



Chinese herbs and anti-infection immunity

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Abstract

Chinese herbology originated in ancient China and has evolved over thousands of years, and is considered one part of complementary and alternative medicine (CAM) in western. Western medicine immune system is distributed throughout the body, and includes the tonsils, adenoids, lymph glands, bone marrow and so on. But there was no any concept for immune system in ancient Chinese medicine books, only used Qi and Blood to describe immune function. Tonic herbs can strengthen Qi and Blood, and keep balance of Qi and Blood to prevent exterior pathogenic influences; Diaphoretic herbs can boost and drive Qi and Blood to eradicate pathogens; some diaphoretic herbs can inhibit or eradicate some kind of bacteria directly. What are Qi and Blood in modern immunology science? How do Chinese herbs strengthen and boost immune system? This paper will provide a general overview of Chinese herbs and their anti-infection mechanisms that were delineated by modern researches.

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Introduction

History of Chinese herbology

Chinese herbs have been used for centuries. The first herbalist in Chinese tradition is Shennong (Liu, 1982), a mythical personage, who is said to have tasted hundreds of herbs and imparted his knowledge of medicinal and poisonous plants to farmers. The first Chinese manual on pharmacology, the Shennong Bencao Jing (Shennong Emperor's Classic of Materia Medica), lists some 365 medicines of which 252 of them are herbs, and dates back somewhere in the 1st century C.E. Han dynasty (Zhang et al., 2008, Yuan et al., 2009).

Li Shizhen completed the first draft of the Compendium of Materia Medica (Bencao Gangmu) in 1578, after conducting readings of 800 other medical reference books and carrying out 30 years of field study (Chen, 1987). For this and many other achievements, Li Shizhen is being compared to the Shennong. The compendium corrected many mistakes and false understandings of the nature of herbs and illness. Li also included many new herbs, added his own discovery in certain drugs, their effectiveness and function, as well as more detailed description according to experiments. The book has details about more than 1,800 drugs (Chinese Medicine), including 1,100 illustrations and 11,000 prescriptions. It also described the type, form, flavor, nature and application in disease treatments of 1,094 herbs (Chen, 1987, Zhen et al., 2002).

Most of directions about modern Chinese medicine were gotten from this book--Bencao Gangmu, and more and more Chinese medical scientist began to research and introduce Chinese herbs to the world (Klein et al., 2001), and also more and more western scientist began to recognize the function of Chinese herbs (Kavoussi, 2007), for example, Lingzhi. Lingzhi ranked number one of the superior medicines that was used to boost immune system to prevent a lot of disease. The ancient Chinese use of medicinal mushrooms has inspired modern day research into mushrooms like shiitake, Agaricus

blazei, Trametes versicolor, and of course lingzhi (Johnson, 2009, Maruyama et al., 2009). Although a 2008 Review, by UC Davis, concluded that there is not enough evidence yet to promote the use of mushrooms or mushroom extracts in the treatment of disease, it stressed the urgency of further research and future clinical trials due to large numbers of promising in vivo and in vitro experiments (Borchers et al., 2008).

Chinese herbs can be used to cure all kinds of disease, here, we just review part of herbs that are related with immune system to prevent or cure infection disease. Before review the topic of Chinese herbs and immune system, we should introduce the theory of Chinese medicine to make it easier to understand how to adjust immune system by Chinese herbs.

Immune system in Chinese medicine and western medicine

In Western medicine and Chinese medicine, the immune system is a functional system that includes many organs and interrelated functions. Chinese medicine focuses on maintaining balance throughout the human organism to maintain a healthy immune system (Li, 2008), and western medicine focuses on strengthen specific immunity against specific pathogen, such as traditional rules, T cell for virus infection and B cell for bacterium etc. (Ou et al., 2003). This must be the big different dogma between Chinese Medicine and Western Medicine (Fig1) (Xu, 2009, Li, 2008, Wang, 2006). In this review, we do not plan to comment that one is more reasonable, we try to combine the different medical system using modern research data.

Western medicine immune system is distributed throughout the body, and includes the tonsils, adenoids, lymph glands, bone marrow, thymus, spleen, appendix and Peyer's patches. The body's defenses, called lymphocytes (T-cells, B-cells, phagocytes and plasma cells), travel through the lymphatic system, a network that parallels blood

veins and arteries. The immune system contains innate immune system and adaptive immune system. When a person catches a cold or has an infected disease, the healthy immune system responds by attacking the foreign bodies with a combination of generalized and targeted cells (Dudley, 1992, Alam, 1998).

