

# **Colds & Flus and The Science Behind ColdQuell**

by

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## **Definition, signs & symptoms, nosology & epidemiology:**

A common cold is a self-limiting illness of the upper respiratory tract caused by a viral infection located in the nose.(1) The common cold is responsible for more days lost from work and school than any other illness.(20) Although the locus of infection is in the nose, colds also involve the sinuses, ears, and bronchial tubes. The symptoms of a common cold include sneezing, runny nose, nasal obstruction, sore or scratchy throat, cough, hoarseness, and mild general symptoms like headache, feverishness, chilliness, and general malaise.(1, 2) Alertness and psychomotor functioning are frequently impaired, reducing productivity before and after symptoms are present.(21) On average, colds last for one week. Mild colds may last only 2-3 days, while severe colds may last for up to two weeks.(1, 2) Although both are caused by viral infection, a cold is a milder illness than influenza or the flu. Influenza typically causes fever, muscle aches, and a more severe cough. However, mild cases of influenza are similar to colds.(3) Adults average 2-3 colds per year and children 6-10 depending on their age and exposure. This higher incidence of colds in children is due to their immature immune system. Typically, the number of colds caught per year in children decreases after six years of age.

## **Etiology:**

As stated above, colds and flus are caused by viral infection. There are over 100 different cold viruses. Rhinoviruses (RV) are the most important of these and cause at least half of all colds.(5) Rhinoviruses are small (30nm), nonenveloped viruses which belong to the Picornaviridae family. This family also includes the genera Enterovirus and Hepatovirus. There are approximately 100 different serotypes of RV currently identified. However, the type of virus involved in a cold or flu is somewhat dependent on the time of year. Rhinovirus, echosackie virus, and coxsackie viruses are the most common causes of spring, summer, and autumn colds, while influenza, para-influenza, and respiratory syncytial viruses are more frequent causes of late fall and winter colds.(22) Antibody-related immunity to a particular virus varies with the virus type, and generally lasts approximately 18 months.(23) While cold weather and wet conditions are not causative agents, it has been demonstrated that exposure to drastic temperature changes and cold may increase the severity of a cold.(23) Recent studies have also demonstrated an increased susceptibility to colds in subjects who smoke,(24) as well as those who are experiencing psychological stress.(25) General health and nutritional status appear to play a role in the severity of the cold.(23) Increased contact with infected individuals increases the likelihood of transmission of cold viruses. Of interest, however, is a 1996 study of adults that demonstrates an increased resistance to infection in hosts with diverse social ties.(26)

## **Pathophysiology:**

Cold viruses can only multiply when they are inside living cells. When on an environmental surface, cold viruses cannot multiply. However, they are still infectious if they are transported from an environmental site into the nose.(6, 7) Cold viruses live only in the noses of humans and not in other animals, except for

chimpanzees and other higher primates.(4) A cold virus is deposited into the front of the nasal passages by contaminated fingers or by aerosolized droplets from coughs and sneezes.(7) Small doses of virus (1-30 particles) are sufficient to produce infection.(8, 9) The virus is then transported to the back of the nose and onto the adenoid area by the nose itself.(10) The virus attaches to a receptor (ICAM-1) which is located on the surface of the nasal cells.(11) The receptor fits into a “docking port” on the surface of the virus. Large amounts of such virus receptors are present on cells of the adenoid.(12) It is also believed that some RV serotypes are capable of up-regulating the ICAM-1 on human epithelial cells in order to increase susceptibility to infection. After attachment to the receptor, the virus is taken into the cell where it starts an infection,(5) and new virus particles are produced in the infected cell. The infected cell eventually dies and ruptures, releasing newly made cold virus to infect other cells in the nose and start the process over again. From the time a cold virus enters the nose, it takes 8-12 hours for the viral reproductive cycle to be completed and for new cold virus to be released in nasal secretions.(13) This interval is called the incubation period. During this period, virus is shed and may be passed on to contacts.(27) Cold symptoms can also begin shortly after virus is first produced in the nose (10-12 hours).(13) The time from the beginning of the infection to the peak of symptoms is typically 36-72 hours. (1, 2) By days 3-5 of the illness, nasal discharge can become mucopurulent from polymorphonuclear leukocytes that have migrated to the infection site in response to chemo-attractants such as interleukin-8. Nasal mucociliary transport is reduced markedly during the illness and may be impaired for weeks. Both secretory immunoglobulin A and serum antibodies are involved in resolving the illness and protecting from reinfection.

