Utilizing Traditional Chinese Herbal Medicine to Treat Infections

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Significance of the Subject

We are aware from ancient literature that physicians have been treating people with infections since the earliest recorded time; this awareness comes about because we know the characteristics of infectious diseases and can detect those manifestations in the brief depictions that are found in fragmentary old writings. While we presume that recommended herbal treatments found in this early literature had some level of success as the reason for the continued use of the therapies over time, we don't have any clear indications of how successful these efforts were, nor do we know the relative effectiveness of particular anti-infection strategies unless we now evaluate them by accepted modern investigative methods, including pharmacology studies and controlled clinical trials.

The basic understanding of pathogens, such as bacteria, and confirming the activity of bacteria-inhibiting substances, such as arsenic compounds, began in the latter part of the 19th century. The ability to inhibit infections with modern drug therapies advanced enormously a few decades later with the introduction of the naturally occurring penicillin as an antibacterial agent in 1942 and the synthetically produced idoxuridine as an antiviral in 1962. Most of us involved with medicine have grown up in the era of ready availability of drugs for infections. Taking these pharmaceuticals for granted, we may not appreciate just how recently they came to be relied upon. New drug development has been systematized since the 1960s, both in terms of having precise three dimensional chemical structure visualization and organizing the bench-to-clinic staging, so that there is an ongoing introduction of new agents, especially among the antivirals. One example of recent progress was the approval of the combination drug ledipasvir with sofosbuvir which yields a very high rate for curing hepatitis C (genotype 1), a disease that became prevalent over the past forty years; more recently, glecaprevir plus pibrentasvir has been approved for six genotypes of hepatitis C with a similarly high cure rate. Although several new antibiotics were introduced, such as delafloxacin, a fluroquinolone joining nearly two dozen other quinolone antibiotics, no new class of those drugs has been discovered in the past 30 years, frustrating those who would like to see a leap in progress.

Prior to medical antibiotics and antivirals, complex natural products were necessarily relied upon; these were derived mainly from plants, but also included animal and mineral substances. The organisms involved in the infection, such as bacteria and amoebas, as well as non-organism entities, mainly viruses, were unknown and undetectable during the historical development of these therapies. Therefore, the treatments were based on a different kind of diagnostic approach and a therapeutic method that fit the interpretation of what was being observed. Partly as a result of the rapid development in the modern understanding of infectious agents and drug therapies that target them, there has been a surge of interest in these kinds of natural treatments that arose during the pre-drug era. Thus, for example, garilic, the widely used food flavoring, became heavily promoted for antibacterial activity, as did several other spices, though to a lesser extent. At the time of this writing, a company that provides chickens for food advertises that their farmers don't apply antibiotic drugs while raising the chickens because they have learned to put oregano and thyme extract in the water the chickens drink, thus providing sufficient antibiotic activity. This kind of alternative is appreciated because of its non-synthetic nature and low incidence of adverse reactions, but especially in light of concerns that excessive reliance on antibiotic drugs leads to development of drug resistant strains.

One of the effective plant drugs for infection that was identified in recent years is artemisinin, a semi-synthetic compound derived originally from the Chinese herb *qinghao* (*Artemisia annua*), which effectively treats malaria, a protozoal disease, and has often used when there is drug resistant malaria. Artemisinin is available also as an herbal supplement, not just a prescription drug. Interest in plant based treatments for infections remains strong for treating cases where drug therapy is only partly effective; Lyme Disease appears to be such a case. Chinese herbs are the subject of this paper; investigations across the globe have stimulated interest in natural treatments for infections from other traditions as well.

Brief Look at the Historical Basis of Infection Treatment by Chinese Herbs

Treatment of infections was one of the essential stimulants to the development of traditional Chinese medicine (TCM). The first Chinese text of herbal formulas belonging to an ongoing tradition was the ***Shang Han Lun*** (ca 200 A.D.; edited at times until about 1100 A.D.). It depicts an epidemic disease with rapidly changing symptoms. Efforts to identify the disease, called *shang han*, have not been successful, though for some time it was thought that several lines of text might refer to cholera; there are symptom patterns described, however, that correspond to malaria and to other diseases. The underlying concept conveyed in this text was that some kind of "evil" influence got into the body and had to be forced out, otherwise it would penetrate further, from surface to interior, and cause more serious damage, with a different herbal strategy for the stages of deeper penetration. Following this idea of dispelling the adverse influence, three primary methods of herbal therapy were sweating, vomiting, and laxation: the pathogen was thought to leave along with the forced emission of bodily fluids. Sometimes, however, the pathogenic influence was fought by countering its *nature*, that is, by addressing its characteristics depicted by common qualities, such as cold and heat, dampness and dryness. The ***Shang Han Lun***, which we have in translation to examine (1) especially dealt with diseases that initially produced fever (sometimes alternatively with chills) but ultimately caused coldness at the interior. Consequently, strongly warming therapies were used in response to the appearance of the symptoms, along with or instead of trying expel the pathogenic influence by inducing perspiration. As a secondary result of coldness, dampness might accumulate or fluid might freely be excreted from the body, thus indicating a lack of control over moisture. Sometimes the dampness would manifest in the form of phlegm accumulation. Redirecting fluid was thus deemed a significant therapeutic target. The table below illustrates herbs used for this kind of epidemic disease revealed in the ancient text. The herbs need not have anti-infection properties in order to alleviate symptoms or help terminate the disease progression, though modern approach to epidemic disease would typically involve an infection-inhibiting therapy if available. None of the herbs listed here are regarded as strong anti-infection agents, even though many of them remain in use as *components* of formulas that are aimed at treating infections.