There was no direct concept of immune system in old Chinese medicine books, but we do found something from these descriptions using our modern researches on immunity and immune organs. In Chinese Medicine theory, the Qi (Bi, 2009) is a concept that circulates on the surface of some organ (spleen, liver, kidney, lung) and the whole body, protecting organs and body from pathogens like bacteria and viruses. This concept of the immune system is thousands of years old. The understanding is that exterior pathogens should be pushed to the surface, and expelled, before entering the meridians and causing pain, or affecting the organ systems with disease (Li et al., 2009). We can use modern immune science to interpret Qi, in fact, Qi should be understood as innate immunity, there are a lot of Chinese herbs (tonic herbs) can strengthen Qi (innate immunity) to prevent exterior pathogenic influences, in modern western medicine, the innate immunity was also described as the first defense to the pathogens (Griffiths, 1999).

There is another “concept” for immune system in ancient Chinese Medicine, named “blood”, what this blood emphasized is not different immune cells (T cell, B cell or NK cell) in blood, but the “circulation” (Bi, 2009). When there is not enough blood circulating to the organs to properly nourish and protect them, the organs become weak and susceptible to pathogens and disease. Deficient conditions would include lower temperature; a poor appetite and the person would be tired (Song et al., 2008). In Chinese medicine, Qi is another power (Li et al., 2009) (except heart) to push and distribute blood to each organ in human body. In western medicine theory, blood is pumped by heart to supply not only the nutrient, but also transfer all

kind of immune cells, cytokines and chemokines from immune organs to infected sites. So, the concept of blood in old Chinese medicine theory should be both innate immunity and adaptive immunity (Zhao et al., 2009). According to modern science research on different Chinese herbs, different diaphoretic herbs can strengthen different immune cells and organs to release pathogens to the exterior, some herbs also like western medicine to kill or inhibit bacteria and virus directly, such as saxifrage (Hu er cao) (Zuo et al., 2005, Zheng et al., 2008) and isatis Leaf (Da qing ye) (Wang et al., 2000, He et al., 2004).

In Chinese medicine, immune system was delineated by “Qi” and “blood” which link some immune organs: lung, spleen, liver, Kidney (Li et al., 2009). Nobody challenge the spleen as the important immune organ, but there are a lot of challenges for lung, kidney and liver as immune organs. Fortunately, more and more modern researches have been describing the functions as immune organs of liver (Gregory et al., 2002, Cousens et al., 2000) and lung (Kohlmeier et al., 2009, Woodland et al., 2009).

Lung: The Lung system is the most exterior organ and is the first internal organ typically affected by exterior pathogens. The Lung system also includes skin and is associated with Qi that can be strengthened by some Chinese herbs (Liu et al., 1998). During a long period, the lung only was looked at a respiratory organ, immunologist only focused on mucosal immunity of lung. Now an increasing number of reports have attempted to interpret lung as an immune organ. The lung airway, lung parenchyma and lung draining lymph nodes are three key parts of pulmonary immune system. Memory T cell and specific B cell from prior respiratory infections are localized to each of sites, with large number of cells present in the airway and parenchyma for several months post infection (Kohlmeier et al., 2009, Woodland et al., 2009).

Spleen: According to Chinese medical theory, the Spleen plays a central role in blood production and is responsible for how we utilize nutrients vital for a healthy immune response. The Spleen system also influences the amount of internal dampness that accumulates in the body. Internal Damp Phlegm creates stagnation throughout the body and throughout the lymphatic system impeding the lymph fluid from transporting toxins out of the body. And in modern science opinion, spleen is only a very important immune organ.

Liver: The liver plays a key role to store blood according to Chinese medical theory. The most important function is clearing the toxic substances, like a filter for blood system, and Chinese herbs can strengthen this function (Enkovaara, 2000, Yu et al., 2009). Modern research also found that liver plays an important role in clearance of systemic bacterial infections. Blood-borne bacteria and bacterial products are quickly trapped in and cleared, by the liver. This rapid clearance of bacteria is generally attributed to the resident liver macrophages, kupffer cell (Gregory et al., 2002, Gregory et al., 1998). Interestingly, evidence supports the participation of hepatocytes in antibacterial defense. Hepatocytes themselves are capable of producing a number of soluble factors that can contribute to resistance. For example, hepatocytes are major producers of acute phase proteins, i.e. C reactive protein, fibrinogen, α_1 proteinase inhibitor, in response to infection (Cousens et al, 2000).