Cold viruses (rhinovirus) infect only a relatively small proportion of the cells lining the nose,(10, 14, 15) and membrane damage is mild. In fact, most of the symptoms of a cold are due to the body's response to the infection. When a nasal cell is infected by a cold virus, the body responds by activating parts of the immune system and some nervous system reflexes.(5) The immune system contains a variety of natural substances called inflammatory mediators. Inflammatory mediators help protect the body from infection and other harmful events. Some inflammatory mediators are released when nasal cells are infected by a cold virus. Some the inflammatory mediators involved in colds include histamine, kinins, interleukins, and the prostaglandins.(5, 16-19) When activated by a cold virus infection, inflammatory mediators cause dilatation and leakage of blood vessels and mucus gland secretion.(5) Inflammatory mediators also activate sneeze and cough reflexes and stimulate pain nerve fibers. These events are what lead to the symptoms of a cold. However, this activity by inflammatory mediators is not necessary for recovery from infection by a cold virus. In fact, 25% of people who are infected by a cold virus do not go on to develop symptoms,(4) and people without cold symptoms recover from this infection just as well as those who become symptomatic. In those who become symptomatic, symptoms persist until adequate immune activity has been mustered and the body begins to destroy the virus. Two to three percent of cold sufferers go on to develop complications due to secondary bacterial infection (typically due to group A and/or B hemolytic streptococcus).

### **Western medical treatment of colds & flus:**

The Western medical treatment of colds and flus is primarily aimed at de-activation of the inflammatory mediators which cause the symptoms of a cold. As yet, antiviral drugs are not generally available in the U.S. There are five main groups of Western drugs, both prescription and over-the-counter (OTC) advised for the treatment of colds and flus. These include 1) antihistamines, 2) nonsteroidal anti-inflammatory drugs (NSAIDs), decongestants (vasoconstrictors), cough suppressants (narcotics), and anticholinergics. Histamine is a natural substance, one of the important inflammatory mediators produced in certain cells in the body. When introduced into the nose, histamine causes dilatation and leakage of blood vessels.(29)

Histamine is also a powerful stimulant of the sneeze reflex. These effects of histamine cause sneezing, coughing, runny nose, and stopped up nose during colds. Histamine may also have a role in causing coughs, but this is less certain. Antihistamines work by preventing histamine from attaching to a cellular receptor, H1. Attachment to this receptor is necessary for histamine activity to occur. Nonsteroidal anti-inflammatory drugs, such as ibuprofen and naproxen, are effective in treating inflammation, pain, and fever. A major action of NSAIDs is to block the production of the inflammatory mediators, prostaglandins. NSAIDs are used in medical practice to treat general symptoms of a cold such as feverishness, chilliness, muscle ache, and general malaise.(30) Decongestants, such as pseudoephedrine, are in the category of alpha-adrenergic agonists. These drugs open the nasal passages by shrinking blood vessels in the mucus membrane of the nose, which is the primary cause of the nasal obstruction of colds. Anticholinergics are a class of drugs that block the action of the parasympathetic nervous system on mucus gland secretion, thereby reducing nasal discharge.(28)

### **The unwanted side effects of Western cold medicines:**

Most nonprescription Western cold medicines have some side effects. These range from dry mouth and drowsiness to dizziness, insomnia, and upset stomach. Although antihistamines typically cause drowsiness in adults, in children they may, paradoxically, cause restlessness, agitation, and insomnia.

### **ColdQuell**

ColdQuell (manufactured and distributed by Blue Poppy Herbs, [www.bluepoppy.com](http://www.bluepoppy.com)) is a high potency (10:1) Chinese herbal extract formula specifically designed to treat both the viral infection that causes colds and flus and the accompanying immune response to that infection. ColdQuell is based on a combination of three of the most famous herbal formulas in Chinese medicine. These are *Xiao Chai Hu Tang* (Minor Bupleurum Decoction), *Yin Qiao San* (Lonicera & Forsythia Powder), and *Si Wu Tang* (Four Materials Decoction).

*Xiao Chai Hu Tang* is the most commonly prescribed Chinese herbal formula in the world today, and it has been in constant use for 1,800 years.(62) It is also one of the most thoroughly researched Chinese herbal formulas, with most of that research having been carried out in Japan. Modern research has confirmed that the seven herbal ingredients in this formula modulate a number of host immune responses. These ingredients include: Radix Bupleuri Falcati (*Chai Hu*), Radix Codonopsis Pilosulae (*Dang Shen*), Radix Scutellariae Baicalensis (*Huang Qin*), Rhizoma Pinelliae Ternatae (*Ban Xia*), mix-fried Radix Glycyrrhizae Uralensis (*Gan Cao*), Fructus Zizyphi Jujubae (*Da Zao*), and uncooked Rhizoma Zingiberis Officinalis (*Sheng Jiang*). For instance, Borchers *et al.* have shown *Xiao Chai Hu Tang* can induce interferons (IFNs) and activate natural killer (NK) cell activity.(31) Research by Kawahita *et al.* confirms that these seven ingredients can, when administered together, induce IFN-alpha/beta production ,(41) and research by both Kaneko *et al.* and Yamaoka *et al.* confirms that this formula is able to augment NK activity after oral administration. (45, 46) According to at least four different studies, *Xiao Chai Hu Tang* can increase production of granulocyte colony-stimulating factor (G-CSF) by peripheral blood mononuclear cells. (32, 39,42, 49) Other studies have also shown that these ingredients can increase production of cytokines, (36, 40) and that this formula has immunomodulating effects on peripheral mononuclear cells.(39) Matsumoto *et al.* have demonstrated that *Xiao Chai Hu Tang* is able to enhance interleukin-1 alpha mediated autocrine growth of human epidermal keratinocytes,(50) while Yamashiki *et al.* have demonstrated that this formula can increase interleukin-10 production by peripheral blood mononuclear cells.(51) Even more recent research by Yamashiki *et al.* has shown that administration of