Table 1. Examples of herbs used for expulsion, warming, and drying dampness in the ***Shang Han Lun***. "Dispel wind" is the terminology related to expelling pathogenic influence through perspiration. Herbs to induce vomiting were less frequently used and thus not included in this table.

Herb Name	Pinyin	Scientific Name	Part	Category
Aconite	*fuzi*	*Aconitum charmichaeli*	root	dispel chill
Alisma	*zexie*	*Alisma aquatica- plantago*	rhizome	remove moisture
Asarum	*xixin*	*Asarum sieboldii*	rhizome	dispel wind-chill
Atractylodes	*baizhu*	*Atractylodes macrocephalla*	rhizome	tonify qi, remove moisture
Atractylodes, red	*cangzhu*	*Atractylodes lancea*	rhizome	resolve wetness
Cinnamon twig	*guizhi*	*Cinnamomum cassia*	twig	dispel wind-chill
Evodia	*wuzhuyu*	*Evodia rutaecarpa*	fruit	dispel chill
Ginger (dry)	*ganjiang*	*Zingiberis officinale*	rhizome	dispel chill
Ginger (fresh)	*shengjiang*	*Zingiberis officinale*	rhizome	dispel wind-chill
Ginseng	*renshen*	*Panax ginseng*	root	warm center
Hoelen	*fuling*	*Poria cocos*	whole	remove moisture
Ma-huang	*mahuang*	*Ephedra sinensis*	stem	dispel wind-chill
Magnolia bark	*houpo*	*Magnolia obovata*	bark	fragrant, resolve wetness
Mirabilitum	*mangxiao*	Magnesium or sodium sulfate	mineral	purgative
Pinellia	*banxia*	*Pinellia ternata*	tuber	resolve cold phlegm
Platycodon	*jiegeng*	*Platycodon grandiflorum*	root	resolve cold phlegm
Polyporus	*zhuling*	*Polyporus umbellatus*	whole	remove moisture
Rhubarb	*dahuang*	*Rheum palmatum*	rhizome	purgative

After many centuries of focus on diseases that were considered to lead to coldness, and with increasing reliance on herbs to counteract cold to the point that leading physicians thought they were being used indiscriminately and overheating some patients, there came a shift in thinking that may have also been stimulated by an actual change in prevalent diseases. The treatments became focused on diseases which generated internal heat, so formulations with many cold natured herbs were then developed (2). The accumulation of dampness could still be a secondary effect, with application of herbs said to alleviate damp-heat (or clear heat, dry damp). The following table illustrates herbs used for these purposes.

Table 2. Examples of herbs used frequently for clearing heat and damp-heat in the attempt to alleviate heat syndromes, as recorded in formula texts of the 16th to 19th centuries. Both rhubarb and mirabilitum, listed in Table 1 as purgatives, are also commonly used in the heat clearing therapies, but are not included in this table to avoid replication.

Herb Name	Pinyin	Scientific Name	Part	Category
Akebia	*mutong*	*Akebia quinata*	stem	remove moisture, heat
Anemarrhena	*zhimu*	*Anemarrhena aspholoides*	rhizome	clear heat
Bamboo	*zhuru*	*Phyllostachys nigra*	stem/leaf	resolve hot phlegm
Coix	*yiyiren*	*Coix lacryma-jobi*	seed	remove moisture, heat
Coptis	*huanglian*	*Coptis chinensis*	rhizome	clear heat, dry damp
Forsythia	*lianqiao*	*Forsythia suspensa*	fruit	clear heat
Gardenia	*zhizi* or *shanzhizi*	*Gardenia jasminoides*	fruit	clear heat, damp-heat
Gentiana	*longdancao*	*Gentiana scabra*	root	clear heat, damp-heat
Gypsum	*shigao*	Gypsum	mineral	clear heat
Lonicera	*jinyinhua*	*Lonicera japonica*	flower	clear heat
Lophatherum	*danzhuye*	*Lophatherum gracile*	leaf	clear heat
Mentha	*bohe*	*Mentha averensis*	tops	dispel wind-heat
Morus leaf	*sangye*	*Morus alba*	leaf	dispel wind-heat
Phellodendron	*huangbai*	*Phellodendron amurense*	bark	clear heat, dry damp
Rehmannia (raw)	*shengdi*	*Rehmannia glutinosa*	root	clear heat, cool blood
Scute	*huangqin*	*Scutellaria baicalensis*	root	clear heat, dry damp
Soja	*dandouchi*	*Glycine max*	seed	dispel wind-heat
Talc	*huashi*	Talc	mineral	remove moisture, heat

The number and variety of herbs used during the later centuries, such as for the treatment of heat diseases starting around the 16th century, was much larger than the collection available in early centuries (such as when the ***Shang Han Lun*** was written), but the second table is organized to present an equal number of example ingredients as in the first. Many of the herbs in table 2 were also used in the ***Shang Han Lun***, but less frequently, being applied for specific manifestations of the disease. In the second table, there are some herbs that are today deemed especially valuable for inhibiting infections: coptis, scute, phellodendron, forsythia, lonicera, gentiana, and gardenia. Still, the majority of the herbs listed in the table or otherwise frequently used at the time are not considered by modern evaluation methods to be especially potent inhibitors of bacteria, viruses, or other organisms.

