laboratory animal studies with some medical reports of adverse effects, the report detailed potential toxic effects of herbs in terms of their contents (alkaloids, glycosides, proteins, etc.); by their site of toxic action (nervous system, respiratory system, digestive system, cardiovascular system, urinary system); and by allergic reactions (including anaphylaxis). As for treatment of such reactions, the authors relied mainly on Western medical techniques. They also advised taking care in prescribing herbs, including:

1. Before administration, understand clearly the properties, actions, dosage, and the side effects of the Chinese medicinal herbs. A doctor's duty is first to make a prescription, and then to provide patients with proper directions.

2. Prescribe according to clinical signs and symptoms, avoid incorrect use, point out the mistaken idea that there is no toxicity and are no side effects from Chinese medicinal herbs. It should be remembered that they can be toxic, especially their active components [when given in isolation and in doses larger than present in crude herb preparations].

3. Don't use any popular prescription without doctor's direction.

4. Ask the allergic history of the patients and the members of their family before administration, especially when using Chinese medicinal herbs via injection.

5. Take care of intolerance signs and idiosyncratic reactions to the herbal drugs used by the patients. The drug should be stopped when the phenomena of itching, fever, erythema, shortness of breath, asthma, and general discomfort have happened.

6. After coming to an understanding of which herb caused the side effects in the patient, one should stop administering the herb or its compound prescriptions.

7. Make use of appropriate therapeutic procedures as soon as acute poisoning or anaphylaxis appears.
APPENDIX 2: Possible Reactions Between Herbs and Drugs

In the Chinese medical literature, reports of adverse interactions between drugs and herbs are not found even though there appears to be openness in the reporting of adverse reactions to herbs themselves. Yet, it is well-established that some pharmaceutical products should not be combined with other pharmaceutical products due to production of adverse effects, and that mixing certain pharmaceuticals with commonly-consumed substances can also have a negative impact on the drug therapy. As examples of the latter:

- Tetracycline should not be taken with milk or milk products because the casein in milk binds the tetracycline and reduces its absorption. Digoxin should not be taken with high fiber foods, which interfere with its absorption.
- Several vegetables, especially green vegetables, should not be taken (or, the amount consumed should not be changed) by patients undergoing anti-coagulation therapy because the vegetables contain varying amounts of vitamin K, a coagulation promoter.
- Alcohol should not be consumed with many drugs, because it alters the drug metabolism or action. In some cases, severe liver toxicity reactions can occur when alcohol is combined with drugs.
- Grapefruit should not be consumed with many drugs (e.g., Seldane), because its flavonoid (naringenin, the same one found in drynaria) inhibits a drug-metabolizing enzyme, thus allowing the level of certain drugs in the blood to attain higher levels and remain high longer (which increases potential for toxic effects of some drugs).

There are also concerns raised by practitioners of traditional Chinese medicine, about interactions between herbs and commonly ingested substances:

- Some herbs are not to be cooked in an iron pot, presumably because the iron that is leached from the pot during cooking inhibits the herb's actions by binding to active constituents and rendering them less absorbable.
- Some herbs are not to be taken with sour-tasting substances, particularly vinegar, because it would impair the herb's actions, possibly by adjusting the functional relationship, as described in the tradition of Chinese medicine, between the liver and the spleen.

The question naturally arises whether or not herbs, which contain chemical substances not inherently different than those comprising pharmaceuticals and those found in foods, might on occasion yield undesired interactions with drugs, with each other, or with various commonly consumed substances.

There are four basic types of problems that might be encountered:

1. Interaction in the gastrointestinal system prior to absorption. The main concern is binding of a drug to an herb substance, thereby rendering the drug less absorbable. It has been suggested that ginger counteracts some cases of nausea because its oleoresin binds up toxins in the digestive system that produce the reaction of nausea. These resins could potentially bind to pharmaceuticals. Also, it has been shown that some herbs inhibit the absorption of cholesterol-presumably by complexing with the cholesterol and reducing its ability pass through the boundaries of the gastro-intestinal tract. Drugs having an oily nature or structure similar to cholesterol might similarly be bound and have their absorption or absorption rate reduced. It has been proposed that one of the ways in which licorice can reduce aconite toxicity is by binding with aconitine and making it less absorbable or active. Tannins, a component of ordinary tea and some astringent Chinese herbs, can bind up alkaloids to make them less available. The potential for inhibiting absorption of drugs is dependent on the dosage of herbs (a small dose could only bind a little of the drug, a large dose could bind more) and the temporal proximity of the ingestion...
of the two materials (the longer the separation between taking the drug and another substance, the less chance of any binding). In the case of tetracycline and binding to casein in milk, patients are instructed not to consume milk at the same time or in close proximity of the time when tetracycline is ingested, but it is not necessary to avoid consuming milk or milk-based products at other times. In a few cases, herbal ingredients might make a drug more easily absorbed, thus raising the potential for toxic reactions to the drug. It is known, for example, the flavonoids enhance the absorption of vitamin C and, in turn, vitamin C enhances the absorption of iron; a similar situation could exist with certain drugs. Although the incidence of absorption problems from herbs is likely to be low, one could avoid this interaction by taking herbs and drugs at least an hour apart.