*Xiao Chai Hu Tang* can increase interleukin-12 (IL-12) by circulating mononuclear cells threefold.(53) Interleukin-12 is an important cytokine for the maintenance of normal systemic defense and bioregulation. *Xiao Chai Hu Tang* can also increase the production of interleukin-6.(55)

It is a well known fact that eating a diet too rich in cholesterol and polyunsaturated fats can depress the immune system, and high fat diets specifically lower immunity for infections.(63) As we have seen above, whether or not a person infected with cold virus becomes symptomatic and the severity and duration of those symptoms is dependent on the person's overall health. Happily, the ingredients of *Xiao Chai Hu Tang* have been shown to improve the lipid metabolism of immune system macrophages.(43, 47, 48) As Y.R, Shen *et al.* state: "Shosaikoto, which is known to modulate the immune system, improves macrophage and lymphocyte functions diminished by hypercholesterolemia..."(48) Yet other research suggests that *Xiao Chai Hu Tang* achieves an anti-inflammatory effect through the promotion of a higher serum concentration of vitamin E.(44) Further, Matsumoto and Shibata have demonstrated that the ingredients of *Xiao Chai Hu Tang* have an antihistaminic effect,(52) and Tauchi *et al.* have demonstrated that this formula acts as a polyclonal B-cell activator which induces IgA production in the mucosal system when administered orally.(54)

In recent years, research has also been done on individual constituents of *Xiao Chai Hu Tang*. The main ingredient in *Xiao Chai Hu Tang* is Radix Bupleuri Falcati (*Chai Hu*) and this herb contains a number of pharmacologically active constituents, most notably the saikosaponins. Bermejo *et al.* have shown that saikosaponin 1 and 2 exert potent in vivo anti-inflammatory effects, possibly through the inhibition of arachidonic acid metabolism.(33) Similarly, Kato *et al.* have shown that saikosaponin-d promotes interleukin-2 (IL-2) production and IL-2 receptor expression. Therefore, saikosaponin-d modulates T lymphocyte function.(34) Ushi and Abe suggest that saikosaponin-d may actually have antiviral ability. In vitro, saikosaponin-d has directly inactivated both measles and herpes simplex viruses with complete loss of infectivity.(35) Whether such saikosaponins are antiviral or not, they most definitely are anti-inflammatory.(37, 38) Another ingredient in *Xiao Chai Hu Tang* is Radix Scutellariae Baicalensis (*Huang Qin*) and one of its active ingredients is baicalein. Research done by Nakahata *et al.* has shown that baicalein can inhibit prostaglandin E2 (PGE2) production.(56) Yet a third ingredient in *Xiao Chai Hu Tang* is Fructus Zizyphi Jujubae (*Da Zao*). According to Yamaoka *et al.*, a polysaccharide fraction of this herb shows an ability to augment NK activity when administered orally.(57) And finally, Fructus Zizyphi Jujubae has been proven to promote airway ciliary motility through the stimulation of epithelial nitric oxide (NO) generation.(58) Thus it is clear, both from the point of view of this formula as a whole and its individual active ingredients, that *Xiao Chai Hu Tang* improves immune function, is anti-inflammatory, and may be antiviral.

However, ColdQuell is not just *Xiao Chai Hu Tang*. This formula also includes all four ingredients of *Si Wu Tang* (Four Materials Decoction): uncooked Radix Rehmanniae (*Sheng Di*), Radix Angelicae Sinensis (*Dang Gui*), Radix Albus Paeoniae Lactiflorae (*Bai Shao*), and Radix Ligustici Wallichii (*Chuan Xiong*). This formula dates back to the Song dynasty and comes from a book published between 1078-1085 CE (AD). Recent research has shown that *Si Wu Tang* has a definite anti-inflammatory ability, most probably due to inhibition of PGE2 release.(59) Research conducted by Kojima *et al.* has also confirmed the anti-inflammatory effects of *Si Wu Tang*. These results demonstrated that an extract of the four ingredients of *Si Wu Tang* reduced angiogenesis, granuloma formation, inflammatory cell migration, and pouch fluid exudation.(60)