This abbreviated rendition of the development of TCM for epidemic and infectious disease points to the key factors the physicians took into consideration: dispelling evil influences (by three major routes) or counteracting them and managing the symptoms. The counteraction and symptom alleviation was particularly in terms of cold, heat, and dampness. Looking back upon the ancient formulas, it is possible to analyze contributions of some individual ingredients to the therapeutic action, such as cough alleviating herb when the infectious disorder generated coughing as a symptom. Direct anti-pathogenic action (inhibiting bacterial or viral activity or reproduction) doesn't seem to have been common: if these treatments worked to shorten the infection duration and severity, the results must have largely been due to physiological adjustments to the disease process, perhaps including enhancing the immunological attack.

The idea of a transmissible agent was beginning to emerge in 19th Century China by observation of epidemic diseases, yet it was western visitors who took the lead. They could replace the concepts of evil influence with details attained by microscope: that there were micro-organisms that convey disease from one person to another, usually by close personal contact. In the 1880s, Louis Pasteur indicated that disease transmission could be prevented by certain precautionary measures, and adopting these methods westerners in China were able to control epidemics via quarantine and by hygienic practices. Their efforts seemed more effective than what the Chinese doctors were doing with their medical therapies to treat those who became ill. Importantly, a tenet of Chinese medicine was that the "superior physician prevents disease, while the ordinary physician treats it." While this aphorism often implied successful treatment of early stage of disease rather than actual primary prevention (as we do today with vaccines), the ability of the western doctors to diminish the spread of an epidemic pointed to a superior approach, degrading the standing of Chinese medicine.

Traditional Chinese medicine and western medicine were divergent methods in China during the 19th century and into the early 20th century, when modern medicine took the lead. But, beginning in the 1950s the two distinctive approaches to health care were combined, or at least put together, mainly as a consequence of political, cultural, and practical considerations. Since modern medicine had shown that infections—as newly defined to involve microorganisms and viruses—were responsible for many diseases, Chinese medicine doctors and researchers began to contemplate finding herbs that could inhibit the infections. A focus on this work was delayed by continued reliance on using traditional formulas. It was not until 1997 that a book was published and translated to English about using traditional Chinese treatment methods for infectious diseases (3). Still, that text presented traditional-style remedies with little or no research basis for the indicated applications; the primary contribution of modern methodology was in identifying the names of the diseases. Unfortunately, the translation of traditional herb names was often very poor and the identity of ingredients not always clear. Many of the formulas were based on herbs that had developed a broad reputation for efficacy even if not confirmed by controlled trials. The book covered seven subjects: influenza, common cold, measles, mumps, herpes zoster, viral encephalitis, and viral hepatitis.

The Trajectory of Modern Efforts

Western influence in China initiated a process of research into traditional herbal remedies during the first half of the twentieth century; during this time, for example, ephedrine was isolated from the Chinese herb *mahuang* and became a widely used drug of modern medicine in the treatment of asthma. In the second half of that century this research effort was greatly stimulated by government policy and increasing understanding of how to carry out research projects. The work was not limited to China, but also took place in other Asian countries, such as Japan and Korea.

The range of research efforts and topics was diverse; there was a primary set of questions to be answered:

1) What is the botanical identity of the traditional herbs, and what range of botanical sources are used for the "same herb"? In many instances, it was found that several different species were in use for a particular herb designation. Sometimes the different source materials had already been identified as having some difference that was recognized traditionally with prefixes that indicated region of origin (e.g. north or south) or some other characteristic.

2) What are the constituents of the traditional herbs, and which might be considered the main active constituents? At the turn of the 20th century, herbal constituents were given simple categories, such as "bitter principles" or "alkaloids" or "mucilage" but advances in analytic chemistry permitted specific structures to be elucidated and named, such as particular alkaloids, flavonoids, and saponins.

3) What impacts could be shown in laboratory testing of the herbal extracts or concentrated active component fractions? Typically, researchers would either look for confirmation of a traditional use or would turn to screening studies, where an animal model or cell culture system was developed and then different herb extracts tested to see which were most effective for the tested activity.

4) What biochemical reactions could be involved in the herb action as revealed by cell culture studies or by other in vitro analysis (e.g., anti-oxidant potential)? What physiological actions could be demonstrated (e.g., neurologic effects, cardiovascular effects)?

5) What could clinical evaluations show in terms of effectiveness rates and any adverse reactions? The majority of such clinical work initially involved case reviews of numerous patients treated at a hospital; over time, some prospective studies were established, where patients were recruited into the study and given a particular treatment (either a single treatment or one of several determined by differential diagnosis) so as to better answer these questions.