Kidney: The Kidney system includes bone marrow (and blood production) in Chinese medicine and is closely associated with DNA and familial attributes of disease patterns. Abundant Jing, or Essence is vital in maintaining a healthy immune system. Now no modern scientist thinks too much about kidney as immune organ, but how about the future?

If Organ Systems become diseased, the proper systems of elimination such as the lymphatic system, Liver, skin, and Kidneys will become less

effective and accumulations will occur. Health in the body relies on the constant movement of Blood, Qi, and interstitial fluids; if fluids stagnate, they heat up just as a stagnant pond accumulates pathogens. Excess conditions would be exacerbated with pressure.

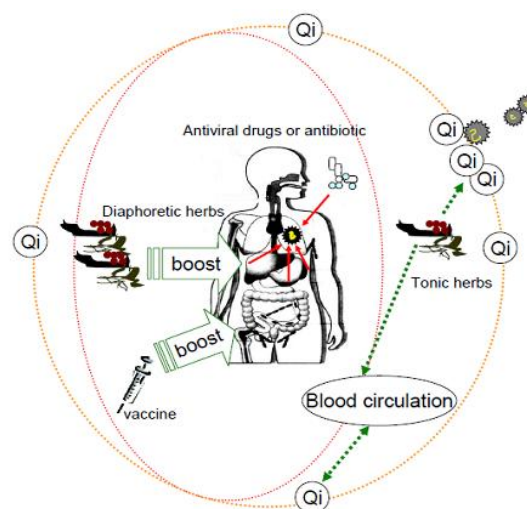


Fig. 1. Functional Chinese herbs, vaccine, antiviral drugs and antibiotic during infection.

Qi circulates on the surface of some organ (spleen, liver, kidney, lung) and the whole body, protecting organs and body from pathogens like bacteria and viruses. Qi also drive Blood to circulate the organs to properly nourish and protect them. The balance of Qi and Blood can keep a health condition; otherwise organs will become weak and susceptible to pathogens and all kind of disease. Tonic herbs can strengthen Qi and Blood, and keep balance of Qi and Blood to prevent exterior pathogenic influences; Diaphoretic herbs can boost and drive Qi and Blood to eradicate all kind of pathogens. The function of vaccine looks more like the diaphoretic herbs to boost immune system, but only prevent special pathogens. It is important to note that antiviral drugs and antibiotic, which is not illustrated in this review, play a different role in virus and bacteria clearance, kill bugs directly without immune system's help.

Modern research on Chinese Herbs and immunity

According to traditional Chinese medicine, defense Qi is located at the exterior surface of the body and offers initial protection against foreign or pathogenic factors. When Qi is strong, pathogenic factors cannot penetrate the body. When it is weak, a variety of infections can occur. Prevention of infections relies on normal function of Qi. From the Western perspective, many herbs that tonify Qi enhance the immune system (Yuan et al., 2000). Herbs that perform such functions include astragalus (huang qi), ganoderma (ling zhi), cordyceps (dong chong xia cao), echinacea, Angelica sinensis (AP, Dang gui), coptis chinensis (Berberine;Huang liang), forsythia suspensa (Lian qiao), Isatis Leaf (Da qing ye), isatis root (Ban lan geng) and saxifrage (Hu er cao) etc. Evidence demonstrates that these herbs are powerful biological response modifiers (BRM), which increase the immune system's capacity to recover from infection, overcome disease and restore health. They achieve this by enhancing production of defensive white blood cells including phagocytes, leukocytes and lymphocytes, providing antibacterial and anti-viral action, increasing red blood cells and haemoglobin, stimulating hormones such as interferon, promoting release of protective proteins called immunoglobulins, reducing inflammation, improving detoxification and increasing the adaptive function of adrenal cortex to resist stress (Kong et al., 2008).

Astragalus (huang qi)--**Tonic herb** is one of the most frequently used Chinese herbs and has historically been used to tonify Qi. It fortifies the lungs, strengthens the Qi and indirectly protects against external pathogenic factors (Cai et al., 2006, Kong, 2006). In terms of Western medicine, modern research has confirmed repeatedly that astragalus increases both specific and non-specific immunity (Cai et al., 2006). In a clinical trial of 115 leucopenic patients, astragalus was found to be associated with an "obvious rise of the white blood cell (WBC) count" with a dose-dependent

relationship (Su et al., 2007). In addition, astragalus works well with concurrent drug therapy in enhancing the overall effectiveness of the treatment. It also potentiates the anti-tumor effect of chemotherapy drugs (Steinmetz et al., 1996) by increasing the content of camp and inhibiting the growth of tumor cells.