The third formula upon which ColdQuell is based is *Yin Qiao San* (Lonicera & Forsythia Powder). This formula comes from the Qing dynasty book *Wen Bing Tiao Bian* (*Systematic Differentiation of Warm*

*Diseases*) published in 1798, and it is a commonly prescribed formula for the treatment of upper respiratory tract infections, influenza, and acute bronchitis.(61) Four ingredients are taken from that formula: Flos Lonicera Japonicae (*Jin Yin Hua*), Fructus Forsythiae Suspensae (*Lian Qiao*), Fructus Arctii Lappae (*Niu Bang Zi*), and Radix Platycodi Grandiflori (*Jie Geng*). Practitioners in the People's Republic of China widely believe that two of these ingredients, Flos Lonicerae Japonicae and Fructus Forsythiae Suspensae, are potent antivirals. In fact, they have been used for the treatment of a wide variety of viral diseases for hundreds if not thousands of years. However, these are not the only antiviral ingredients in this formula. Radix Isatidis Seu Baphicacanthi (*Ban Lan Gen*), Radix Scutellariae Baicalensis (*Huang Qin*), and Radix Glycyrrhizae Uralensis (*Gan Cao*) are also widely believed to be directly antiviral. Below is a complete listing of the Western gross pharmacodynamic effects of each ingredient in ColdQuell.

Radix Isatidis Seu Baphicacanthi (*Ban Lan Gen*): antiviral, antibacterial

Fructus Forsythiae Suspensae (*Lian Qiao*): antiviral, antibacterial, antifungal, anti-inflammatory, lymphatic decongestant, antipyretic, phagocyte stimulant

Flos Lonicerae Japonicae (*Jin Yin Hua*): antipyretic, antiviral, antibacterial, antifungal, leukocyte production stimulant, anti-inflammatory, lymphatic decongestant

Radix Scrophulariae Ningpoensis (*Xuan Shen*): antibacterial, anti-inflammatory

uncooked Radix Rehmanniae (*Sheng Di*): antibacterial, antifungal, anti-inflammatory, interferon inducer, demulcent, lowers blood lipids

Radix Ligustici Wallichii (*Chuan Xiong*): antispasmodic, antibacterial, antifungal, tranquilizing

Radix Scutellariae Baicalensis (*Huang Qin*): antiviral, suppresses replication of influenza A & B viruses, antibacterial, antifungal, anti-inflammatory

Radix Bupleuri (*Chai Hu*): antipyretic, anti-inflammatory

Radix Codonopsis Pilosulae (*Dang Shen*): immune system stimulant, promotes digestion, absorption, and metabolism

Rhizoma Pinelliae Ternatae (*Ban Xia*): expectorant/mucolytic, antitussive, antiemetic

Fructus Zizyphi Jujubae (*Da Zao*): antihistaminic, expectorant/mucolytic, mild sedative

uncooked Rhizoma Zingiberis Officinalis (*Sheng Jiang*): antibacterial, expectorant/mucolytic

Fructus Arctii Lappae (*Niu Bang Zi*): antipyretic, anti-inflammatory, antibacterial, demulcent

Radix Albus Paeoniae Lactiflorae (*Bai Shao*): antispasmodic, analgesic, sedative, antibacterial, antifungal, immune stimulant, interferon inducer, antipyretic

Radix Angelicae Sinensis (*Dang Gui*): immune stimulant, promotes phagocytosis of mononuclear macrophages, interferon inducer, antibacterial, antifungal

Radix Glycyrrhizae Uralensis (*Gan Cao*): anti-inflammatory, expectorant, demulcent, antiviral, antibacterial, interferon inducent, antispasmodic, antihistaminic

Radix Platycodi Grandiflori (*Jie Geng*): expectorant, antitussive, demulcent, antifungal, anti-inflammatory

Given the above pharmacodynamic actions of the ingredients of ColdQuell, it is no wonder that this formula has proven so effective in treating colds and flus in thousands of people in North America and Europe. Based upon reports by practitioners and their patients, if taken upon the first sign of a cold (such as sore throat, slight fever, and chills), this formula can often eliminate all symptoms without further progression of the illness. When that is not possible, it can decrease the severity of those symptoms and decrease the duration of the illness. Based on the above-documented research, we believe this ability of ColdQuell to stop colds and flus dead in their tracks is a function of these Chinese herbs' unique abilities to kill viruses and suppress their replication as well as their anti-inflammatory, immune-enhancing, antitussive, antihistaminic, and expectorant and mucolytic activities. If these are the recommended activities for treating a common cold, ColdQuell fulfills this bill exceptionally well in a safe and natural way free from the typical unwanted side effects of Western drugs.

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