With regard to treatment of infections, the dominant research method has been the screening of herb extracts for their impact on bacteria, viruses, and other pathogens in the laboratory; most of this work had its origins in the mid-1970s and has been ongoing. The findings from such laboratory tests do not necessarily predict clinical results, because the application of herbal constituents to organisms directly may not reflect what happens when the herb material is ingested, partially absorbed, diluted in the blood stream, and reaching the target pathogen or affected cells in much lower concentration. The testing is a starting point for potential development of a drug from the active constituent, where synthetic improvement of the compound may be carried out for refined targeting the pathogen yet having low toxicity. In fact, none of the modern drugs for treating infections used internationally are directly derived from Chinese herbal active constituents apart from one highly successful instance previously mentioned, with artemisinin, and even then artemisinin has been shifted in use from a single drug therapy to part of a paired drug treatment because artemisinin resistance has now been found in several countries. The lack of other anti-infection drug development from herbs is not necessarily an indication that Chinese herbs don't hold further promise. Rather, the development of infection inhibiting drugs was already well underway before scientists involved with pharmaceutical development would think to turn to Chinese herbs as a potential resource. Put simply, drug development had already established a pathway that did not require looking for plant based components. Nutraceuticals, which are isolated active components or standardized extracts of herbs, have been one route by which Chinese herbs (and herbs of other traditions) have gotten use as drug-like substances. An example is the alkaloid berberine, which has anti-infection properties and is extracted from Chinese herb sources, such as phellodendron.

In the Chinese culture where use of herbs has been widespread, herbal products for infections have been produced that have both a popular reputation and research backing. A good example is the herb *banlangen*, the root of isatis, which is used extensively for treating infections. Best known as a remedy for early stage influenza, it is incorporated into numerous formulations and applied to many infections, especially those of viral origin. It is precisely this kind of knowledge that practitioners of botanical medicine in the west can utilize, because these herbs are available for use and have some degree of scientific support that might have been lacking before. It is possible for individual practitioners to review the literature using common search tools within medical journal resources (such as PubMed), but it can be helpful to have some guidance, as provided here, in finding which herbs have been of special interest and the extent of information about them.

The Path to Current Use in the U.S.

The Institute for Traditional Medicine (ITM) was one of the first organizations outside of China to pursue the practical application of the anti-infection herbs in clinical practice. This situation came about from a convergence of several events within a short period of time. In 1976, the U.S. FDA shifted its policy on Chinese herbal medicine from one of blocking entry of the medicinal items, which they had classified as unapproved drugs, to allowing these materials as part of the Chinese culture. This was at a time when there was a growing number of Chinese immigrants. After the Chinese revolution, Chinese immigration to the United States rose dramatically, first from Hong Kong, Macau, and Taiwan, and then, after the end of the Cultural Revolution, from the mainland. This increase in Chinese residents, especially where they had gathered into close-knit communities (Chinatowns), gave rise to a demand for use of their traditional medicines, so that once the change in policy occurred, Chinese herb imports and the Chinese herb medicine shops and distributors that dispensed them arose almost immediately.

The Institute's Director (current author) visited China in 1977, as one of the representatives of the first western herb company to attend the Canton Trade Fair, followed in subsequent years by visits to research centers, herb growing and collection areas, traditional medicine factories, hospitals, and academic institutions. These visits provided insights into the status of Chinese medicine in China and the types of resources that could be tapped into so as to get information for the small but growing group of acupuncturists in the west. Thus, for example, during a visit to Heilongjiang Province in 1981 a Chinese medicine researcher, Fu Kezhi, was introduced and soon after ITM had him open a small branch office of the Institute to gather publications on selected topics and then to provide translations, which he did for nearly twenty years.

Another influence was the AIDS epidemic; it had begun in the U.S. without notice in 1976 and was first recognized in 1981; ITM members and students working in the San Francisco Bay Area had seen patients with this syndrome before 1981, not knowing what it was, but applying Chinese medicine concepts to the observed symptoms. The AIDS epidemic brought attention to treatment of many infectious diseases, since the debilitated immune system HIV infected individuals could not fight many ordinarily restrained infections.

The Chinese University of Hong Kong had developed a Chinese Medicinal Materials Research Center and as its data base of herb information, publications, and international contacts grew, they sponsored a major conference titled "Advances in Chinese Medicinal Materials Research" in 1984, presented in English with proceedings published in 1985 (4) and the Center then produced a massive collection of research summaries in two volumes (1986-1987) called **Pharmacology and Applications of Chinese Materia Medica** (5), followed by an abstract service, accompanied by some review articles, that began in 1987 called Abstracts of Chinese Medicine (6), all of these in English translation.

While other factors could be mentioned, in essence, during this short period from 1976-1987 a variety of circumstances had brought Chinese people and their medical tradition to the U.S., Chinese research information had become easier to access, and a medical crisis arose that focused attention on the treatment of infections that were not being adequately controlled by the immune system. The Institute for Traditional Medicine had members who traveled to China, attended the Hong Kong conference, and obtained the books and abstract service, and became involved in treatment of AIDS patients. The severity of disease conditions among the AIDS patients and initial lack of successful drug therapy for them provided a sense of urgency that propelled the investigations. Other infection-based diseases also came under scrutiny through the same resources, such as viral hepatitis

Chinese Research and Publications

In depth study of anti-infection herbs can be traced back to the mid-1970s in China, yet it had a relatively low priority among the research efforts. For example, at the 1984 conference in Hong Kong there was only one submitted paper on herbs for an infectious disease, viral hepatitis, but no indications that the herbs discussed actually had an inhibitory effect on the virus. A submitted poster on infection depicted four infrequently used Chinese herbs that showed antibacterial action in laboratory studies. In a review of developments in Chinese herbal pharmacology from 1985-1988 (7), only one paragraph mentioned anti-infection activity, briefly listing 11 herbs, eight of which are rarely used. Rather, other medical topics took precedence.