Ganoderma (ling zhi)--**Tonic herb** increases the number of white blood cells and inhibits the growth of various viruses and bacteria associated with the flu (Niedermeyer, 2005). It has been demonstrated to enhance the immune system in various clinical studies. The specific effects of ganoderma include an increase in monocytes, macrophages and T-lymphocytes (VanderHem, 1995, Haak et al., 1993). There is also an increased production of cytokine, interleukin, tumor necrosis factor and interferon. Furthermore, ganoderma has a broad spectrum of antibacterial activities, inhibiting the growth of pneumococci, streptococci (type A), staphylococci, e. coli, b. dysenteriae and pseudomonas, among others (Yoon et al., 1994, Ofodile, 2005).

Cordyceps (dong chong xia cao)--**Tonic herb** has traditionally been used in chronic debilitated patients. It is an excellent herb to tonify the kidney yin and yang and improve overall bodily constitution (Zhu et al., 1998). Cordyceps is another herb that has marked immunomodulatory functions. It enhances overall immunity by increasing lymphocytes and natural killer cells and the production of interleukin, interferon and tumor necrosis factor (Liu et al., 1992, Xu et al., 1992, Liu et al., 1992).

Echinacea--**Tonic herb** is in stimulating phagocytosis, or the consumption of invading organisms by white blood cells, NK cells and lymphocytes (Mose, 1983, Goel, 2005). To prove this, scientists incubate human white blood cells, yeast cells and echinacea extract. They examine the blood cells microscopically and count the numbers of yeast cells gobbled up by the blood cells. Extracts of echinacea can increase phagocytosis by 20-40%

(Goel, 2005, Joksic et al., 2009). Another test, called "the carbon clearance" test, measures the speed with which injected carbon particles are removed from the bloodstream of a mouse. The quicker the mouse can remove the injected foreign particles, the more its immune system has been stimulated. In this test too, echinacea extracts excel, confirming the fact that this remarkable plant increases the activity of immune system cells so they can more quickly eliminate invading organisms and foreign particles (Schumacher et al., 1991, Bauer et al., 1998). Echinacea also stimulates the production of interferon as well as other important products of the immune system, including TNF α (Goel, 2005, Elsasser, 1996, Hwang et al., 2004), which is important to the body's response against cancer. Echinacea also inhibits an enzyme (hyaluronidase), which is secreted by bacteria, and helps them gain access to healthy cells (Facino, 1993). While echinacea is usually used internally for the treatment of viruses and bacteria, it is being used more externally for the treatment of wounds. It also kills yeast and slows or stops the growth of bacteria, and helps to stimulate the growth of new tissue. It combats inflammation too, further supporting its use in the treatment of wounds (Goel, 2005, Chaves et al., 2007, Matthias et al., 2008)

Angelica sinensis (AP, Dang gui) --**Tonic herb** is good for women, it also helps treat the heart, spleen, liver and kidneys that help both men and women (Chen et al., 1994). The effect of the herb in treating menstrual cramps is explained by the compounds that help relax the muscle tissue and relieves pain (Chen et al., 1994, Wang et al., 1996). Dang gui also stimulates the central nervous system, which can remedy menstrual weakness and headaches. Recent study show that, *Angelica sinensis* (AP), in the range of 30-300 mg/L, the total AP and its fractions, directly stimulated the proliferation of murine splenocytes, and significantly enhanced the proliferation of lymphocytes in MLR and T lymphocytes. The percentage of CD4(+) T lymphocytes in total splenocytes was also enhanced by them (Yang et al., 2005), AP is also one Chinese

herb which can regulate the immune response through upregulating IL-2, IFN- γ expression and activating Th1 cell (Yang et al., 2006).