2. Alteration of drug metabolizing enzymes. Drugs (and herbs) are often eliminated from the system by the action of enzyme systems that break them down into components that are more easily excreted. If the enzyme system is inhibited, the drug will remain in the body longer, and thus its effects will be greater (with repeated doses of drugs, the toxicity of the drug could become a problem). It has been shown in laboratory experiments (34) that some Chinese herbs inhibit the drug metabolizing enzymes (on much rarer occasions, an herb is found to stimulate the enzymes). The effect of those herbs (when used in a dosage that is sufficient to significantly affect the enzyme activity) on drugs metabolized by those enzymes is to make it possible to use a lower dosage of the drug and still get the same level of effect. This is a potential benefit. It has been reported in the Japanese literature, for example, that use of bupleurum formulas can reduce the dosage of corticosteroids necessary to treat various inflammatory diseases—inhbition of drug metabolizing enzymes might be the mechanism by which this is accomplished (it is also possible, however, that anti-inflammatory actions of the herbs make the requirement for steroids lower). Similarly, it has been suggested that rehmannia-based formulas can reduce the amount of insulin needed by diabetics; the mode of action has not been determined, but might include longer survival of insulin in the blood stream. The alteration of drug-metabolizing enzymes probably occurs only with high-dosage herb therapies. Individuals suffering from liver or kidney diseases may be more susceptible to such problems since the enzyme systems and elimination mechanisms may already be inhibited. To avoid this problem, when using high dosage forms of herbs (decoctions or isolated active constituents), one should introduce the herbs gradually, building up the dosage over time, and closely observing any changes that occur.

3. Target-cell binding. Some drugs act by binding to surface components of cells, an action which then induces an alteration of cellular functions. If an herb component binds to the same surface component without having the same effect on cellular functions, then it could reduce the effectiveness of the drug therapy by preventing the drug from having its intended effect. The technique of blocking "receptor" sites on a cell surface is an important strategy in many new drug therapies, but unintentional blocking by ingestion of herbs could limit the effect of some drugs. One of the proposed mechanisms of action of the isoflavones (such as those found in soy beans) is that they influence some of the estrogen receptors on cell surfaces. Target-binding effects are strictly dose dependent and very specific for the drug in question. It is difficult to know whether or not a problem can arise, but the problem should be limited to the high dosage forms of herbs.

4. Alternative pathways. If a drug therapy has a particular end result (physiologic action) produced by one mechanism, and the herb therapy used at the same time produces the same physiologic action but by a different mechanism, the total effect could be greater than that desired. This enhanced or "synergistic" action would allow a reduction of the amount of drug ingested, but if the drug dose were not reduced, side effects might be generated. An example of a potential problem (theoretical, not yet reported) would be the ingestion of an anti-coagulant drug and simultaneous ingestion of a blood-vitalizing herb formula. If the two act by different mechanisms, the reduction of clotting could be sufficient to render the individual susceptible to spontaneous
bleeding (if they acted by the same mechanism, the drug effect might be so much greater than the herb effect that the herb would appear to cause no effect at all, though additive action would still be possible). Licorice, which can lead to increased potassium secretion might enhance the potassium excreting action of certain diuretic drugs (e.g., Lasix), resulting in irregular heart rhythm. Thus, one might avoid matching a drug and an herb therapy that have a very similar specific outcome, unless one is seeking to increase the intensity of the outcome.

While no one may actually suffer from a problem of drug and herb interaction, the potential is there and might be increased with the continued introduction of both new herbs and new drugs. Prudent measures to avoid potential problems would include:

1. taking the herbs and drugs at different times so that they don't mix before absorption;
2. starting out with low to moderate herb dosage to allow time to check for potential interactions and to make suitable adjustments if deemed necessary after about one week of therapy;
3. using some caution in administering herb formulas that have a focused effect (as opposed to a very broad action obtained from some combinations) that is the same as the drug effect.

Chinese herbalists routinely combine a huge variety of herbs together; at present there does not appear to be any reason to avoid mixing together any combination deemed suitable for the individual being treated. According to an ancient concept, there are a few herb incompatibilities (when the two herbs are combined, the results are toxic). However, recent testing has failed to show that there is any significant adverse effect from the combination of those herbs. Laboratory work with a number of animals and single-cell organisms has not revealed any toxicity or other problem when the purported incompatibilities are combined. It may be assumed that the doctrine of incompatible herbs arose from a few observations of negative reactions of patients to herbal formulas with a mistaken conclusion as to the cause. Once incompatibilities were reported in the medical literature, doctors generally avoided using the combination (which might have revealed its lack of toxicity) and simply recited the cautionary statements. The majority of incompatibilities involved at least one herb that had toxic effects, and it could have been the effect of that herb in one or more individuals that gave rise to the concern about the combination of herbs.

Because of the diversity of active components in an herb formula, and the relatively low dosage of each individual component compared to the dosage of a chemical in a pharmaceutical product, the potential problems of herb/drug interactions are usually not a serious problem.

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