The two volume book compiling literature surveys done at the Chinese Medical Material Research Center had within it the most comprehensive information about Chinese research on anti-infection properties. This book covered just over 400 Chinese herbs; of these, 10 were listed as being inhibitors of amoebas, 120 were deemed antibacterial, 60 were antifungal, 8 antimalarial, and over 40 were deemed antiviral; in many instances, these were secondary properties revealed by laboratory screening studies, but several of the herbs had some history of use for infectious diseases. Some herbs were counted in more than one category, but altogether about 150 different herbs had at least one of these anti-pathogenic effects; in addition, there were 15 herbs were deemed inhibitors of intestinal worms (anthelmintic) and 11 were inhibitors of schistosoma (trematodes). In terms of clinical studies, influenza, encephalitis B, early childhood viral infections (such as measles, mumps, chicken pox, and whooping cough), and skin diseases were the prominent subjects.

The high incidence of reporting antibacterial and antiviral activity reflects the ease with which herb extracts can show inhibitory action in vitro. Still, some of these herbs revealed clinical utility for infectious diseases. The table below lists several of the herbs that appear especially promising.

Table 3. Broad spectrum anti-infection herbs from **Pharmacology and Applications of Traditional Chinese Medicine**. This is a partial list, but includes many of the frequently used herbs. There are four herbs that are the same as those in Table 2. A designation accompanying many of the herbs is "clean toxin" or "detoxicant" which is a general concept that includes infections, but is not limited to that particular pathology (clean toxin herbs are used, for example, to treat snake and insect bites and cancerous swellings).

Herb Name	Pinyin	Scientific Name	Part	Category
Andrographis	*chuanxinlian*	*Andrographis paniculata*	rhizome	clear heat
Ching-hao	*qinghao*	*Artemisia apiaceae or annua*	top	clear heat
Coptis	*huanglian*	*Coptis chinensis*	rhizome	clear heat, dry damp
Forsythia	*lianqiao*	*Forsythia suspensa*	fruit	clear heat
Houttuynia	*yuxingcao*	*Houttuynia cordata*	fruit	clear heat, dry damp
Hu-chang	*huzhang*	*Polygonum cuspidatum*	rhizome	clear heat
Isatis Leaf	*daqingye*	*Isatis tinctoria*	leaf	clear heat
Isatis Root	*banlangen*	*Baphicacanthus cusia*	root	clear heat
Lonicera	*jinyinhua*	*Lonicera japonica*	flower	clear heat
Oldenlandia	*baihuasheshecao*	*Oldenlandia diffusa*	top	clear heat
Patrinia or Thlaspi	*baijiangcao*	*Patrinia villosa*	whole	clear heat
Phellodendron	*huangbai*	*Phellodendron amurense*	bark	clear heat
Prunella	*xiakucao*	*Prunella vulgaris*	top	clear heat
Scute	*huangqin*	*Scutellaria baicalensis*	root	clear heat, dry damp
Sophora	*kushen*	*Sophora angustifolia*	root	clear heat, dry damp
Taraxacum	*pugongying*	*Taraxacum mongolicus*	whole	clear heat
Viola	*zihuadiding*	*Viola yedoensis*	whole	clear heat

If one examines TCM formulations that come to us from ancient texts and still in use today, less than half of the herbs in Table 3 are included (at least with any frequency), which demonstrates the influence of modern research on determining anti-infection herbs. Nonetheless, the selection of the herbs to be tested in research projects was partly inspired by prior uses that implied a potential anti-pathogenic effect. Because of the frequency of infectious diseases inducing a fever response and inflammation, these herbs have been classified in the modern Materia Medica as herbs that "clear heat." In the book **Traditional Chinese Treatment for Infectious Diseases** many of the formulas contain three or more of the ingredients in Table 3 and typically also contain one or two of the ingredients in Table 2.

Sample Research Summaries

In **Pharmacology and Applications of Chinese Materia Medica**, summaries of research findings are presented by therapeutic category. Three examples are relayed here, selecting some portions of the text related to anti-infection activities.

Huzhang: In vitro studies showed that *huzhang* decoction, [and its active components] polygonin and polydatin, were inhibitory to *Staphylococcus aureus, S. albus, Neisseria catarrhalis*, alpha and beta *Streptococcus, Escherichia coli, Proteus vulgaris, Pseudomonas aeruginosa, Salmonella typhi,* and *Shigella flexneri*. It also had a lethal effect on *Leptospira* in vitro. Huzhang decoction inhibited Asian influenza virus type A and herpes simplex virus, adenovirus type III, poliomyelitis virus type II, *Coxsackie* virus groups A and B, encephalitis B….

Yuxingcao: Various in vitro studies proved that the herb decoction was inhibitory to *Staphylococcus aureus, S. albus, Streptococcus hemolyticus, Diplococcus pneumoniae, Neisseria catarrhalis, Corynebacterium diphteriae, Proteus vulgaris, Shigella shigae, S. schmitzi, S. flexneri, S. sonnei, Salmonella enteritis, Vibrio cholera suis,* and *Leptospira* species. The various preparations of *yuxingcao* afforded satisfactory therapeutic effects on upper respiratory tract infections and chest infections such as bronchopneumonia, lobar pneumonia, lung abscess, and chronic bronchitis. The *yuxingcao* tablet [extract derived from]15-30 grams administered daily by mouth upon contact with contaminated water afforded a prophylactic effect against leptospirosis. Other authors reported the efficacy of *yuxingcao* alone or with *Artemisia annua* (*qinghao*) in the management of leptospirosis. *Yuxingcao* has curative and prophylactic values in postoperative infections and acute phlebitis following infusion or transfusion.