Coptis chinensis (Berberine;Huang liang)--**Diaphoretic herb** is usually combined with other bitter-tasting herbs such as phellodendron, scutellaria and gardenia. This herb has many uses including the treatment of skin diseases, intestinal infections and hypertension (Berberinen, 2000). Modern researches focus on extract of *Coptis chinensis*—Berberine (Berberinen, 2000), also has significant antimicrobial activity against a variety of organisms including bacteria, viruses, fungi, protozoans, helminths, and chlamydia. In modern China, the predominant clinical uses of *Coptis chinensis* (berberine) are bacterial diarrhea (Berberinen, 2000). Several mechanisms that may explain its ability to inhibit bacterial diarrhea. An animal study found berberine reduced the intestinal secretion of water and electrolytes induced by cholera toxin (Swabb et al, 1981). Other studies have shown berberine directly inhibits some *V. cholera* and *E. coli* enterotoxins (Sack et al., 1982), significantly reduces smooth muscle contraction and intestinal motility (Akhter et al., 1979), and delays intestinal transit time in humans (Yuan et al., 1994). Berberine sulfate has also been found to be directly bacteriocidal to *V. cholera* (Amin et al., 1969). In the case of *E. coli*, in vitro research indicated berberine sulfate was capable of inhibiting bacterial adherence to mucosal or epithelial surfaces, the first step in the infective process. This may be a result of berberine's inhibitory effect on fimbrial structure formation on the surface of the treated bacteria (Sun et al., 1988).

Forsythia suspensa (Lian qiao)--**Diaphoretic herb** A new compound, 2-(1,4-dihydroxy cyclohexanyl)-acetic acid isolated from the seeds of *Forsythia suspensa* (Thunb.) Vahl, has been assessed for potent antiviral effect on RSV for the first time in vitro by cell morphology methods. Its structure was elucidated on the basis of spectroscopic evidence (IR, MS, ¹H-NMR, ¹³C-

NMR) (Zhang et al., 2002). Forsythia suspensa can inhibit RANTES secretion in H1N1-infected A549 bronchial epithelial cells to stop accumulation of inflammatory cells in the infective sites that has been reported to play a crucial role in the progression of chronic inflammation and multiple sclerosis after viral infection (Koetal, 2006). This is the reason why it can be used for influenza treatment.

Isatis Leaf (Da qing ye) and Isatis Root (Ban lan geng) -- Diaphoretic herbs are the leaf and root of the same plant. The leaf is a stronger direct antiviral. The root works more to modulate the immune response, increasing immune function, but dampening the excess inflammation that a robust immune response can create. Isatis leaves contain an alkaloid known as tryptanthrin, which is strongly inhibitory to the cyclooxygenase-2 (COX-2) enzyme, and is theorized to be largely responsible for the anti-inflammatory action of Isatis (Liu et al., 2007). The leaves also contain several derivatives of hydroxycinnamic acid, including ferulic acid and sinapic acid (Hartled et al., 1995). These agents are thought to be important in the anti-inflammatory and anti-allergic activity of Isatis leaf preparations. For infection, Isatis leaves have been used in traditional medicine mainly for treatment of infections; specifically, encephalitis, upper respiratory infection, and gastroenteritis (Wang et al., 2000, He et al., 2004). Isatis root extracts have also been used to treat infection (Qi et al., 2007, Hsuan et al., 2009). The anti-microbial action of the root is likely more broad-spectrum than that of the leaves. In vitro and human studies from China have shown Isatis root extract to be antibacterial, antiviral, and antiparasitic (He et al., 2004).

Saxifrage (Hu er cao) -- Diaphoretic herb is not very famous Chinese herb, but has strong antiviral (Zuo et al., 2005), antibacterial (Zheng et al., 2008) or antiphlogistic ability. There are growth-promoting substances in the leaves. The whole plant is depurative, febrifuge and suppurative. Its use promotes the drainage of pus.

A decoction is used in the treatment of boils and abscesses, poisonous snakebites, otitis media, acute attacks of convulsions and haematemesis. The leaf juice is applied to aching ears, abscesses and inflammations (Zheng et al., 2008, Gujarathi et al., 2009)

Concluding remarks

Our understanding of the mechanisms that Chinese herbs employ to inhibit and eliminate virus and bacteria has grown considerably over the past decade. The discovery of different Chinese herbs and the role they play to strengthen and boost immune system has also been illustrated by modern immune researches. The dissection of different Chinese herbs function by modern research has allowed us to determine the important of using Chinese herbs as one part of complementary and alternative medicine (CAM), but one thing should be emphasized here, research only focus on simple gradient or single herbs should be changed to collection of herbs according to Chinese medical theory, it is apparent that kind of research is far more complex than originally thought, but it is really a good way for herbs research (Shen, 2000). Future studies investigating the anti-infection immunity, for example anti-influenza immune response, in every greater detail will be required to develop a comprehensive picture for Chinese herbs (Lu et al., 2008).

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