Banlangen: The decoction or aqueous extract of the herb had inhibitory action against *Staphylococcus aureus, Diplococcus pneumoniae,* alpha *Streptococcus, Haemophilus influenzae, Escherichia coli, Salmonella typhi,* and *Shigella dysenteriae*. Satisfactory therapeutic effects were achieved with the decoction or injection preparation of the herb in the treatment of encephalitis B. Both the decoction and injection preparation of the herb had therapeutic effects in acute and chronic hepatitis. They effected the remission or subsidence of symptoms and promoted the improvement of liver function. Various degrees of therapeutic effect were achieved with the herb used to treat viral diseases of the skin such as herpes simplex, herpes zoster, pityriasis rosea, and verruca plana. For epidemic cerebrospinal meningitis, six cases were cured by the oral decoction of the herb. All symptoms and signs essentially disappeared between the 8th and 9th days of medication.

In the reporting on *banlangen,* several other disease conditions were said to be clinically responsive including influenza, infectious mononucleosis, and diphtheria; eye drops made from the herb were reported to be useful in treating fulminant conjunctivitis.

Practical Examples

When Chinese herbs began coming into the United States, they were initially in three forms: the crude herbs that would be used for making decoctions; dried decoctions (granules); and patent medicines, the prepared formulas from dozens of factories in China. One of the most popular of the patents was from a manufacturer in Tianjin, China, a large coastal city near Beijing. The product is *Yin Qiao Jie Du Pian*, which remains popular to this day. The manufactured product is based on a 19th century formula of the heat-clearing school called *Yin Qiao San*.

Yin Qiao San (sample dosing pattern; this could be varied)

Lonicera (*jinyinhua*)	10 grams
Forsythia (*lianqiao*)	10 grams
Platycodon (*jiegeng*)	6 grams
Arctium (*niubangzi*)	10 grams
Mentha (*bohe*)	10 grams
Soja (*dandouchi*)	10 grams
Schizonepeta (*jingjie*)	12 grams
Lophatherum (*danzhuye*)	10 grams
Licorice (*gancao*)	6 grams

The name of the formula is derived from two key ingredients *jinyinhua* (lonicera) and *lianqiao* (forsythia). These two herbs were likely included in the formulation for the original reason of helping to alleviate fever, but became understood to be serving as anti-infection herbs, especially useful for inhibiting viruses. The formula was primarily utilized for influenza, a disease that had contributed a huge death rate, most especially right after World War I in the worldwide pandemic that hit China hard, but also ongoing as a major cause of death to those weakened by other diseases or old age. *Yin Qiao Jie Du Pian* has also been applied to early stage of viral infections apart from influenza based on the positive effect on the respiratory virus and the idea that other viruses would likely respond, which appears to occur in some cases.

During visits to China one of the patent remedies found everywhere was an extract of isatis root (*banlangen*). The preparation type was known as a "chong ji" which is the extract integrated into sugar crystals. Putting this material into hot water restores the extract to a tea form, and the sugar, which serves also as a preservative and a bulking agent (for the relatively small amount of extract), sweetens the tea to make the bitter taste of isatis tolerable. This extract was used for influenza and deemed highly effective. A British company interested in introducing Chinese herbs to the U.K. (and U.S.) came across this patent early in their efforts and, having been inspired by its popularity in China, brought back many thousands of these packets. Unfortunately, there was no mechanism of introducing this unusual product at the time. Westerners interested in herbs and other natural therapies had become skeptical about consuming sugar, which in China was not considered a problem, and most flu remedies were in the form of capsule, tablet, or small dose of liquid, so the form was strange. Further, isatis was largely unknown, though "dyer's woad," the same isatis plant named for its indigo color for dying cloth, had been known to some western herbalists as a medicinal plant.

Thesis: Adding Similar Compounds

Clinical experience of several Chinese herb formulas suggest that the disease-causing organism or virus is impacted, and it is not just the symptoms that are being suppressed. This experience includes administration of the formulas at the earliest stage of infection and having the disease process terminate, using the formula prophylactically and apparently having success in prevention, and translating a formula designed for a particular kind of infection, such as respiratory, to application in other infections and still having successful response. Modern Chinese herb formulas for infection usually include many research-confirmed anti-infection herbs (such as those listed in Table 3). The action of these complex formula might be understood in terms of the herbs each contributing a *different* mechanism of inhibition that would add up to a potent effect. For example, one of the herbs might inhibit entry of a virus into cells; another might inhibit viral replication; another might inhibit viral release; another might stimulate immune attack against the virus. The modern drug approach to difficult viral infections, such as for HIV or hepatitis C, is to combine two powerful inhibitory actions so as to virtually shut down the virus while avoiding the potential for resistant strains to arise. The herbs could serve as a milder form of this strategy, suppressing though not eliminating the virus.

In the formulation *Yin Qiao San* and its tablet version only two of the herbs have a reputation for anti-infection activity, the two herbs of the formula name, lonicera and forsythia, while the other ingredients appear to be for common symptoms, such as sore throat, headache, and cough. It is difficult to explain from the perspective of modern pharmacology how these two ingredients can be present in sufficient dosage to actually impede the viral activity; further, with the other herbs aimed at respiratory tract infection symptoms, it is difficult to envision this complex formula having an effect on other types of viral infection. The thesis offered here is that in successful formulas comprised of very few of the notable anti-infection herbs, the "secondary" herbs include active constituents that are similar enough to those in the anti-infection herbs that they can produce an additive effect, reaching the necessary dosage to act against the pathogen.

Plants serve as chemical factories that usually produce multiple variants of a basic ingredient type. For example, if a plant synthesizes a particular dominant monoterpene it will always synthesize several other monoterpenes. These are different end points to the natural synthetic processes. Each of these variants will usually share a certain therapeutic action, but some of them will be more potent than others. The combination of the several variants may produce a *stronger* action than any one of them individually by virtue of reinforcing the same type of activity through different cell types that respond to the variants differently. When combining two herbs that produce the same category of constituent, the dosage of that constituent group is raised, and the number of variants may also increase. Together, those can generate a strong action.

In a prior article (8), I suggested that triterpenoid glycosides and steroidal glycosides were sometimes combined in this way: that is, adding up several herbs with similar ingredients, without the original herbalists designing the formula having any knowledge of the active constituent types. These were formulas for treating a subgroup of lung diseases, those interpreted, in modern understaning, as involving abscesses.

In the case of *Yin Qiao San*, the ingredient lophatherum (*danzhuye*), likely included because of its traditional reputation to treat sore and dry throat, has been found to have flavone-C-glycosides, especially derivatives of luteolin, that have anti-viral activity. Luteolin is a major constituent of lonicera. Arctium (*niubangzi*), an herb likely used also for sore throat and also for headache based on traditional applications, contains arctigenin, a lignin that has anti-viral effects. Forsythia also contains arctigenin and other lignans as active constituents. These are only two examples for this complex formula. In all, the overlapping constituents can yield a substantial quantity of each type, allowing for about three groups of constituents: flavonoids, saponins, and lignans with enough dosage to have the necessary anti-viral action. Had the developer of *Yin Qiao San* selected the herbs to include in the formula slightly differently, the combination of herbs might not have worked as well because of lacking overlap of ingredients with anti-pathogenic activity, and that different selection is what happened to dozens of other formulas of similar design: they faded away. Herbs that have the same attributed therapeutic action may have considerably different active constituents, therefore, when selecting an herb or herbs for sore throat, instead of selecting lophatherum and arctium, the herbalist could have picked two others that did not have the similar active constituents to the key herbs, lonicera and forsythia.

One has to be careful in following this train of thought, as the majority of flowering plants have some flavonoids, and many medicinal herbs have saponins as active constituents. Therefore, simply finding similar constituent types is not sufficient; these have to be present in sufficient quantity to make a difference in activity as well as having similar chemical structure. The range of flavonoids and saponins is very broad, so that one must compare the actual structures and not just the categories.

Modern Formulas in the Treatment of Impetigo with Chinese Herbs

Impetigo is a bacterial skin infection caused mainly by *Staphylococcus aureus* (in more than 90% of cases) but sometimes by group A *Streptococcus*, both pathogens leading to formation of pustules. Its treatment can help illustrate how modern Chinese herb formulas are designed. By the traditional concepts, impetigo is thought to be produced by the combination of "internal damp-heat and external toxic-evil" (9), meaning that an infection of the skin is made possible by an imbalance of damp-heat arising internally due to dietary factors or weakness of the organs that distribute moisture and regulate heat. The accumulated *dampness* from fatty, moist, and salty foods, and from food residue that remains too long as a result of weak stomach function is also thought to "transform" into *heat*, creating or worsening the internal damp-heat condition. The primary therapy is to clear heat and toxin and eliminate dampness. An example of a formula is:

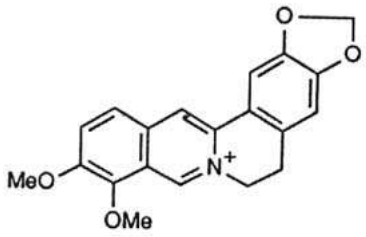
Patrinia (*baijiangcao*)	15 grams
Taraxacum (*pugongying*)	12 grams
Scute (*huangqin*)	10 grams
Coptis (*huanglian*)	10 grams
Lonicera (*jinyinhua*)	10 grams
Forsythia (*lianqiao*)	10 grams
Gardenia (*zhizi*)	10 grams
Chiang-huo (*qianghuo*)	10 grams
Alisma (*zexie*)	12 grams
Hoelen (*fuling*)	15 grams
Red Atractylodes (*cangzhu*)	10 grams

This combination of herbs is decocted and taken orally; the gram amounts are for a one day dose, the tea typically taken in two half-batches. All of these herbs, but one, chiang-huo, different than ching-hao (*qinghao*), are mentioned in at least one of the three tables of this article, with the first seven included in the anti-infection herbs list of Table 3. In addition to this internal remedy, a powder of rhubarb, phellodendron, scute, and sophora is combined with enough water to moisten it and applied topically to the affected area (or a skin wash can be prepared with the herbs). A similar treatment recommendation is found in the **Encyclopedia of Practical Traditional Chinese Medicine** (10), deleting the herbs for dampness (alisma, hoelen, red atractylodes):

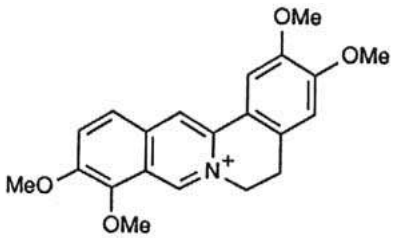
Lonicera (*jinyinhua*)	15 grams
Chrysanthemum (*juhua*)	15 grams
Scute (*huangqin*)	9 grams
Coptis (*huanglian*)	9 grams
Gardenia (*zhizi*)	9 grams
Phellodendron (*huangbai*)	9 grams
Viola (*zihuadiding*)	15 grams
Semiaquilegia (*tiankuizi*)	9 grams
Taraxacum (*pugongying*)	15 grams

The formula is prepared as a decoction. All of these herbs, except chrysanthemum and semiaquilegia, are listed in Table 3, and semiaquilegia is known also to have antibacterial properties; it did not get into Table 3 because of less frequent use. For topical therapy, a combination of lonicera, chrysanthemum, phellodendron, sophora, and alum (a mineral) is recommended in the same section of the book.

The alkaloids of coptis, an herb in these formulas for bacterial infection, include berberine and palmatine, both of which have antiseptic action against *Staphylococcus* and *Streptococcus* and, as mentioned previously, berberine has been developed as a nutraceutical. When evaluated for *Staphylococcus* infection, it was found that coptis alone was not as effective as coptis combined with scute and licorice (11). Thus combinations of herbs have the potential to increase pathogen inhibitory action.



Berberine



Palmatine

References

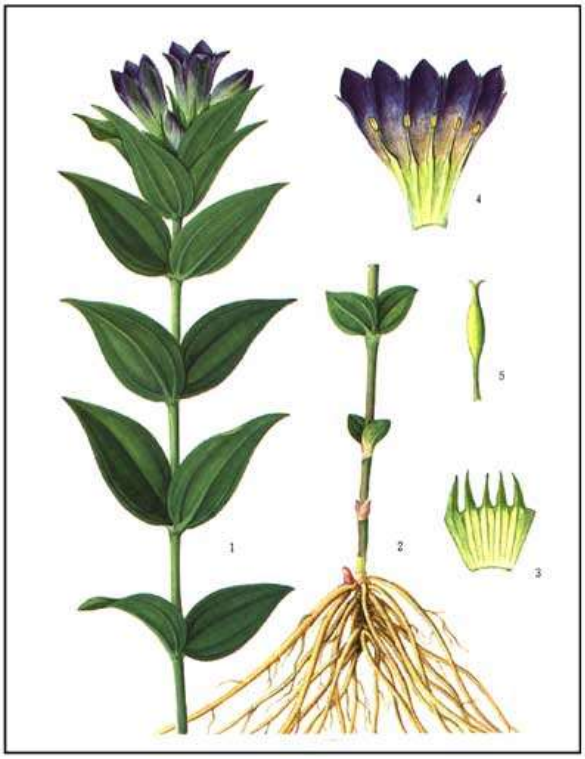
1. Hsu HY and Peacher WG (editors), ***Shang Han Lun*: The Great Classic of Chinese Medicine**, 1981 Oriental Healing Arts Institute, Long Beach, CA.
2. Hsu HY and Wang SY, **The Theory of Feverish Diseases and Its Clinical Applications**, 1985 Oriental Healing Arts Institute, Long Beach, CA.
3. Hou Jinglun, et al. (editors), **Traditional Chinese Treatment of Infectious Diseases**, 1997 Academy Press, Beijing.
4. Chang HM, et al., **Advances in Chinese Medicinal Materials Research**, 1985 World Scientific, Singapore.
5. Chang HM and But PPH (editors), **Pharmacology and Applications of Chinese Materia Medica**, (2 vols.), 1986 World Scientific, Singapore.
6. Abstracts of Chinese Medicine (published 1987–1996); Medicinal Materials Research Center, Chinese University of Hong Kong, Shatin, N.T., Hong Kong.
7. Xu GJ and Wang ZT, *Advances of Pharmacognosy in China from 1985-1988*, Abstracts of Chinese Medicine 1989; 3(4): 398-413.
8. Dharmananda S, *Chinese herbs containing triterpene and steroid glycosides (saponins) with dramatic therapeutic effects*, 2016 START Group Manuscripts, ITM, Portland, OR
9. Li Lin, **Practical Traditional Chinese Dermatology**, 1995 Hai Feng Publishing Company, Hong Kong.
10. Xu Xiangcai (chief editor), **English-Chinese Encyclopedia of Practical Traditional Chinese Medicine (v. 16, Dermatology)**, 1990 Higher Education Press, Beijing.
11. Yan M, et al., *Observation on inhibitory effect of coptis alone and its combination with scute and licorice on the growth of Staphylococcus aureus*, Journal of Chinese Herbs 1998; 23(6): 375-377.

Upper left:
Lonicera japonica.
flower

Upper right:
Forsythia suspensa.
fruit

Lower left:
Gentiana scabra
root

Lower right:
Sophora angustifolia
root



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